Glucose dysregulation in advanced Parkinson's Disease: too much glucose or not enough insulin?

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Symposium

Saturday, June 16 2018

EAN/MDS-ES: Tauopathies: pathophysiology, clinical features and experimental therapies

SYMP01_1

Tau protein in normal and pathological brain

T.F. Outeiro
Göttingen, Germany

Abstract: Tau protein is traditionally known as a microtubule binding protein, but its precise function is still unclear. Under certain conditions we do not fully understand, Tau can become hyperphosphorylated, leading to its accumulation in pathological protein inclusions that occur in various neurodegenerative disorders such as Alzheimer's disease, frontotemporal dementia, and parkinsonism. In an effort to understand the biology and pathobiology of Tau, we have investigated its interactions with other proteins associated with neurodegenerative diseases.

We used a variety of cell and molecular approaches to identify Tau-interactors, and performed additional studies in animal models of tauopathy.

We found that Tau interacts various aggregation-prone proteins, such as alpha-synuclein and huntingtin. In addition, we found that Tau also interacts with PTEN (phosphatase and tensin homologue on chromosome 10), and that it can regulate brain insulin signalling. This highlights a novel function of Tau that raise the hypothesis that loss of Tau function favours brain insulin resistance, a key process in cognitive and metabolic impairments in Alzheimer's disease patients. In total, understanding the role of Tau in normal and pathological conditions is essential for the development of novel therapeutic strategies for tauopathies.
Disclosure: Nothing to disclose

SYMP01_2

Progressive supranuclear palsy and corticobasal degeneration: one disease or two

C. Colosimo
Terni, Italy

Abstract: Progressive supranuclear palsy (PSP) and corticobasal degeneration (CBD) were first described in the sixties as new and distinctive clinocopathological entities, both of which were later classified on molecular grounds as 4-repeat (4R) tauopathies. In the last two decades the overlap between these two diseases has become indeed even stronger. It is now well accepted that up to a quarter of cases having pathologically-proven PSP may in life present with the classical clinical picture of CBD, also known as corticobasal syndrome. On the other hand, smaller number of people with pathologically definite CBD may present in life with a clinical syndrome resembling typical PSP. This matter has been fully recognised by the most recent consensus criteria for CBD published in 2013, and by those for PSP published last year. In the Movement Disorder Society–endorsed PSP criteria, in particular, this has been fully recognized introducing the new diagnostic category of 4R tauopathy, which characterises cases in whom is impossible to predict during life the final pathological diagnosis of PSP or CBD. The addition of diagnostic biomarkers would hopefully increase diagnostic specificity for these individuals in the near future.
Disclosure: Nothing to disclose.

SYMP01_4

Emerging disease-modifying treatments for tauopathies

G.U. Hoeglinger

Munich, Germany

Abstract: The currently proposed therapies for tauopathies are oriented towards symptomatic improvements and have limited efficacy. No officially approved drugs are available for disease modification, i.e. slowing of disease progression. Recent advances in the understanding of the pathological changes in tauopathies have allowed to develop novel rational therapeutic strategies, aimed to interfere at the core pathological disease mechanisms. These approaches include antisense oligonucleotides, aggregation inhibitors, microtubule stabilizers, kinase inhibitors, OGA inhibitors, and tau antibodies. This talk will provide a timely overview on the current developments in this rapidly evolving field of research.

Disclosure: Nothing to disclose.

Overarching Theme: Diagnosing genetic epilepsies

SYMP02_1

Is epilepsy a genetic disease?

S.D. Shorvon
London, United Kingdom

Abstract: Of course epilepsy has a genetic component, almost all conditions and diseases and most human physical and mental characteristics do. However, the genetic influences are often complex involving epigenetic, epistatic and non-genetic components. Genetic influences are most prominent in the early epileptic encephalopathies and in the epilepsies due to rare metabolic and congenital disorders, but in the great majority of other cases, including the idiopathic epilepsies, the genetic influence is not clear cut and often small. It is intellectually lazy to relabel these epilepsies 'genetic', as has been the recent ILAE proposal. In this talk, a brief overview of the epilepsies in which there are a strong genetic contribution and the genetic mechanisms involved will be given, followed by a short description of some of the issues relating to the epilepsies with weak genetic influence and epilepsy pharmacogenetics. The importance and social implications of accurate terminology will be stressed.

Disclosure: Nothing to disclose

SYMP02_2

Molecular diagnosis in genetic epilepsies: why we need to test

S. Weckhuysen
Antwerpen-Wilrijk, Belgium

Abstract: Recent advances in genetic techniques have led to the discovery of an increasing amount of epilepsy genes. While most progress has been made in the field of severe childhood epilepsies, several gene findings have now also proven a role of genetics in the etiology of focal epilepsy syndromes with later onset age. The identification of a genetic cause will in the first place reduce the need for further (sometimes invasive) diagnostic testing, and guide counseling about prognosis and recurrence risk. Most importantly however, for a selection of genetic epilepsies, establishing a genetic diagnosis also has important treatment implications. An increasing amount of case reports and small cohort studies report on the benefits of selected treatments in specific genetic epilepsies. The sometimes conflicting results in clinical practice do however also illustrate the difficulties encountered when designing "precision medicine" trials for often rare genetic epilepsies.

Disclosure: Nothing to disclose

EAN/ESO: Cerebral small vessel disease - recent advances and clinical implications

SYMP03_2

New insights into what causes SVD- and treatment implications

H. Markus

London, United Kingdom

Abstract: Cerebral small vessel disease (SVD) is one of the most important cerebrovascular conditions worldwide, causing a quarter of all strokes and being the most common pathology underlying vascular dementia. Despite its importance there are few treatments. A major factor underlying this is a lack of understanding of the disease mechanisms. Recent insights particularly from imaging and genetics have provided new insights into disease mechanisms, and potential therapeutic possibilities. These have highlighted the importance of endothelial dysfunction, and blood brain barrier breakdown. The talk will provide an overview of these advances, and what our current thinking of disease pathogenesis is. It will look forward to how these advances may helkp development of future treatments.

Disclosure: Nothing to disclose

EAN/EAPC: Palliative care and neurology

SYMP04_1

Palliative care from a neurologist's perspective: the evidence

D. Oliver

Canterbury, United Kingdom

Abstract: Awareness of the role of palliative care for patients with neurological disease is increasing with the aim of providing a holistic approach – considering physical, emotional, social and spiritual aspects of patients and their families. There is increasing evidence that this approach may improve the quality of life, help in symptom management and may even increase survival.

Studies have shown that as specialist palliative care service for neurological patients may lead to the improvement in quality of life and the symptoms of pain, breathlessness, bowel symptoms and sleep and the mortality is not increased. Palliative care for MS patients improved symptoms and caregiver burden and was cost effective.

Other studies have shown that a specialist multidisciplinary team approach, including palliative care, for people with amyotrophic lateral sclerosis improved the quality of life of patient and their families and an increase in survival was shown – a median survival improvement from 11 months to 19 months.

The role of palliative care has been strengthened by the publication of the Consensus document on palliative care from the European Academy of Neurology and the European Association for Palliative Care. This report recommends the increased involvement of palliative care, with all neurology services providing a palliative care approach – listening to patients and their families and assessing and managing these issues – in collaboration with more specialist palliative care services for more complex areas. In this way the quality of life, and the care at the end of life, for patients and families can be improved.

Disclosure: Nothing to disclose.

SYMP04_2

Guidelines in progress across Europe

R. Voltz

Cologne, Germany

Abstract: Recently, The Lancet Neurology highlighted the topic of palliative care in neurology in an Editorial (2017;16:489). This was prompted by the European Association for Neuro-Oncology guideline on palliative care in glioblastoma (Lancet Oncology 2017;18:e330-340). An EAN Task Force is currently working on a European Guideline on Palliative Care and Multiple Sclerosis. Earlier, a consensus review on the general principles in palliative care for patients with chronic and progressive neurological disease was published, jointly developed by the EAN and the European Association for Palliative Care (EAPC, Eur J Neurol 2016;23:30-38).

With this growing interest and number of guidelines, the question arises how general and disease-specific guidelines can complement each other. A solution could be based on the palliative care framework of the German Guideline Program in Oncology (www.leitlinienprogramm-onkologie.de/english-language/) which encompasses general palliative care principles that are independent from the underlying diagnoses (ie, a horizontal guideline), together with guidelines on disease-specific aspects. Specific guidelines should refer to the principles outlined in the horizontal guideline and provide only guidance on disease-specific aspects.

To achieve the high-quality evidence for such guidelines and to guide patient care, increased funding for research in this area is clearly needed. We hope that funders and reviewers of proposals in the future acknowledge the clinical relevance of this new and important topic in neurology.

Disclosure: Nothing to disclose.

SYMP04_3

What can a neurologist learn from palliative care specialists?

S. Veronese

Turin, Italy

Abstract: Palliative medicine and neurology are medical specialties that share many issues in clinical practice and in the process of care for patients affected by incurable, progressive and potentially life-threatening diseases.

Since the 90's the AAN published several statements and clinical recommendations on ethics, aimed at encouraging neurologists to learn and put in practice the principles of palliative care, recognising how most of their patients will not be curable and will die as a direct consequence of the neurological disorder that they have diagnosed.

According to the recently published EAN / EAPC consensus review on palliative care in neurology, the main areas of improvement for neurologists facing the challenge of caring for incurable patients are: communication, proactive needs assessment, accurate symptom control, prevention of crisis, care of psychosocial and spiritual existential issues, awareness of EoL choices, role of advanced directives, recognition of deterioration and dying phase, bereavement for the relatives.

These issues now need to be developed and implemented. There are tools that may help, such as structured communication models for breaking bad news (SPIKES), Patients' reported outcome measures tools (IPOS_NEURO), prognostic indicator tools for palliative care involvement (GSF toolkit, SPICT, NECPAL), end of life pathways, prevention of crisis interventions (Just in case kit).

By close collaboration, and mutual education, neurologists and palliative care specialists can develop a better understanding of the role of palliative care can offer and how to effectively collaborate so that the management of neurological patients may improve throughout the disease progression, including the end of life.

Disclosure: Nothing to disclose

EAN/ECTRIMS: Therapeutic challenges in progressive Multiple Sclerosis

SYMP09_2

Understanding progression: the contribution of clinical trials and natural history studies

J. Sastre-Garriga
Barcelona, Spain

In view of the new therapeutic options that will be soon available for patients with primary and secondary progressive multiple sclerosis, a better understanding of factors related to clinical worsening is clearly needed. Seminal studies in the late '80s showed that lesion loads in patients with primary progressive multiple sclerosis were lower in comparison with relapse-onset patients with comparable disability, indicating that lesion-related magnetic resonance markers might be less useful in this disease phenotype. However, studies in the early phases of primary progressive multiple sclerosis as well as natural history studies have shown that magnetic resonance imaging parameters are useful tools to monitor and predict disease evolution. Recent clinical trials have reinforced this idea, greatly adding to our knowledge with regards to the importance of inflammatory (presence of new lesions and lesions with gadolinium enhancement) and neurodegenerative magnetic resonance imaging markers (brain and spinal cord atrophy). In this talk a review of natural history and clinical trial data focusing on the potential use of magnetic resonance imaging as a valid surrogate will be presented.

SYMP09_3

Present and future treatment options in progressive MS

T. Derfuss
Basel, Switzerland

Abstract: Despite considerable progress in the treatment of relapsing-remitting MS there is still a tremendous need for an effective treatment of progressive forms of MS. Results from clinical trials during the last years indicate that an immunosuppressive/-modulatory treatment during the progressive stages has only a modest impact on disability progression. The S1P modulator siponimod has demonstrated a significant but modest reduction in disability progression along with an improvement in MRI parameters in secondary progressive MS. The monoclonal, B cell depleting anti-CD20 antibody ocrelizumab has shown comparable results in a phase III trial of primary progressive MS. These trial results indicate that the inflammatory component during later stages of MS has only a partial and probably minor influence on disability progression. Another problem of treating progressive MS comes from the notion that the inflammation might be compartimentalized in the brain. Treatments that do not affect inflammatory cells within the brain including brain-resident microglia and infiltrated lymphocytes and macrophages will have no impact even on inflammation related disability progression. This is exemplified by the negative results of the clinical trial of natalizumab in secondary progressive MS. Therefore there is a great interest in and demand for neuro-/myelin protective/regenerating therapies. Indeed clinical trials during recent years give a glimpse of hope. Neuroprotective strategies with sodium channel blockers like phenytoin and myelin regenerative/protective therapies like Biotin, anti-LINGO, and clemastine showed promising results in phase II trials. However, improvement in these trials was often limited to surrogate markers without a significant effect on clinical outcomes, with the only exception of biotin that showed an improvement of clinical disability in a trial of progressive MS. There is still an urgent need for more trials in progressive MS but it seems that we are at the beginning of a new era where anti-inflammatory treatments might be combined with neuro-/myelin protective/regenerating therapies to improve the disability and prognosis of patients with progressive MS.
Disclosure: Nothing to disclose.

Monday, June 18 2018

The spectrum of dementias

SYMP05_1

Alzheimer's disease

R. Schmidt
Graz, Austria

Abstract: Over the last 10 years research in Alzheimer´s disease (AD) has focused on revisions of diagnostic criteria. The main goal of these revisions is to diagnose AD earlier, incorporate the entire clinical spectrum of the disease including atypical forms, and to prove that a pathophysiological process of AD creates the basis of symptomatology. Assessment of AD biomarkers is considered instrumental for diagnosis-making. The most recent development is a unifying update of the 2011 NIA-AA criteria considerd to be a "research framework" because its intended use is for observational and interventional research, not routine clinical care. AD diagnosis is purely based on biomarker positivity irrespective of clinical symptoms with biomarkers being grouped into those of beta-amyloid deposition, pathologic tau, and neurodegeneration [AT(N)]. The lecture will present these new criteria and discuss possible consequences and shortcomings. The authors themselves appreciate the concern that this biomarker-based research framework has the potential to be misused. Overall, at the preclinical and prodromal stage more than 30 groups can be separated based on their biomarker pattern and clinical presentation. Each group may have differing risk for conversion to dementia or cognitive decline and it will last decades to know the respective figures of conversion and time to conversion for trial planning. The hope of the authors is that the new NIA-AA research frame work will enable a more precise approach to interventional trials where specific pathways can be targeted in the disease process and in the appropriate people is shared by the lecturer. Nonetheless, a major point of discussion is that AD may be become a laboratory-based diagnosis and interventional research may be inclined to treat the proteinopathy alone but not the clinical syndrome.
Disclosure: Nothing to disclose.

SYMP05_2

Vascular dementia

J.M.M.C. Ferro
Lisbon, Portugal

Abstract: Vascular dementia and vascular cognitive impairment are second to Alzheimer's pathology as a cause of cognitive decline and associated dependency. Vascular dementia is more frequent in low and middle income countries and in those with a high prevalence of stroke and of uncontrolled vascular risk factors. Cerebrovascular pathology also often combines with degenerative pathology. Vascular dementia can results from multiple pathophysiological mechanisms. The most relevant subtype of vascular dementia is that due to subcortical small vessel disease, which has a human genetic model (CADASIL), a characteristic clinical (subcortical vascular dementia) and imaging (lacunes, micro-bleeds and white matter lesions) phenotype.
We will present an update review on vascular dementia and on the contributory role of vascular pathology to the cognitive decline in the elderly. We will emphasize the clinical, neuroimaging, biochemical and genetic biomarkers of vascular dementia. Current management will be addressed, with focus on methodological issues of experimental studies and new targets for prevention and treatment
Disclosure: Nothing to disclose.

SYMP05_3

Frontal lobe dementias

J.M. Schott
London, United Kingdom

Abstract: The frontal lobe dementias represent a diverse groups of disorders with a variety of phenotypes, underlying pathologies and in a substantial proportion of cases, genetic underpinnings.

In this session I will provide a clinical overview of the canonical clinical syndromes - behavioural variant frontotemporal dementia, progressive non-fluent aphasia, and semantic dementia - using video cases and covering contemporary clinical diagnostic criteria, also considering overlap syndromes e.g. with corticobasal syndrome and motor neuron diseases.

I will outline the various pathologies underpinning these disorders and autosomal dominant genetic causes, and the extent to which they relate both to one another and to the various clinical syndromes; current and emerging disease biomarkers; and current and future prospects for treatment.

Disclosure: I report no disclosures relevant to this talk, but have received research funding and PET tracer from Eli Lilly, have consulted for Roche, Eli Lilly, Biogen and Merck, received royalties from Oxford University Press and Henry Stewart Talks, given education lectures sponsored by Eli Lilly and Biogen, and serve on a Data Safety Monitoring Committee for Axon Neuroscience SE.

SYMP05_4

Lewy Body dementia

E. Lemstra
Leiden, Netherlands

Abstract: Dementia with Lewy bodies and Parkinson's disease dementia, together called Lewy body dementias, are the second most common type of degenerative dementia in the elderly after Alzheimer's disease. However, Lewy body dementias receive relatively little attention and patients are often misdiagnosed. Patients with Lewy body dementia not only suffer from dementia but face other challenging symptoms such as hallucinations, parkinsonism, autonomic dysfunction and sleep disorders. Accurate diagnosis is crucial because these patients need a specific treatment approach. Much has been gained in the past decade in the improvement of diagnostic accuracy and the understanding of pathophysiological mechanisms. Recently, diagnostic criteria have been revised now incorporating distinctive biomarkers. During this symposium these new criteria will be reviewed. Lewy body dementias are alpha-synucleinopathies but concomitant Alzheimer-pathology in varying degree often occurs. Alzheimer-pathology in Lewy body dementias probably influences disease manifestation. The issue of overlapping pathologies and the relationship to clinical phenotypes will be discussed. Furthermore, large genetic studies on Lewy body dementias have been performed recently, shedding new light on pathophysiological mechanisms in these diseases. The main findings will be presented in this symposium.

Disclosure: Nothing to disclose.

Coma: Neuromodulation, imaging and neurobiology

SYMP06_1

Mechanisms of impaired consciousness

D. Kondziella
Copenhagen, Denmark

Abstract: According to neurological doctrine, consciousness is lost or impaired following strategic lesions in the brainstem, bilateral damage to the cerebral hemispheres or global metabolic dysfunction; and patients may recover from coma by successively passing through stages of limited consciousness to full consciousness with or without remaining cognitive deficits. However, functional neuroimaging, elaborate EEG paradigms and standardised clinical bedside techniques have paved the way for a more nuanced understanding of the many facets of disorders of consciousness, and we as clinical neurologists are increasingly thinking in terms of neuronal connectivity and brain networks as opposed to isolated pathological lesions. Yet, it is still not appreciated widely enough that patients exist who are clearly conscious but have lost all means of communicating it to the outside world because they no longer have any motor output at all. In this lecture, the pathophysiological mechanisms of impaired consciousness are discussed, highlighting the origin of specific clinical signs and syndromes, the recognition of which are crucial to discerning the state of consciousness of a given patient. Although this talk is tailored to the needs of the general neurologist at the bedside, we will make the case that key concepts of clinical consciousness research have been described by novelists and poets a long time before they entered the minds of neurologists, and that important principles to the understanding of the origin of human consciousness and its disorders may be derived from unsuspected fields such as comparative biology and phylogenetics.
Disclosure: Nothing to disclose.

SYMP06_2

Where structural changes predict outcome

L. Puybasset
Paris, France

Abstract: We developed a score derived from MRI to predict 1-year outcome of patients unresponsive to simple orders after traumatic brain injury, aneurysmal subarachnoid haemorrhage, and cardiac arrest in the day 7 - day 45 period post brain injury. Recent studies reported late awakeners cases, even in cardiac arrest and, in contrary, that around 10% of patients with acute brain injury remain with permanent disorders of consciousness. The need of reliable prognosis tool at the early phase, while the patient is still in the ICU, is critical. ComaScore, based on the quantitative analysis of diffusion tensor imaging, was developed from a derivation cohort of 506 patients. It is much more performing than existing tools (IMPACT, OHCA) in this respect. In absence of reliable tool for prognostication, the reality is that patients' management and care titration highly depend on the hospital/service where the patient is cared, leading to unequal access to care and decision regarding care withdrawal. The implementation in clinical routine may be fast because (i) only nearly conventional MRI sequences are required and (ii) a prototype of the medical device (https://comaweb.org) is already functioning (iii) this web-application has been used for data collection by 10 French centers since 2015. Growing social and economic challenges of intensive care must encourage health agencies to establish standards for care management of comatose patients. We believe that the use of comaScore is a pillar of these standards.
Disclosure: Nothing to disclose.

SYMP06_3

Cognitive-motor dissociation: cave!

K. Diserens
Lausanne, Switzerland

Abstract: Disorders of consciousness (DOC) are a common consequence of severe brain injuries. Physicians in neuro-intensive care units are faced with the challenge of providing a diagnosis and a prognostic orientation, the latter eventually leading to complex therapeutic and ethical decisions. Bedside clinical examination of non-communicating DOC patients is based on validated coma scales scoring essentially motor efference and verbal interaction to evaluate consciousness. In the very acute phase after stop of sedation this evaluation may be hampered by several factors (e.g. neurological deficits, concomitant medical conditions, fluctuation in arousal, assessor variability). The use of the Motor Behaviour Tool (MBT, Pignat et al. 2016), a supplemental tool to the robust JFK Coma Recovery Scale-Revised (CRS-r) (Giacino et al., 2004), helps the examiners to identify several pitfalls alerting them to the high risk of misdiagnosis especially in case of Cognitive Motor Dissociation (CMD) patients (Schiff N et al., 2018). Results from clinical observations of a consequent sample of DOC patients in the very acute phase will be presented. Finally, the controversy of the methodological approach to improve diagnostic accuracy of CMD will be discussed.
Disclosure: Nothing to disclose.

SYMP06_4

Neuromodulation: outlook into the future

S. Laureys
Liege, Belgium

Abstract: Neuromodulation techniques aimed at normalising the neurophysiologic disturbance produced by brain lesions or dysfunction. They have been studied for years in attempts to modulate brain activity to treat several neurological diseases. Non-invasive brain stimulations offer an opportunity to improve the recovery of severely brain injured patients with disorders of consciousness (DOC), a population that lacks of effective treatment options, especially at the chronic stage.

In this presentation, we will expose the neural mechanisms of neuromodulation and how these novels techniques can, from a mechanistically point of view, improve the recovery of severely brain injured patients. We will also describe non-invasive techniques, namely transcranial direct current stimulation (tDCS) and transcranial magnetic stimulation (TMS), as therapeutic (and diagnosis) options for patients with DOC. The first studies on tDCS, targeting the left prefrontal cortex, have shown encouraging results, with significant behavioral improvements, in both acute and chronic patients. More recent studies targeting other brain regions (e.g., posterior parietal or motor cortex) or aiming at better understand the mechanisms of action of tDCS (using neuroimaging techniques) in severely brain injured patients have also been performed, confirming the clinical potential of tDCS in this population of patients. Sor far, prefrontal tDCS has shown to reproductively improve patients' signs of consciousness following one, five and twenty days of stimulation. TMS has also been investigating with excellent results for diagnosis purpose but less so for therapeutic treatments. TMS has also been investigating with excellent results for diagnosis purpose, when combined with EEG, it allows to differentiate between unresponsive/vegetative and minimally conscious patients at the single level. The therapeutic effects of repetitive TMS are encouraging but it still needs more validation. Lastly, we will discuss the therapeutical (e.g., benefit/risk ratio) and ethical issues (e.g., end-of-life decision) that arisen with such a challenging population.

Even if more work has to be done to strengthen our understanding of the mechanisms and potential treatments to promote the recovery of consciousness in patients with DOC, the field of neuromodulation seems to be a promising therapeutic option to improve patients' rehabilitation.
Disclosure: Nothing to disclose

Tuesday, June 19 2018

A new look in neuropathogenesis of Multiple Sclerosis

SYMP07_1

Role of environmental factors for MS

R. Gold
Bochum, Germany

Abstract: The genetic aspects of Multiple Sclerosis have been recognised early, based on observations in monozygotic twins and in afflicted families. Yet, even with the most sophisticated multicentre genetic studies these factors come to a maximum of 35% contribution for susceptibility to MS. At the same time, prevalence data of MS in Northern and Central European countries have risen 2-3 times, coming to a gross figure of 1:400 MS risk in these populations. Although there has been progress in MRI techniques and updates in MS diagnostic criteria, these figures by far exceed the expected range.

The most fundamental changes in modern civilisation have occurred with respect to nutrition and environment. There is overall decrease of fiber rich food such as fruit and vegetables, paralleled by intake of high-sugar and long-chain fatty enriched 'fast food'. In the recent years, sophisticated transgenic models have been established and studied which allude to these factors. They also allow to study the respective microbiota, which can be easily transferred into patients with specific disease courses of MS. In addition, the influence of salt and spices has been assessed as additional confounding factors. Exposure to cigarette smoking further modulates the risk factors.

In this presentation, the available molecular, cellular and clinical data will be discussed which further support the modulation of susceptibility for multiple sclerosis.
Disclosure: Nothing to disclose.

SYMP07_3

Challenges for modern MS therapy on back-ground of pathogenesis

L. Massacesi
Florence, Italy

Abstract: Pathogenesis of Multiple Sclerosis (MS) varies over time in the same individual from purely immune-mediated to degenerative, requiring different therapeutic strategies according to the disease phase. Initially the immune system damages the central nervous system (CNS) from the periphery, then it gradually compartimentalises in the CNS, damaging from inside. To this inflammatory mechanism gradually over the years overlap toxic-degenerative mechansms of neuron disruption due to reparing/scaring processes, progressively contributing to deplete neuron reserve of patients and determining irreversible disability. Then, the only effective therapeutc strategy in MS is preventing this depletion. This can be done with the available treatments active on the immune system, optimally in the very early stages of the disease, preventing new waves of inflammation from outside the CNS. However only a few of these treatments can reach the foci of inflammation compartmentalized in the CNS crossing the blood brain barrier (BBB). Then, these are the treatments that should be more effective against the compartmentalized immune response. Available markers of compartmentalization are both clinical and paraclinical. The clinical are time/ space dissemination changes (from relapsing remitting and multifocal to progressive and pauci-focal) and interindividual variability of the course (from highly heterogeneous to homogeneous). The paraclinical ones are intrathecal Ig production and visualization by MRi of leptomeningeal infiltrates. Protection of the neurons and of myelin (and myelin regeneration) –when available-should also optimally be pursued early in the course of the disease, when neuron damage is still minimal, but particularly early in the course of any new lesion.
Disclosure: LM: declares honoraria for speaking in scientific meetings or for participation in advisory boards, by Genzyme, Biogen, Mylan and Roche; travel support for scientific meetings from Merck-Serono, Biogen, Teva, Genzyme and Novartis.

SYMP07_4

The contribution of MRI for better understanding of MS

D. Chard

London, United Kingdom

Abstract: Our understanding of the neuropathogenesis of MS has changed recently with, for example, an increasing recognition of the extent and clinical relevance of grey matter pathology, and emerging evidence that factors outside the brain may substantially influence pathology within it. In this session we will consider how MRI has contributed to this, and how it has helped to bridge the gap between neuropathological studies and clinical outcomes. We will also look at new and emerging MRI techniques for assessing MS pathology in life, and their potential role in the diagnosis of MS and in treatment trials.

Advances in molecular characterisation and personalised therapies in brain tumors

SYMP08_1

Targeting the immune cells or the glial cells in glioblastoma: the new question

M. Weller
Zurich, Switzerland

Abstract: The current standard of care for glioblastoma of neurosurgical resection as feasible followed by involved-field radiotherapy and concomitant and maintenance temozolomide chemotherapy prolongs survival to a median of 16 months in clinical trial populations, but survival with glioblastoma is still in the range of one year on a population level. Immunosuppression is one of the hallmarks of the glioblastoma microenvironment, prompting the clinical development of various immunotherapeutic strategies that are currently being studied in clinical trials of phase I, II or III. Efforts focusing on the antagonism of glioma-associated immunosuppression alone, e.g., blocking the transforming growth factor (TGF)-β pathway or programmed cell death ligand (PD-L)-1, have not been successful. Similarly, counteracting inhibitory signalling to T-cells at the target cell level via cytotoxic T lymphocyte-associated protein (CTLA)-4 or programmed death (PD)-1 using various neutralizing antibodies has not been demonstrated to improve outcome yet. Various vaccination approaches have also been tested, including dendritic cell-based vaccines, using either crude tumor lysates (DCVax) or tailored mRNA or peptide stimulation (ICT-107), or defined peptides alone, like the epidermal growth factor receptor (EGFR) variant III vaccine, rindopepimut. Efficacy for any of theses vaccines remains to be demonstrated. Thus, it appears that alleviating the immunosuppression generated by glioma cells remains a prime goal for better treatment successes in glioblastoma, but attention should at the same time be directed to render immune effectors more active against target cells, and more resistant to inhibition, e.g., by generating CAR T-cells refractory to immune inhibitory signalling.
Disclosure: MW has received research grants from Abbvie, Acceleron, Actelion, Bayer, Merck, Sharp & Dohme (MSD), Merck (EMD), Novocure, OGD2, Piqur, Roche and Tragara, and honoraria for lectures or advisory board participation or consulting from Abbvie, BMS, Celgene, Celldex, Merck, Sharp & Dohme (MSD), Merck (EMD), Novocure, Orbus, Pfizer, Progenics, Roche, Teva and Tocagen.

SYMP08_2

Subependymal giant cell astrocytoma (SEGA): a model of targeting tumor growth and seizures

F. Ducray
Lyons, France

Abstract: Seizures are a major problem in brain tumor patients. This presentation will focus on how advances in molecular characterisation and personalised therapies in brain tumors may help managing epilepsy. For this purpose this presentation will review the pathophysiology of brain tumor related epilepsy and analyze the impact on epilepsy management of advances in the molecular characterization of subependymal giant cell astrocytoma (SEGA) but also IDH-mutant gliomas and glioneuronal tumors (including DNET and gangliogliomas).
Disclosure: Nothing to disclose.

SYMP08_3

Specific inhibitors of molecular pathways in brain metastases: from improved response to improved survival

R. Soffietti, R. Rudà, A. Pellerino
Turin, Italy

Abstract: Few clinical trials of systemic agents have been conducted to date in patients with brain metastases, and this population has frequently been excluded from clinical trials of emerging investigational drugs. Historically, the use of systemic therapy in patients with brain metastases has been limited by the presence of the blood brain barrier (BBB), that limites the access of hydrophilic and/or large agents into the CNS. However, the BBB is disrupted in macroscopic brain metastases resulting in an increased exposure to systemic drugs. Recent advances in understanding the molecular basis of tumor growth in many solid tumors have allowed the development of agents targeting molecular pathways both in the extracranial and intracranial disease. Encouraging results have emerged for tyrosine kinase inhibitors and monoclonal antibodies in subgroups of patient with brain metastases. Regarding brain and leptomeningeal metastases from non-small cell lung cancer (NSCLC), EGFR and ALK inhibitors yield a high rate of durable responses. In this regard, the capacity of the first two generations of compounds (gefitinib, erlotinib, afatinib, crizotinib, ceritinib) to cross an intact BBB was very limited, while it is now greatly improved with the next generation of compounds (osimertinib, alectinib, brigatinib). HER2 positive breast cancer brain metastases can now be targeted by specific inhibitors (lapatinib, neratinib), and the same is true for brain metastases from BRAF-mutated melanoma (vemurafeninb, dabrafenib). One of the major limitations with targeted therapies employing small molecules is the risk of the emergence of a resistance, due to the development of novel mutations.
Disclosure: Nothing to disclose

SYMP08_4

New molecular subtypes of medulloblastomas and ependymomas: different outcome and treatment options

S. Pfister
Heidelberg, Germany

Abstract: Medulloblastoma (MB) are two of the most common malignant pediatric brain tumors. Both of them display extensive inter-tumoral heterogeneity, which probably reflects different cells-of-origin. These molecular subgroups and subtypes, which are often associated with specific genetic hits, need to be taken into account for patient stratification as well as the interpretation of clinical trial results. The talk will address the biological and clinical differences of medulloblastoma and ependymoma subgroups as well as their reliable detection in a clinical setting and potential implications for novel therapies.
Disclosure: Nothing to disclose.

Oral Sessions

Saturday, 16 June 2018

Neurological manifestations of systemic diseases

O101

EXPLORE: a prospective, multinational natural history study of patients with acute hepatic porphyria with recurrent attacks

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Background and aims: Acute Hepatic Porphyrias (AHPs) are rare, genetic diseases caused by mutations in the heme pathway. Central to AHPs is the upregulation of aminolevulinic acid synthase1 (ALAS1), the first, rate-limiting enzyme which causes accumulation of neurotoxic heme intermediates, aminolevulinic acid (ALA) and porphobilinogen (PBG). This results in life-threatening attacks and chronic, debilitating manifestations due to injury to the nervous systems, including neurovisceral pain, fatigue, and motor weakness.

Methods: EXPLORE is the first observational study characterizing clinical management of patients with AHPs with ≥3 attacks/year, including patients receiving prophylactic treatment to prevent attacks. We will be presenting updated ≥12 month data.

Results: 112 patients enrolled from 13 countries. Patients reported a mean of 9.3 attacks in 12 months prior to the study, with pain (99%), mood/sleep, and digestive (each 96%) symptoms being the most common. Annualized attack rate on study was 4.9 attacks/person, of which 77% required treatment. For those on hemin prophylactically, mean attack rate/person-year=4.0. Chronic symptoms were reported by 65% of patients, with pain (63%), mood/sleep (44%), and digestive (36%) manifestations most frequent. The EQ5D quality of life score was 66 (1-100); 35% had some difficulty walking and 57% had difficulty with usual activities or anxiety/depression. Mean ALA and PBG levels at screening (during non-attack) were increased to 8Xs and 20Xs ULN, respectively.

Conclusion: EXPLORE demonstrates that patients suffer from chronic symptoms in addition to frequent attacks that decrease quality of life. Given morbidity and mortality, there remains an unmet need for novel therapies to prevent attacks and treat chronic symptoms.

Disclosure: This is supported by Alnylam.

O102

Clinical characterisation of Wilson's Disease patients: a retrospective study at a tertiary-care centre in Lisbon

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Background and aims: Wilson's Disease (WD) is an autosomal recessive metabolic disorder caused by ATP7B gene mutations, producing toxic copper accumulation, mainly in the liver and the brain. We aim to characterise the population of patients with WD followed at our centre and to identify possible factors that may correlate with neurological involvement in WD.

Methods: We identified all patients with the diagnosis of WD listed in our centre's database between 2009 and 2017. We reviewed case records and collected clinical, laboratorial, genetic and imaging data.

Results: We identified 24 patients, 17 (81%) of them were females. Median age at diagnosis was 17 years (SD±14). ATP7B gene sequencing result reported c.2123T>C as the most frequent mutation. Mixed hepatic and neurological presentation was the most common form (45.8%, 11 cases). Pure hepatic and neurological presentations were found in 10 (41.7%) and 3 (12.5%) patients, respectively. Patients with neurological involvement were older at diagnosis than patients with only hepatic involvement (29 vs. 17 years). Rigidity, bradykinesia and tremor were the most reported neurological signs, with bradykinesia being more frequent in the younger patients. Normal liver transaminase levels at diagnosis correlated with presence of neurological disease (p=0.000034). Six patients with neurological symptoms presented brain MRI changes compatible with WD. Follow-up reported improvement with treatment in 8/11 (73%) patients with neurological symptoms.

Conclusion: Initial assessment of liver transaminase levels may help to identify WD patients who are more likely to develop in time neurological symptoms, alerting to the need of regular neurological evaluations.

Disclosure: Nothing to disclose

O103

Impact of Patisiran, an investigational RNAi Therapeutic, on nutritional status in patients with hereditary Transthyretin-Mediated Amyloidosis

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Background and aims: Patients with hereditary transthyretin mediated amyloidosis (hATTR), a multi-systemic, rapidly-progressive, life-threatening disease, often have poor nutritional status and overall weight loss due in part to severe gastrointestinal manifestations as well as cardiac disease. In the phase 3 APOLLO study, Patisiran demonstrated significant improvements in neuropathy (mNIS+7) and quality of life (QOL) compared to placebo in hATTR amyloidosis patients with polyneuropathy, and was generally well-tolerated. We present the impact of Patisiran on nutritional status, as measured by modified body mass index (mBMI) the APOLLO study.

Methods: APOLLO was a multi-center, international, randomized (2:1), double-blind study of Patisiran 0.3mg/kg or placebo IV q3W in hATTR amyloidosis patients with polyneuropathy (NCT01960348). Primary endpoint was change from baseline at 18-months in mNIS+7. One of the secondary endpoints was change in mBMI, defined as the product of BMI and albumin levels.

Results: APOLLO enrolled 225 patients: mean age 60.5 years (24-83), 74% males and 43% V30M. At baseline, mBMI was similar in the Patisiran and placebo groups. In the placebo group, mBMI declined by a LS mean of 119.4 kg/m2 x g/L over 18-months relative to baseline, whereas LS mean decline was only 3.7 with Patisiran. This improvement compared to placebo was seen as early as 3-months of treatment with Patisiran.

Conclusion: Patients treated with Patisiran maintained their nutritional status over 18 months. The favorable effect of Patisiran on mBMI relative to placebo indicates stabilization of mBMI decline in hATTR amyloidosis patients, therefore improving overall nutritional status.

Disclosure: This research was supported by Alnylam Pharmaceuticals.

O104

Impact of prior TTR stabilizer use in patients with hereditary Transthyretin-Mediated Amyloidosis in the APOLLO phase-3 study of Patisiran

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Background and aims: Hereditary transthyretin-mediated (hATTR) amyloidosis is a multi-systemic, life-threatening disease caused by transthyretin (TTR) mutations resulting in TTR protein destabilization forming multi-organ amyloid fibril deposits. TTR tetramer stabilizers have been used in hATTR amyloidosis patients; however, some studies have shown disease progression is still observed. In the APOLLO study, Patisiran, an investigational RNAi therapeutic, resulted in significant improvement in neuropathy (mNIS+7) and Norfolk Quality of Life Diabetic Neuropathy (Norfolk QOL-DN) compared to placebo in hATTR amyloidosis patients and was generally well-tolerated. We evaluated the impact of prior treatment with TTR tetramer stabilizers on Patisiran efficacy from the APOLLO study.

Methods: APOLLO was a Phase 3, randomized (2:1), double-blind, study of patisiran 0.3mg/kg or placebo IV q3W (NCT01960348) in hATTR amyloidosis patients with polyneuropathy. Primary endpoint was change from baseline at 18-months in mNIS+7. TTR tetramer stabilizer discontinuation was required 14 or 3 days prior to study entry for tafamidis or diflunisal, respectively.

Results: APOLLO enrolled 225 patients: mean age 60.5 years (24-83); 74% males; 43% V30M. Prior to study entry, 53% of patients had previously received a TTR stabilizer (Tafamidis: n=74(33%); Diflunisal; n=45(20%). An

improvement in mNIS+7 and Norfolk QOL-DN was seen in patients with or without prior stabilizer use (Table 1) at 18-months. Additional efficacy and safety data to be presented.

Analysis	Patient Population	Placebo Patients (n)	Patisiran Patients (n)	LS Mean Treatment Difference (Patisiran-Placebo)	95% Confidence Interval
mNIS+7	Overall	77	148	-34.0	-39.9,-28.1
	Previous Stabilizer Use	25	76	-38.3	-46.1,-30.5
	No Previous Stabilizer Use	26	61	-29.9	-39.1,-20.8
Norfolk QOL-DN	Overall	77	148	-21.1	-27.2,-15.0
	Previous Stabilizer Use	41	78	-17.6	-25.7,-9.4
	No Previous Stabilizer Use	36	70	-25.9	-36.2,-15.6

Table 1. mNIS+7 and Norfolk QOL-DN Results

Conclusion: Patisiran demonstrated significant benefit relative to placebo in mNIS+7 and Norfolk QOL-DN in patients with or without prior TTR tetramer stabilizer use, thus providing evidence that hATTR amyloidosis patients with prior stabilizer use may benefit from Patisiran.

Disclosure: This research was supported by Alnylam Pharmaceuticals.

O105

Phase 1/2, randomized, placebo controlled and open-label extension studies of Givosiran an investigational RNA interference (RNAi) therapeutic, in patients with Acute Intermittent Porphyria

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Background and aims: Acute hepatic porphyrias (AHPs) are rare genetic diseases resulting from loss-of-function mutations that cause upregulation of Aminolevulinic Acid Synthase 1 (ALAS1), the first and rate-limiting enzyme in the heme pathway. The resulting accumulation of neurotoxic intermediates Aminolevulinic Acid (ALA) and porphobilinogen (PBG) leads to neurovisceral attacks and chronic symptoms. Common neurological symptoms include pain, fatigue, muscle weakness, peripheral neuropathy, and neuropsychological manifestations. Givosiran acts via RNA interference (RNAi) to inhibit liver ALAS1 synthesis.

Methods: A Phase 1/2 (ClinicalTrials.gov Identifier: NCT02452372), multinational study evaluated the safety, tolerability, pharmacokinetics, and pharmacodynamics of subcutaneously administered Givosiran (2.5mg/kg monthly). Impact on clinical activity, including chronic symptoms, annualized attack rates, and hemin use were explored. Patients completing the study were eligible for the open label extension (OLE) study (NCT0294983).

Results: Givosiran was generally well tolerated with no clinically significant laboratory abnormalities related to study drug. One unexpected serious adverse event (SAE; hypersensitivity) related to Givosiran occurred. Urinary ALA and PBG were reduced by 77% and 76% versus baseline, respectively. Additionally, Givosiran decreased mean annualized attack rate versus placebo by 73% and decreased annualized hemin doses versus run-in period by 73%. The OLE (n=8) data showed maintenance of clinical activity as observed in Phase 1.

Conclusion: Givosiran was generally well-tolerated and resulted in rapid and durable lowering of neurotoxic intermediates. ALA and PBG lowering were associated with marked reductions in both the annualised attack rate and hemin use. Complete Phase 1/2 and interim OLE data will be presented.

Disclosure: This was supported by Alnylam Pharmaceuticals

Movement disorders 1

O107

Glucose dysregulation in advanced Parkinson's Disease: too much glucose or not enough insulin?

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Background and aims: Glucose metabolism has recently been reported to be altered in Parkinson's Disease (PD) as a non-motor consequence of the disease. Since insulin pancreatic production and secretion is modulated by the autonomic nervous system, the severity of dysautonomia in PD could be linked with blood glucose dysregulation. We aimed to detect changes in glucose regulation in PD patients compared to healthy controls in response to oral glucose intake.
Methods: Blood glucose and insulin kinetics during a 75-g Oral Glucose Tolerance Test were compared between 50 PD patients and 50 healthy controls (CT) matched for Body Mass Index (BMI), age and sex. Potential relationships between changes in glucose kinetics and clinical parameters were analyzed including PD severity and autonomic function using SCOPA-AUT (Scales for Outcomes in Parkinson's disease, Autonomic dysfunction).
Results: Blood glucose was significantly higher at T90 (p=0.04) and T150 (p=0.01) in PD patients compared to CT. Moreover, the total area under time curve for blood glucose was significantly higher in PD patients compared to healthy controls (1187±229 vs 1101±201 mmol.min.l-1; p=0.05). Simultaneously, no significant increase of insulin levels was observed in PD patients compared to controls. Higher blood glucose levels were associated with higher BMI (p<0.001), female gender (p<0.033), longer duration of PD (p=0.001), lower dose of dopaminergic treatment (p=0.023), and higher score of dysautonomia (p=0.017).
Conclusion: Glucose control is impaired in advanced non-diabetic PD patients, due to impaired adaptive insulin response which may be a novel non-motor consequence of PD associated dysautonomia.
Disclosure: Nothing to disclose

O108

Skin nerve phosphorylated α-synuclein deposits in Parkinson's disease with orthostatic hypotension

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Background and aims: We aimed to investigate phosphorylated α-synuclein (p-syn) deposits in skin nerves and clinical characteristics in patients with Parkinson's Disease (PD) and Orthostatic Hypotension (OH) vs PD patients without dysautonomia (PD-OH) to clarify the peripheral nerves involvement in these two conditions.
Methods: We enrolled 28 idiopathic PD patients with abnormal nigro-striatal DatScan and cardiac MIBG: 1) 14 PD+OH; and 2) 14 disease duration matched PD-OH; 7 of them were re-evaluated over a long follow-up (4±2 years). Corrected Mini-Mental State Examination (MMSEc) was normal in all recruited patients. All patients underwent skin biopsy in proximal (i.e. C7 paravertebral spine region) and distal (i.e. thigh and leg) sites.
Results: PD+OH patients showed a higher incidence of REM sleep behavior disorder (RBD) than PD-OH. PD+OH showed a higher p-syn deposition than PD-OH with a widespread autonomic cholinergic and adrenergic skin nerves involvement. Over the follow-up PD-OH patients showed a marked increase in motor dysfunctions scores without autonomic symptoms and a slight increase of skin p-syn deposition but still lower than PD+OH.
Conclusion: 1) PD+OH showed a wide involvement of p-syn deposits in autonomic cholinergic and adrenergic skin nerves and higher incidence of RBD compared to PD-OH; 2) skin p-syn in PD-OH was mainly restricted to adrenergic fibers of skin vessels. A slight increase of skin p-syn deposition was found over a follow-up but still lower than PD+OH. These data supported a different pathogenesis between PD+OH and PD-OH and may help to identify a specific diagnostic trait for PD+OH patients.
Disclosure: Nothing to disclose

O109

Clinical predictors of screen-defined dementia in early Parkinson's disease

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Background and aims: Predicting early dementia in Parkinson's disease (PD) has important implications for individual prognosis, designing clinical trials and targeting novel treatments, but there remains a lack of evidence in this area. This study examined which clinical factors predicted early dementia in a large cohort of early PD subjects.

Methods: Parkinson's patients assessed within 3.5 years of diagnosis were recruited between 2010-2015 (the Discovery cohort, UK) and then re-assessed after 18 months. The Montreal cognitive assessment was used to assess cognition, using a score of <23 for screen-defined dementia. A broad spectrum of other motor and non-motor symptoms were also assessed. A logistic regression model with a backward stepwise selection was used to determine which baseline clinical assessments were independent predictors of dementia at 18 months.

Results: 61 of the 488 included PD patients developed new dementia at 18 month follow-up. Older age at diagnosis with poor performance on phonemic fluency, cube copying, and the Purdue assembly task were all included in the final model as independent predictors of dementia (figure 1).

The area under the ROC curve for this model is estimated at 0.81 (95% CI 0.74-0.89) (figure 2).
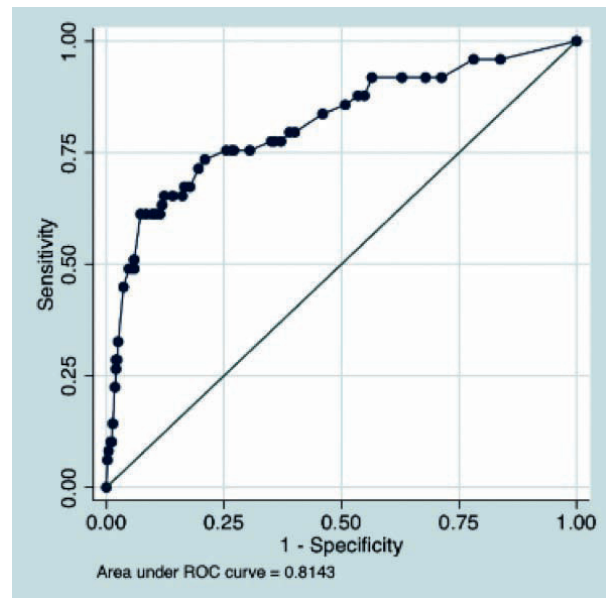
Figure 1 - Odds ratios of model for factors predicting dementia, with their 95% confidence intervals. Age at diagnosis was analysed as a 5 level ordinal variable, cube copying errors was analysed as a 3 level ordinal variable, and both phonemic fluency and purdue assembly were analysed as a dichotomous variables (poor performers <20th centile).
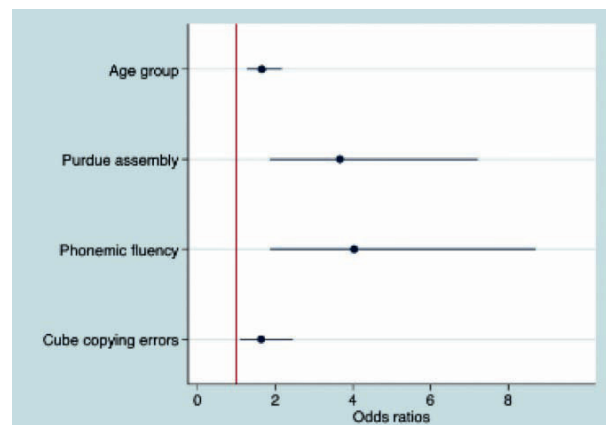
Figure 2 - ROC curve depicting model of factors predicting dementia including age at diagnosis, Purdue assembly task, phonemic fluency and cube copying connection errors.

Conclusion: Poor performance on three simple clinical tests performed early in PD (the Purdue assembly task, phonemic fluency and cube copying) can be used to predict early dementia. This has implications for both clinical practice and clinical trials.

O110

Temporal evolution of biomarkers in isolated REM sleep behavior disorder and early Parkinson's disease

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Background and aims: We aimed to study the temporal evolution of biomarkers of various modalities in healthy ageing controls (HC), the prodromal condition of idiopathic REM sleep behavior disorder (iRBD) and in Parkinson's disease (PD).

Methods: We investigated previously identified biomarkers for early PD in 34 iRBD subjects and compared these to 88 HC and 91 PD patients. We stratified the PD group into 31 patients with RBD (PD+RBD) and 60 patients without (PD-RBD). Baseline and follow-up investigations after 24 months covered questionnaires On Non-Motor signs (NMS), cognitive testing, video-polysomnography (PSG), ECG, olfactory testing, magnetic resonance imaging with Voxel Based Morphometry (VBM) and Cerebrospinal Fluid (CSF) measures.

Results: Most biomarkers in the iRBD group lay between HC and the PD groups. ECG frequency, that was elevated in PD, was normal in iRBD and HC (p<0.01). Other biomarkers already showed abnormalities similar to PD: a high NMS burden (p<0.01) and a non-significant decrease of β-amyloid 1-42 and total tau protein in CSF. There was also a trend towards more abnormalities in iRBD patients compared to the PD group, but did not reach statistical significance: more severe hippocampal atrophy by VBM, more pronounced cognitive decline. The CSF levels of α-synuclein were lower in the iRBD compared to the PD+RBD group (p=0.03)

Conclusion: In prodromal PD abnormalities in NMS, imaging and fluidic markers are already obviously pointing towards the development of overt disease. Based on these results iRBD represents a prodromal state of various α-synuclein aggregation disorders and may develop into a specific, motor phenotype.

Disclosure: The study was supported by unrestricted research grants from the Paracelsus-Elena-Klinik, Kassel, TEVA Pharma/Lundbeck, GE Healthcare and the Parkinson Fonds Deutschland.

O111

Brain Lewy body density is associated with a lower prevalence of artherosclerotic cardiovascular disease risk factors in patients with Parkinson's disease

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Background and aims: Epidemiological studies suggest that Atherosclerotic Cardiovascular Disease (ASCVD) risk factors increase the risk of developing Parkinson's disease (PD). However, conflicting data suggest lower rates of ASCVD in PD. The objective of this study is to determine, with data from a longitudinal clinicopathological study, whether ASCVD risk factors are associated with a PD diagnosis and/or brain alpha-synuclein pathology load.

Methods: All subjects were enrolled in the Arizona Study of Aging and Neurodegenerative Disorders (AZSAND). Multivariable logistic regression models, including age, gender, and smoking history, were used to investigate the association of a PD diagnosis or brain alpha-synuclein pathology load with ASCVD risk factors

Results: 150 subjects were included (PD n=60, controls n=90). The regression models showed significant inverse associations. The multivariable Odds Ratio (OR) of brain alpha-synuclein pathology load for carotid artery disease was 0.93 (95% CI: .86 to .98; p=0.02), for anticoagulant use .95 (95% CI: .90 to .99; p=0.04) and for lower heart weight .96 (95% CI: .92 to .99; p=0.01).

Conclusion: This study shows a significant association of higher brain alpha-synuclein pathology load with a lower prevalence of both clinical and pathologic indices of ASCVD in PD subjects versus age-similar controls. We hypothesize this is due to alpha-synuclein pathology-induced sympathetic denervation in PD.

Disclosure: Nothing to disclose

O112

Multimodal MRI markers modifications in Multiple System Atrophy: a longitudinal study

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Background and aims: Multimodal MRI (mMRI) approach is based on combination of MRI parameters sensitive to different tissue characteristics (e.g. volume atrophy, iron deposition, and microstructural damage). The combination of different MR biomarkers could help to discriminate different pathologies with parkinsonian syndrome (Péran et al. Mov Disord.; 2018). Using mMRI, the aim of the study was to evaluate brain changes due to disease progression in Multiple System Atrophy (MSA) patients.

Methods: 19 MSA patients underwent 3-T MRI exam twice at time of inclusion and after one year of follow-up. This MRI comprised: T2*-weighted, T1-weighted and diffusion tensor imaging scans. We used the same method as in the previous work (Péran et al., Brain, 2010) to extract MRI markers (grey density, R2* value, mean diffusity (MD) and fractional anisotropy). The GD, R2*, MD, and FA maps were compared using non-parametric paired t-tests. Statistical significance threshold was set to $p < .05$ corrected for family wise error.

Results: Figure 1 shows changes due to disease progression from voxel-based analysis in R2* (red), MD (green) and FA (blue) maps. The main results showed significant increase of MD in brainstem and in cerebellum. MSA patients showed also lower FA mainly in left inferior longitudinal fasciculus. Additionally, MSA patients showed a decrease of R2* mainly in cerebellum and in fusiform gyrus. We did not find significant modifications for GD maps.
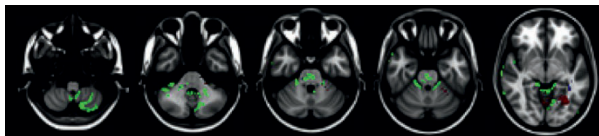

Figure 1

Conclusion: This study demonstrates that mMRI is able to detect longitudinal modifications after one year of MSA progression. Further analyses are on-going to determine the relationships between clinical and MRI markers.

Disclosure: Nothing to disclose

MS and related disorders 1

O113

Spinal cord area is a stronger predictor of physical disability than brain volume in secondary progressive Multiple Sclerosis

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Background and aims: Spinal cord atrophy may be a more sensitive measure of disability worsening than brain atrophy in Multiple Sclerosis (MS).

We aimed at investigate the contribution of spinal cord area and brain volume to disability in people with secondary progressive MS (SPMS).

Methods: A group of SPMS patients randomised in a phase 2 clinical trial (MS-SMART) were included in this study. Patients underwent neurological assessments, brain and cervical cord MRI. We measured the following MRI and clinical parameters: Mean Upper Cervical-Cord Cross-Sectional Area (Mucca), Normalised Brain Volume (Nbv), Expanded Disability Status Scale (Edss), Ms Functional composite (MSFC), and Symbol Digit Modalities Test (SDMT). We analysed associations of MRI variables with clinical scores using multivariable linear regression models adjusting for age and gender. Fig.1A-B shows the MRI analysis pipelines.

Fig. 1A-B MRI analysis pipeline A: cross-sectional area of the cervical cord at C2-C3 level. B: normalised brain volume analysis.

Results: Sixty subjects were analysed. The baseline characteristics are shown in Table 1. Multivariable linear regression analyses (Fig.2) showed that MUCCA (standardised-beta= -0.35, standard-error [SE]=0.12,

p=0.005) and NBV (standardised-beta= -0.32, SE=0.14; p=0.02) were independently associated with EDSS. MUCCA, but not NBV, was significantly associated with MSFC (standardised-beta=0.28 SE=0.13; p=0.031). Both MUCCA (standardised-beta=0.3 SE=0.12; p=0.013) and NBV (standardised-beta=0.42, SE=0.14; p=0.006) were independently associated with SDMT.

16 axial scans from a high resolution 3D-PSIR sequence (0.5x0.5x3) are acquired/centered from/in C2-C3. MUCCA is calculated using a semi-automated software (Jim7, Xinapse Systems, UK). Firstly, a marker is manually positioned in the center of the 5 slices between C2-C3 (slices 7-11). Subsequently, Jim7 automatically finds the cord area of the 5 slices, that are finally averaged to get MUCCA. PSIR= Phase Inversion Recovery. MUCCA= mean upper cervical-cord cross-sectional area.

Lesions were contoured on the PD scans based on hyperintensity in the PD/T2 and FLAIR scans using a semi-automatic method (Jim 7 Software, Xinapse Systems, UK). The lesion mask was then used to fill the lesion on the 3DT1-weighed image. Brain was then segmented automatically using the GIF algorithm the brain mask was then registered to the MNI template to obtain final normalised brain volume. PD= proton density. FLAIR: Fluid attenuated inversion recovery. GIF= geodesic information flows.

Table 1. Baseline characteristics of the patients

Variable	All subjects N= 60
Age (years) mean (SD)	53.8 (7)
Gender (female:male)	23:37
Disease duration (years) mean (SD)	23.4 (8.9)
EDSS median (range)	6 (4-6.5)
SDMT (correct answers) median (range)	49 (17-70)
MSFC mean (SD)	0.13 (0.52)
MUCCA (mm²) mean (SD)	67.4 (10.3)
NBV (ml) mean (SD)	1398.4 (89.2)

SD= standard deviation. EDSS= expanded disability status scale. SDMT= symbol digit modalities test. MSFC= multiple sclerosis functional composite. MUCCA= mean upper cervical-cord cross-sectional area. NBV= normalised brain volume.

Fig.2 Multivariable linear regression plots of the statistically significant associations. Plots are based on raw data (i.e. non-standardised data) for a better understanding of the relationships.

Conclusion: MUCCA was the strongest predictor of EDSS, NBV the strongest predictor of SDMT, and MUCCA the only predictor of MSFC. Our findings demonstrate that spinal cord area shows increasing promise as a marker of disability in progressive disease.

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O114

Long-term prognosis of disease evolution and evidence for sustained Fingolimod treatment effect by plasma neurofilament light in RRMS patients

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Background and aims: Neurofilament light chain (NfL), an intracellular protein exclusively expressed by neurons, is elevated in the cerebrospinal fluid and blood of patients with multiple sclerosis (MS). We studied the mid- and long-term prognostic potential of plasma NfL for disease evolution and progression and long-term fingolimod effect on plasma NfL levels in patients with relapsing–remitting MS (RRMS).

Methods: Plasma NfL was measured at baseline (N=542), Month (M) 6 (N=467), M12 (N=471), M24 (N=225), and M120 (N=79) using Single Molecule Array (SIMOA) technology in participants from two Phase 3 studies (pooled FREEDOMS, TRANSFORMS) who continued fingolimod treatment in an extension study until M120. The relationship between NfL levels in the initial 12 months (NfL-area under the curve [AUC] classified as low, <30pg/mL; medium, 30–60pg/mL; and high, >60pg/mL) and MS outcomes was assessed using regression models adjusted for age, log[baseline NfL] and baseline characteristics.

Results: At M48, assignment to the high NfL-AUC category compared with low NfL-AUC predicted time to (TT) first relapse, mean cumulative number of new T2 lesions, annual rate of brain atrophy, TT EDSS>=4, TT SPMS and 6M-confirmed disease worsening. NfL levels in patients taking fingolimod were reduced and remained low relative to baseline (from 29.9 to 21.6pg/mL at M24 and from 30.6 to 18.4pg/mL at M120; p<0.0001, both).

Conclusion: Our data support the value of plasma NfL as a mid- to long-term prognostic biomarker of disease evolution and progression in RRMS. The reduction of NfL levels achieved by fingolimod treatment was sustained over 10 years.

Disclosure: This study was funded by Novartis Pharma AG, Basel, Switzerland. Detailed disclosure of each author will be included in the poster/oral presentation.

O115

Alemtuzumab provides durable clinical efficacy in patients with active rrms in the absence of continuous treatment: 7-Year follow-up of CARE-MS I (TOPAZ Study)

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Background and aims: In CARE-MS I (NCT00530348), alemtuzumab 12 mg/day (baseline: 5 days; 12 months later: 3 days) significantly improved clinical/MRI outcomes versus SC IFNB-1a over 2 years in treatment-naive RRMS patients. Durable efficacy was observed in a 4-years extension (NCT00930553; 95% of CARE-MS I patients enrolled, 92% completed Y6), in which patients could receive alemtuzumab retreatment as-needed for relapse/MRI activity or receive other DMTs per investigator's discretion. Further evaluation is ongoing (TOPAZ extension; NCT02255656). We present efficacy/safety outcomes over 7 years (2 years core study plus 4 years extension and TOPAZ Y1) in alemtuzumab-treated patients from CARE-MS I.

Methods: Assessments: Annualised relapse rate (ARR); EDSS scores; 6-month confirmed disability worsening (CDW); 6-month confirmed disability improvement (CDI); no evidence of disease activity (NEDA); and AEs.

Results: 299 patients (93%) completed TOPAZ Y1. 59% received neither alemtuzumab retreatment nor other DMT after the initial 2 courses. ARR remained low (Y7: 0.13); 60% were relapse-free in Y3 7. The percentage with stable/improved EDSS scores versus baseline remained high at Y7 (78% [improved, 21%; stable, 57%]). The mean change in EDSS score from baseline to Y7 was 0.09. At Y7, 74% were 6-month CDW-free; 37% achieved 6-month CDI. The majority of patients achieved NEDA each year (Y7: 61%). Overall AE incidence decreased over time.

Conclusion: Alemtuzumab efficacy was maintained for 7 years in treatment-naive patients, despite 59% receiving no additional treatment since the initial 2 courses. Alemtuzumab

safety profile remained consistent. Alemtuzumab provides a unique treatment approach for RRMS patients, offering durable efficacy without continuous treatment.

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O116

Effects of Fingolimod on MRI outcomes in patients with paediatric-onset Multiple Sclerosis: results from the Phase-3 PARADIGMS study

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Background and aims: Approximately 3–5% of Multiple Sclerosis (MS) cases manifest in childhood and adolescence, characteristically with highly active inflammatory disease course. Paediatric-onset MS (POMS) has an impact on brain integrity and may increase Brain Volume Loss (BVL) above age-expected rates. This study assessed the effect of oral Fingolimod up to 0.5mg daily versus intramuscular interferon (IFN) beta-1a 30µg once weekly on MRI outcomes in POMS patients.

Methods: In this double-blind, double-dummy, active-controlled, multicentre study, patients with POMS (aged 10–<18 years) received either Fingolimod (dose adjusted for body weight; N=107) or IFN beta-1a (N=107) for up to 2 years. MRI was performed at baseline and every 6 months until the End Of The Study (EOS) core phase. Key MRI outcomes were the number of new/newly enlarging T2 (n/neT2) lesions and Gd-enhancing T1 (Gd+T1) lesions, Annual Rate Of Brain Volume Change (ARBVC), annualised rate of number of new T1 hypointense lesions, change in total T2 Hyperintense Lesion Volume (T2LV) and the number of Combined Unique Active Lesions (CUAL).

Results: At the EOS, compared with IFN beta-1a, fingolimod significantly reduced the annualised rate of n/neT2 lesions (52.6%; p<0.001), number of Gd+T1 lesions per scan (66.0%; p<0.001), ARBVC (−0.48% vs. −0.80%, p=0.014), annualised rate of number of new T1 hypointense lesions (62.8%; p<0.001), T2LV (percent change from baseline: 18.4% vs. 32.4%, p<0.001) and CUAL per scan (60.7%; p<0.001).

Conclusion: Fingolimod significantly reduced MRI activity and slowed BVL for up to 2 years vs. IFN beta-1a in paediatric-onset MS.

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O117

Characterizing the Slowly Evolving Lesions (SELs) in a cohort of secondary progressive Multiple Sclerosis patients

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Background and aims: There is a need to develop markers of progression in Multiple Sclerosis (MS). Slowly Evolving Lesions (SELs) on MRI have been recently identified in longitudinal trials of Primary Progressive MS (PP-MS) using non-linear registration-based analysis techniques [1]. Magnetization Transfer Ratio (MTR) highly correlates with demyelination and axonal loss within MS lesions [2].

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[2] K. Schmierer, F. Scaravilli, D. R. Altmann, G. J. Barker, and D. H. Miller, "Magnetization transfer ratio and myelin in postmortem multiple sclerosis brain," *Ann. Neurol.*, vol. 56, no. 3, pp. 407–415, Sep. 2004.

Methods: We included 79 secondary progressive (SP-MS) patients from the MS-SMART trial (NCT01912059) who underwent brain PD/T2, FLAIR and MTR scans at baseline, 24 and 96 weeks. Manually delineated lesions showing Jacobian expansion were selected as "candidates". Final SELs were chosen through a sum score of their concentricity and constancy (figure 1). We calculated baseline MTR values within the different lesion types (SEL, non-SEL and non-candidates) and compared MTR changes from baseline to 96-week.

Figure 1. Two-steps selection of SELs
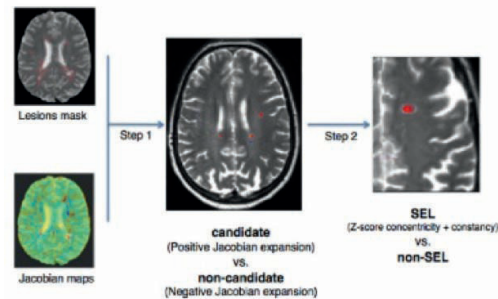
Results: From 4756 lesions screened, 1140 candidates were identified and ultimately 140 SELs (2.9%) were detected. Baseline MTR within SEL was lower compared to the non-SELs and non-candidates (24.51, 26.26 and 28.89, respectively; p-values<0.001). MTR decrease between baseline and week 96 within SELs was significantly greater compared to non-SELs (p=0.02) and to non-candidates (p=0.01) (Figure 2). In contrast, there were no significant differences in MTR change between non-SEL and non-candidates (p=0.50).

Figure 2. MTR change baseline – week 96
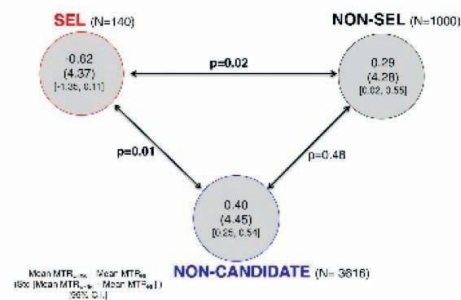
Conclusion: We confirm that, as in PP-MS, there are lesions in SP-MS that can be classified as SELs. Given their more destructive signature on MTR, SELs are promising biomarkers of chronic plaque evolution in progressive MS. Future studies will investigate whether there is a relationship between the occurrence of SELs and clinical disability.

O118
Characterizing dynamic functional network connectivity in the main clinical phenotypes of Multiple Sclerosis

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Background and aims: Resting-state (RS) dynamic Functional Network Connectivity (dFNC) in Multiple Sclerosis (MS) has rarely been studied. Here, we investigated dFNC changes occurring in MS patients according to their clinical phenotype.

Methods: RS fMRI data were acquired from 126 MS patients and 40 healthy controls (HC). There were 52 relapsing remitting (RR) MS, 16 benign (B) MS, 34 secondary progressive (SP) MS and 24 primary progressive (PP) MS patients. Between-group dFNC differences in 42 relevant networks were assessed: 1) in MS patients vs HC, and 2) among different clinical MS phenotypes.

Results: Clustering analysis revealed 3 dFNC states in HC and MS patients: State 1 (frequency=57%, low dFNC strength), State 2 (frequency=19%, middle-high dFNC strength), and State 3 (frequency=24%, low FNC strength except for high dFNC strength in the sensorimotor and visual networks). Compared to HC, MS patients showed an overall reduction of dFNC in the main sensorimotor, cognitive and subcortical networks, while increased dFNC was found for the frontal-attention network. The same pattern of dFNC changes was detected when comparing RRMS and PPMS patients vs HC. Compared to RRMS, SPMS showed strong dFNC reductions in most functional networks, mainly in States 2 and 3, and a markedly increased dFNC for the frontal-attention network in States 1 and 2. Conversely, frontal-attention dFNC was significantly decreased in BMS vs RRMS patients.

Conclusion: Significant dFNC changes contribute to explain MS phenotypic heterogeneity. While the prevalent reduction of dFNC might reflect the progressive accumulation of structural damage, compensatory/maladaptative mechanisms may take place in frontal/attentional circuits.

Peripheral nerve disorders 1

O119

Axonal function predicts response to subcutaneous immunoglobulin in chronic inflammatory demyelinating polyneuropathy: the PATH study

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Background and aims: Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) is an immune mediated disease starting with functional impairment and demyelination; in later stages, axonal degeneration may occur.

Methods: PATH was a randomised, double-blind study investigating 0.2 (low) and 0.4 g/kg (high) weekly doses of maintenance SCIG IgPro20 (Hizentra®, CSL Behring) versus placebo (N=172). After Ig dependency testing, and IVIG restabilisation, patients were randomised to SCIG or placebo for 25 weeks or until early termination. Nerve conduction studies (NCS) were performed before study drug administration. Relapse rate (defined as a 1 point increase by adjusted Inflammatory Neuropathy Cause and Treatment score) comparisons were undertaken on patients with assumed non-axonal damage versus assumed axonal damage based on cut-off amplitudes at the distal stimulation site: 1 mV for the foot and 2 mV for the wrist.

Results: Patients with assumed non-axonal damage who received placebo had a 73% relapse rate versus 39% on low-dose and 19% on high-dose SCIG. Patients with assumed axonal damage had relapse rates of 25%, 30% and 19% for placebo, low-dose and high-dose SCIG, respectively.

Conclusion: CIDP patients with assumed non-axonal damage had a high relapse rate when switched from IVIG to placebo that was significantly reduced in patients switched to SCIG therapy. Relapse rates were lower in assumed axonal damage patients and were not influenced by SCIG. These findings could help in redesigning future trials including maintenance regimens based on NCS categorisation of patients.

Disclosure: This study was sponsored by CSL Behring.

O120

Corneal confocal microscopy and skin biopsy in the evaluation of diabetic small fiber neuropathy

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Background and aims: Corneal Confocal Microscopy (CCM) is a comparatively new diagnostic method that enables morphological evaluation of small sensory nerve fibers in the cornea. Currently, Intraepidermal Nerve Fiber Density (IENFD) is considered a gold standard for the diagnosis of Small Fiber Neuropathy (SFN). The aim was to compare sensitivity of CCM and IENFD in the detection of SFN in patients with Diabetic distal symmetrical Polyneuropathy (DPN).

Methods: A group of 81 patients with the diagnosis of definite DPN (mean age 58.2; 50 men, 31 women; 27 patients had painful DPN - pDPN) based on clinical signs and symptoms and nerve conduction studies, and a group of 32 healthy controls (HC) of similar age and gender were assessed using skin biopsy and CCM with evaluation of Corneal Nerve Fiber Density (CNFD), Length (CNFL), Branch Density (CFBD) and Tortuosity (CNFT).

Results: All CCM parameters showed significantly higher proportion of abnormal values not only in DPN group compared to HC (p<0.001), but the proportion of abnormalities of all CCM parameters (except CNFT) was significantly higher in pDPN subgroup compared to non-painful cases (p<0.05). CCM sensitivity in detection of SFN in DPN group was similar (72%) to that of IENFD (74%). Individual values of CCM parameters, however, showed insignificant correlation with IENFD values (p<0.05).

Conclusion: CCM is able to prove significant involvement of small sensory nerve fibers in patients with symptomatic DPN with comparable sensitivity as IENFD obtained via semi-invasive skin biopsy procedure. Higher proportion of CCM abnormalities in pDPN possibly reflects higher severity of neuropathy in painful cases.

Disclosure: Nothing to disclose

O121

Charcot-Marie-Tooth disease type 4B with myelin outfoldings (CMT4B): a multicentre retrospective study

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Background and aims: Charcot-Marie-Tooth neuropathy B1 and B2 (CMT4B1/B2) are characterized by recessive inheritance, early onset, severe course, slowed nerve conduction, myelin outfoldings, loss-of-function mutations in Myotubularin-related protein-2 and -13 (MTMR2, MTMR13/SBF2), respectively, involved in phosphoinositides metabolism. We conducted a multicentre retrospective study to better characterise CMT4B in view of possible clinical trials.

Methods: In 16 centres, we collected clinical, genetic, instrumental data from CMT4B subjects.

Results: There were 44 patients (27 CMT4B1, 17 CMT4B2). CMT4B1 patients were younger and with earlier onset than CMT4B2. Onset age: 2.8+/-2.8 years (range 0-13) in CMT4B1, 7.6+/-8.7 (1-36) in CMT4B2; delayed motor milestones in 14/26 CMT4B1 and 4/17 CMT4B2 subjects. Twelve CMT4B1 but only two CMT4B2 patients became chair-bound. Both types are characterised by vocal cord involvement (10/25 CMT4B1, 9/17 CMT4B2); respiratory involvement was seen almost exclusively in CMT4B1 patients (n=8, four NIV, one tracheostomy; one CMT4B2 patient on NIV). Glaucoma (n=6) and buphthalmos (n=3) occurred only in CMT4B2.

CMTNS and CMTES-motor scores were significantly higher in CMT4B1 patients in spite of their younger age, indicating more severe disease: CMT4B1=CMTES mean 17.9+/-5.9 (n=20; range 9-28/28), CMTNS mean 30.1+/-4.7 (n=10; 19-36/36), CMTES-motor mean 13.2+/-2.9 (n=21; 8-16/16); CMT4B2=CMTES mean 15.8+/-4.4 (n=17; 6-24/28), CMTNS mean 23+/-5 (n=16; 13-32/36); CMTES-motor mean 9.2+/-3.9 (n=17; 4-16/16).

Conclusion: CMT4B1 is more severe than CMT4B2. MTMR2, a catalytically active phosphatase, interacts with MTMR13, which is known to increase MTMR2 enzymatic activity but is catalytically inactive. CMT4B2 nerves may have a residual enzymatic activity of MTMR2 which results in less severe phenotype than CMT4B1.

Disclosure: Partly supported by LAM Therapeutics

O122

Cryoglobulinaemia-associated peripheral neuropathies: clinical characteristics and prognosis from 20 years experience of neuromuscular clinic

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Background and aims: Cryoglobulinaemia is associated with peripheral neuropathies. We assessed prognostic role of clinical and neurophysiological variables among 28 patients over 20 years.

Methods: 28 patients with cryoglobulinaemia-associated neuropathy were enrolled at University of Modena during period 1998-2017. Evaluated independent clinical variables were gender, age at onset, cryoglobulin type, HCV co-infection, type of neuropathy (axonal or demyelinating), copathologies, therapies. Degree of neurological involvement (mild, moderate, severe) was assessed using disability scales (MRC, INCAT, tremor rating scale) and electrophysiological examinations. Probability of death or neurological worsening was estimated from binomial, multinomial, ordered logistic regression, Cox models. P-values <0.05 were considered significant.

Results: 20 patients were female (71%; M:F ratio 1:2.5). Median age was 66 years (range 31-83). Median follow-up time was 33 months. Eighteen patients had type II cryoglobulins (64%), 7 type III (25%), 3 type I (11%). 16 patients had HCV-RNA (57%). Sensorymotor demyelinating neuropathy was prevalent (65%). Neuropathy was mild in 46.3%, moderate in 32.1%, severe in 23% of patients. Cumulative incidence of worsening over time was 39%. None of independent variables had predictive role on neurological worsening or death, except type II cryoglobulin at multivariable ordered logistic regression (OR 12.5, 95% CI 1.24-126, p 0.03). HCV co-infection showed borderline significance (OR 3.93, 95% CI 0.86-17.8, p 0.07). Kaplan-Meyer estimate of worsening in respect of stratified age at onset showed more severe course in subjects above 70 years.
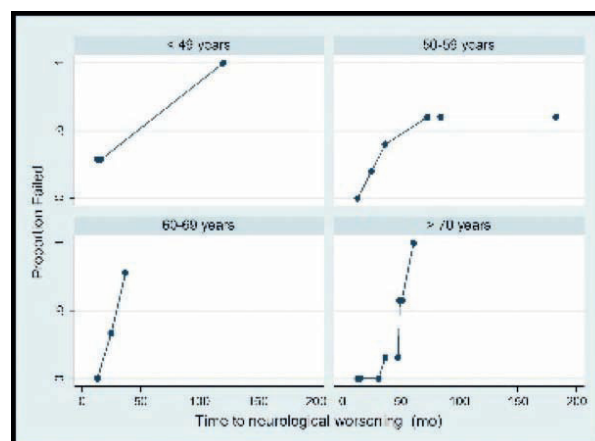
Graph 1

Conclusion: Type II cryoglobulins was associated with more severe peripheral neuropathy especially in aged subjects.

Disclosure: Nothing to disclose

O123

Long-term efficacy and safety of Inotersen in patients with hereditary transthyretin (hATTR) amyloidosis treated in the open-label extension of the phase-3 study NEURO-TTR

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Background and aims: hATTR is a rare, progressive, fatal disease manifested by systemic build-up of TTR protein, resulting in organ failure. The disease causes significant morbidity and progressive decline in Quality of Life (QOL) and robs patients of their independence owing to limitations on activities of daily living. We report results of the Open-Label Extension (OLE) study of NEURO-TTR, highlighting the long-term efficacy and safety of inotersen, an antisense oligonucleotide inhibitor of TTR protein production, in patients with hATTR.

Methods: Patients with hATTR who completed the double-blind, placebo-controlled, phase 3 study NEURO-TTR (NCT01737398) were eligible to receive Inotersen (300-mg weekly subcutaneous doses) for up to 5 years in this OLE. The OLE monitored adverse events and change from baseline in the Norfolk Quality of Life—Diabetic Neuropathy (Norfolk QOL-DN) total score (136 points total, higher scores indicate worse QOL) and modified neuropathy impairment score +7 (mNIS+7) (346 points total, higher scores indicate worse neuropathy).

Results: At the time of the interim analysis, 114 patients had enrolled in the OLE. Most patients were white (95%) and male (70%), and, at OLE baseline, mean age was 61.4 years and 69% of patients had cardiomyopathy. Mean disease duration from time of symptom onset to OLE baseline was 81.8 months. Mean OLE baseline mNIS+7 composite scores and Norfolk QOL-DN total scores were 92.0 and 55.2, respectively. One-year OLE follow-up results will be presented.

Conclusion: Results of the OLE showed continued benefit, as measured by Norfolk QOL-DN and mNIS+7. No new safety concerns were identified.

Disclosure: This study was sponsored by Ionis Pharmaceuticals (Carlsbad, CA, USA).

Neurogenetics

O124

Estimated lifetime prevalences of autosomal mitochondrial disorders based on allele frequencies of pathogenic variants in exome databases

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Background and aims: Currently, only limited epidemiological data about mitochondrial diseases are reported, and a large proportion of them may be seriously underestimated. We expected to provide an accurate description approximating the actual prevalence of autosomal mitochondrial diseases.

Methods: We estimated the lifetime prevalence of autosomal mitochondrial diseases based on the allele frequency of pathogenic and likely pathogenic variants using the Hardy-Weinberg equilibrium. 22 autosomal recessive mitochondrial disorders were assessed (Table). Publicly available exome databases (gnomAD) and our in-house database as of August 2017 were queried to collect a list of variants of all candidate genes. Phenylketonuria (PKU) served as a proof of concept to verify the validity of our method.

Results: The estimated lifetime prevalence of PKU was 15.4 (12.1-19.3)/100,000, thus being very similar to the numbers known from the German newborn screening (18.7 (21.6-16.9)/100,000). The total estimated lifetime prevalence of the 22 investigated autosomal mitochondrial disorders was 14.0 (9.6-20.3)/100,000 in our in-house database, 16.8 (14.6-19.5)/100,000 in European (Non-Finnish) population and 10.0 (8.8-11.4)/100,000 in worldwide population according to the gnomAD dataset. The individual estimated lifetime prevalences of the 22 investigated disorders can be provided upon request.

Conclusion: In view of the marked difficulties in performing traditional epidemiological studies in rare disorders, the estimation of lifetime prevalences by using allele frequencies of pathogenic variants in exome databases seems to be a useful approach.

Disclosure: Nothing to disclose

O125

UFM1 founder mutation in the Roma population causes severe variant of Hypomyelination with Atrophy of the Basal ganglia and Cerebellum (H-ABC)

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Background and aims: Hypomyelination with Atrophy of the Basal ganglia and Cerebellum (H-ABC) is a rare leukodystrophy caused by dominant mutations in TUBB4A. A few cases are negative for TUBB4A mutations. We aimed at identifying a second gene defect in H-ABC.

Methods: We performed homozygosity mapping and Whole Exome Sequencing (WES) to detect the disease-causing variant. We used a Taqman assay for population screening. We developed a luciferase reporter construct to investigate the effect of the promoter mutation on expression.

Results: 16 patients fulfilling the MRI criteria for H-ABC presented distinctive caudate nucleus abnormalities (figure 1) and exhibited severe encephalopathy. The majority had a Roma ethnic background. Single nucleotide polymorphism array analysis in 5 patients identified one large overlapping homozygous region on chromosome 13. WES in 2 patients revealed a homozygous deletion in the promoter region of UFM1. Sanger sequencing confirmed homozygosity for this variant in all patients. All patients shared a common haplotype, indicative of a founder effect. Screening of 1000 controls from different European Roma panels demonstrated an overall carrier rate of the mutation of 4.5% (range 3% up to 25% in a small isolate). Transfection assays showed that the deletion reduced expression in specific central nervous system cell lines.

Figure 1 | MRI features in autosomal recessive H-ABC. T2-weighted image showing an abnormal, hyperintense white matter signal, consistent with hypomyelination.

The putamen is absent (red arrowhead) and the caudate nucleus is small; the lateral part of the head of caudate nucleus has an abnormally high signal (yellow arrow).
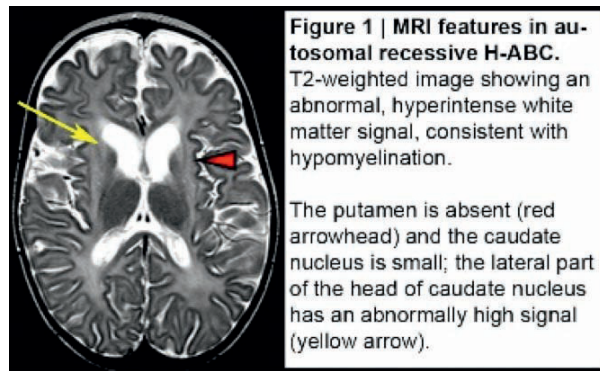
Conclusion: UFM1 encodes ubiquitin-fold modifier 1 (UFM1), a member of the ubiquitin-like family involved in posttranslational modification of proteins. Its exact biological role is unclear. This study is the first to associate a UFM1 gene defect with a disease phenotype and sheds new light on possible UFM1 functional networks.

Disclosure: Nothing to disclose

O126

Phenotypic and neuroimaging expression of NKX6-2 mutations lead to a new distinct disease with spastic ataxia and hypomyelination

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[1]UCL Institute of Neurology, London, United Kingdom, [2]KFSHRC, Riyadh, Saudi Arabia, [3]Institute of Human Genetics, Hamburg, Germany, [4]University of Medicine and Pharmacy "Victor Babes", Timisoara, Romania

Background and aims: Despite advances in genetic testing a large number of hyopomyelinating disorders remain a genetic mystery. We identified a new distinct phenotype of spastic-ataxia with hyopomyelination negative for previously known hyopomyelinating genes.

Methods: We used a combination of homozygozity mapping, exome sequencing, immunobloting, clinical and neuroimaging for novel gene discovery. Using gene expression and network analysis with Weighed Genes Co-expression we placed the new gene within a regulatory pathway.

Results: We mapped this phenotype to deleterious bi-allellic mutations in NKX6-2 in 14 cases of different ethnic backgrounds providing evidence for a high NKX6-2 mutation burden in hypomyelinating leukodystrophy disease spectrum. We show that the phenotypic and neuroimaging expression in NKX6-2 is mutation-specific and that phenotypes with epilepsy in the absence of overt hypomyelination, as well as diffuse hypomyelination without seizures can occur. Our data suggests that the phenotypic consequences of NKX6-2 mutations is classified in three main subgroups: severe global psychomotor delay with widespread hypomyelination, spastic-ataxia with hypomyelination and spastic-ataxia with seizures.In-silico analysis of human brain expression and network data shows that NKX6-2 is involved in oligodendrocyte maturation and may act within the same pathways of genes already associated with central hypomyelination.

Conclusion: Combining genetic, phenotypic and functional data this study contributes with the discovery of novel NKX6-2 pathogenic mutations and provides new insights into NKX6-2 related disease. Therefore, our case series suggests that NKX6-2 mutations should be considered in patients with autosomal recessive, very early onset of nystagmus, cerebellar ataxia with spasticity particularly when associated with typical neuroimaging signs of hypomyelination.

Disclosure: Nothing to disclose

O127

The natural history of mitochondrial stroke-like episodes: observational cohort study from the UK

Y.S. Ng[1], A. Schaefer[1], R. Pitceathly[2], V. Nesbitt[3], J. Hall[4], M. Farrugia[5], M. Roberts[6], J. Poulton[7], M. Hanna[8], R.W. Taylor[1], D. Turnbull[1], R. McFarland[1], G. Gorman[1]

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Background and aims: Stroke-Like Episodes (SLE) are one of the most devastating neurological features identified in mitochondrial disease. However, the natural history of SLE due to different genotypes is not well characterised.

Methods: An observational, national cohort study over an 18-year period (2000-2017).

Results: 108 patients presenting with SLE were identified. The most common genetic defect was the m.3243A>G mutation (66%), followed by recessive POLG mutations (20%) and other mtDNA point mutations (14%). The mean age of occurrence of the first SLE was significantly higher in mtDNA group compared to POLG group (35 vs 19 years, p<0.001). Patients with POLG mutations were more likely to present with an explosive onset SLE without preceding clinical symptoms compared to mtDNA mutations (47% vs 9%, p<0.001). Common neurological features associated with SLE were headache, focal seizures (motor and/or occipital), visual field loss and dysphasia. MRI signal abnormalities involving the parietal and occipital lobes were common, irrespective of the genotype. Stroke-like lesions involving the prefrontal cortex and thalamic lesions were more common in POLG than mtDNA mutations (frontal: 32% vs. 13%; thalamic: 53% vs. 10%, p<0.05). Higher mortality was observed in POLG group compared to the mtDNA group (62% vs. 38%, p=0.049) during the follow-up; the mean age of death was significantly different between two groups (28 vs 46 years, p=0.001) (Figure 1).

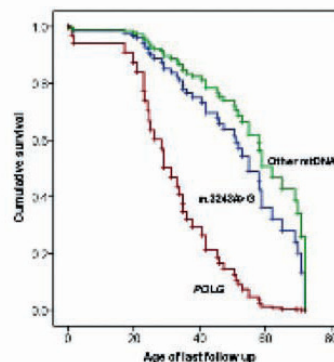Figure 1. Comparison of survival in different genotypes. Log rank, p<0.001

Conclusion: These findings highlight that focal seizures are intrinsic to the development of SLE and the outcomes are dependent on the underlying genetic defect.

O128

Next Generation Sequencing results in an Italian cohort of hereditary optic neuropathy patients

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Background and aims: Hereditary Optic Neuropathies (HON) have a common pathophysiologic mechanism involving in most cases mitochondrial dysfunction. In more than 50% of cases the causative genes are unknown. Next Generation Sequencing (NGS) allows screening simultaneously several candidate genes. We aimed at genetically screening consecutive HON patients negative for LHON and OPA1 mutations.

Methods: Using the Illumina sequencing platform, we designed a custom panel of 35 targeted nuclear genes already described or suspected to be causative for HON, syndromic or non-syndromic. So far, we investigated 129 unrelated HON probands.

Results: Mutations in HON related genes were identified in 47/129 cases (36%), even if in 24 cases these variants must be further validated (segregation analysis, in vitro studies). Among the 23 consolidated positive results, we found mutations in ACO2 (n=5), AFG3L2 (n=5), WFS1 (n=4), OPA1 (n=4), SPG7 (n=2), RTN4IP1 (n=1), SDHA (n=1) and TMEM126A (n=1) genes. The most frequent mutated genes in our cohort (including also the cases under validation) were WFS1, ACO2 and AFG3L2. Interestingly, AFG3L2 gene mutations, previously described only in two non-syndromic HON families, were found in additional five families. Also its paralogous gene, SPG7, has been found mutated in two additional recessive cases with isolated ON. Finally, ACO2 turns out as a frequent gene associated with not-syndromic HON.

Conclusion: In conclusion, NGS-based diagnostics improves the rate of successful identification of unsolved HON cases, enlarging their genetic landscape. Furthermore, this approach allowed expanding the clinical spectrum of genes involved in mitochondrial functions previously associated with multisystemic disorders.

Disclosure: Nothing to disclose

O129

A randomized trial of Deferiprone for Pantothenate Kinase-Associated Neurodegeneration (PKAN)

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Background and aims: Pantothenate Kinase-Associated Neurodegeneration (PKAN) is the most common form of Neurodegeneration with Brain Iron Accumulation (NBIA), a heterogeneous group of rare hereditary neurodegenerative disorders. Treatment with an appropriate iron chelator holds promise to decrease brain iron levels in NBIA, which may slow or stop disease progression.

Methods: Randomized, double-blind, placebo-controlled trial designed to evaluate efficacy and safety of deferiprone (DFP) in PKAN. Patients were randomly assigned in a 2:1 ratio to receive DFP or placebo for 18 months.

Results: Of 100 screened subjects, 89 were enrolled, with 59 randomized to DFP and 30 to placebo. After 18 months, there was a marked decrease of iron in the globus pallidus (as measured by quantitative MRI R2* mapping) in the DFP group (R2* change -36.1 Hz) but virtually no change in the placebo group (R2* change -0.5 Hz, p<0.0001). The primary endpoint was a change in the total Barry-Albright dystonia scale. Patients in both treatment groups worsened over time but the progression in the DFP group was slower (-2.48 points) than that in the placebo group (-3.99 points). The overall difference between the two groups approached statistical significance (p=0.0761) and was significant in favor of Deferiprone for patients with atypical PKAN. DFP was associated with an excellent safety profile.

Conclusion: DFP led to marked reduction of iron accumulation in the brain and showed a trend towards slowing of clinical progression in this devastating disease. Upcoming data from an open extension trial will provide additional data on 36 months of DFP treatment.

Disclosure: This study was funded by the European Commission 7th Framework Programme (FP7/2007-2013, HEALTH-F2-2011, grant agreement No. 277984, TIRCON). Study drug and Placebo as well as additional funding was provided by the drug manufacturer, ApoPharma Inc., Toronto, Canada.

Neuroimmunology

O130

Neurofilament Light chain (NfL) serum concentration reflects disease severity in patients with MOG-Ab associated disorders

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Background and aims: Neurofilament Light chain (NfL) is a marker of axonal injury, increased in Serum/Cerebrospinal Fluid (CSF) of patients with several neurological disorders, including inflammatory conditions associated with Myelin Oligodendrocyte Glycoprotein Antibodies (MOG-Ab). Analysis of NfL levels according to clinical status has never been reported in this condition.

Methods: We collected clinical, MRI, and laboratory data of consecutive patients positive for serum MOG-Ab, tested with a live-cell immunofluorescence assay at the Neuropathology Laboratory, University of Verona, between March 2014 and December 2017. Serum and, when available, CSF and follow-up samples were analysed for NfL concentration using a high sensitive technology (Simoa, Quanterix). A group of aquaporin-4 antibodies (AQP4-Ab) positive cases and Healthy Controls (HC) were also included.

Results: 48 patients were enrolled (25 MOG-Ab positive, 11 AQP4-Ab positive and 12 HC) with comparable age at first sampling. Serum NfL concentration was higher in MOG-Ab positive subjects (median 11.4 pg/ml, range 2.5-97) than in HC (median 6.62, range 3.76-11.54) and, to a lesser extent, AQP4-Ab positive cases (median 8.8, range 2-80.3). NfL levels were higher in MOG-Ab positive patients with a severe attack at sampling (severe motor impairment/severe encephalopathy/severe visual impairment with visual acuity <2; median 17.15, range 4-97) compared with cases with a mild-to-moderate event (median 10.9, range 2.5-21.4) and tended to decrease during the follow-up. Further analyses according to other clinical features and MRI status are ongoing.

Conclusion: Our data confirm the presence of axonal damage in MOG-ab associated disorders and support the role of NfL as possible biomarker in these diseases.

Disclosure: Nothing to disclose

O131

Mimics of Autoimmune Encephalitis

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Background and aims: The identification of multiple antibodies has evoked a growing interest in Autoimmune Encephalitis (AIE), especially as these are treatable. The recently published criteria for AIE include a novel diagnosis of "presumed seronegative AIE", a diagnosis by exclusion and based on strict criteria. The aim of our study was to evaluate these criteria, determine the occurrence for AIE mimics and how to differentiate these from AIE.

Methods: In this retrospective cohort study, we included children and adults referred for AIE to our academic center for neuro-inflammation, the Dutch national reference center (July 2016-December 2017). Ancillary testing included lumbar puncture, MRI, and cerebral biopsy when considered necessary. All patients underwent extensive antibody testing in serum or CSF. Patients were classified according to the 2016 Graus criteria.

Results: 93 patients were referred, 62% female. The median age was 50 years (range 1-79). Antibodies were identified in 45 patients, while 15 patients fulfilled criteria for specific neuroinflammatory disorders (like CLIPPERS). Seronegative AIE was diagnosed in 10 patients, while the other 23 had AIE mimics. Most frequently AIE mimics were CNS malignancies, primary psychiatric disorders and functional disorders (all n=4). Confounding factors were non-specific antibodies (like VGKC or TPO), false positive cell-based assays, and (temporary) steroid responsiveness.

Conclusion: AIE mimics are found within the group of seronegative AIE and AIE associated with non-specific antibodies. AIE is a diagnosis not to miss, but physicians should avoid making this diagnosis lightly, as treatment and prognosis differ.

O132
Evaluation of treatment response in adults with relapsing MOG-Ab associated

A. Cobo-Calvo[1], M. Sepulveda[2], T. Armangué[3], A. Ruiz[4], E. Maillart[5], B. Audoin[6], H. Zephir[7], D. Biotti[8], J. Ciron[8], F. Durand Dubief[1], N. Collongues[9], X. Ayrignac[10], E. Thouvenot[11], A. Montcuquet[12], F. Rollot[13], N. Solà Valls[14], S. Llufriu[14], Y. Blanco[14], S. Vukusic[1], A. Saiz[14], R. Marignier[1]

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Background and aims: Myelin Oligodendrocyte Glycoprotein Antibodies (MOG-Ab) in adult patients are related to relapsing acquired demyelinating syndromes. However, the treatment response in this population is currently unknown. We aimed to describe the clinical characteristics at first attack, and response to different therapies strategies in adult patients with relapsing MOG-Ab-associated diseases

Methods: Retrospective study from France and Spain including 125 relapsing (≥2 episodes) patients aged ≥18. First, we performed survival analysis to investigate time to relapse between treated with immunosuppressants (Azathioprine, Mycophenolate Mophetil, [MMF], rituximab, cyclophosphamide or corticoids/immunoglobulins), Multiple Sclerosis (MS)-disease Modifying Drugs (DMD) and non-treated patients, adjusting by a Propensity Score method. Second, we Assessed Annualized Relapse Rates (ARR) and disability pretreatment and on-treatment, in those patients with at least 6 months of follow-up

Results: Median age at onset was 34.1 years (range 18.0-67.1), the female:male ratio 1.2:1 and 96% were caucasian. After a median follow-up of 53.7 months (range 2.0-564.5), 82 (65%) patients had received immunosuppresants, and 10 (8%) MS-DMD. Patients starting immunosuppressants were at lower risk to experience a further relapse in comparison to non-treated (HR 0.51, 95%CI, 0.29-0.95; p<0.025). No differences were observed between MS-DMD and non-treated patients. ARR mean (standard deviation) was reduced from 1.05 (1.20) to 0.42(0.79) with Azathioprine (n=11, p=0.040), from 1.19(1.11) to 0.23(0.60) with MMF (n=11, p=0.032), and from 1.08(0.98) to 0.42(0.88) with rituximab (n=26, p= 0.010). No differences were observed with MS-DMD.

Conclusion: In adults with relapsing MOG-Ab-associated diseases, immunosuppressant therapy (Azathioprine, MMF and Rituximab) but no MS-DMD is associated with reduced risk of further relapse.

Disclosure: Nothing to disclose

O133
Syndrome and outcome of antibody-negative limbic encephalitis

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Background and aims: To report the clinical characteristics of 12 patients with limbic encephalitis (LE) who were antibody-negative after a comprehensive immunological study.

Methods: Review of clinical records of 163 patients with LE. Immunohistochemistry on rat brain, cultured neurons, and cell-based assays were used to identify neuronal autoantibodies. Patients were included if 1) there was adequate clinical, CSF, and MRI information to classify the syndrome as LE, 2) MRI images were accesible for central review, and 3) serum and CSF were available and confirmed negative for neuronal antibodies.

Results: 12 (7%)/163 LE patients (median age: 62 years; range: 40-79; 9 [75%] male) without neuronal autoantibodies were identified. The most frequent initial complain's were deficits in short-term memory leading to hospital admission in a few weeks (median time: 2 weeks; range: 0.5-12). In four patients the short-term memory dysfunction remained as isolated symptom during the entire course of the disease. Seizures, drowsiness, and psychiatric problems were unusual. Four patients had solid tumors (1 lung, 1 esophagus, 2 metastatic cervical adenopathies of unknown primary tumor) and 1 chronic lymphocytic leukemia. CSF showed pleocytosis in 7 (58%) with a median of 13 white blood cells /mm3 (range: 9-25). Immunotherapy included corticosteroids, intravenous immunoglobulins, and combinations of both drugs or with rituximab. Clinical improvement occurred in 6 (58%) of 12 assessable patients.

Conclusion: Antibody-negative LE is more frequent in older males and usually develops with predominant or isolated short-term memory loss. Despite the absence of antibodies, patients may have an underlying cancer and respond to immunotherapy.

Disclosure: Nothing to disclose

O134

Aquaporin-4 autoantibodies from Neuromyelitis Optica Spectrum Disorder patients cause complement-independent spinal cord pathologies and motor deficits in mice

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Background and aims: Neuromyelitis Optica Spectrum Disorders (NMOSD) are CNS inflammatory disorders. Autoantibodies against aquaporin-4 (AQP4-IgG) are pathogenic in NMOSD. Neuroinflammation is initiated upon binding of AQP4-IgG to astrocytic AQP4. The role of complement-independent pathophysiologies is uncertain. We aim to study the complement-independent pathological effects of AQP4-IgG in mice.

Methods: Mice were pretreated with complete Freund's adjuvant and pertussis toxin to disrupt blood-brain barrier, then received daily intraperitoneal injection of IgG purified from AQP4-IgG-seropositive NMOSD patients (IgG(AQP4+)) or healthy individuals (IgG(Healthy)) for 8 days. Motor function was tested by walking across narrow beams. Cervical cord was collected for immunofluorescent analysis.

Results: Human IgG infiltrated into spinal cord parenchyma. There was no deposition of complement activation product (C5b9). Mice received IgG(AQPd+) showed astrocytic injuries/loss compared to mice received IgG(Healthy) indicated by significant loss of AQP4 and glial fibrillary acidic protein immunoreactivities. These mice displayed decrease in the glutamate transporter, excitatory amino acid transporter 2, on immunostaining. There were extensive microglial/macrophage activation on ionized calcium-binding adapter molecule 1 (Iba1) and cluster of CD68 immunostaining, respectively. Spinal cord of mice received IgG(AQP4+) had patchy demyelination and axonal injuries/loss on myelin basic protein and neurofilament immunostaining. Mice received IgG(AQP4+) required longer time with more paw slips to walk across narrow beams compared to mice received IgG(Healthy). Treatment with NMDA receptor antagonist, MK-801, significantly improved motor function of IgG(AQP4+) mice.

Conclusion: AQP4-IgG mediated complement-independent pathologies including AQP4 and astrocytic loss, neuroinflammation, demyelination and axonal injuries/loss may involve glutamate excitotoxicity and microglia/macrophage activation; these pathologies may be improved by NMDA receptor antagonist.

Disclosure: Nothing to disclose

O135

Thrombotic and non-thrombotic neurological manifestations in Primary Antiphospholipid Syndrome

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Background and aims: Central nervous system involvement in primary Antiphospholipid Syndrome (pAPS) can be thrombotic (t-pAPS - stroke, TIA, Sneddon syndrome, and cerebral venous thrombosis) or non-thrombotic (nt-pAPS - epilepsy, headaches, movement disorders, myelitis, neuropsychiatric deficits).

Methods: Retrospective review of clinical records in a series of 73 pAPS patients from Neurology and Immunology outpatient clinic of Centro Hospitalar do Porto – Portugal.

Results: 53 patients (72.6%) had history of neurological manifestations; 37 of them were women (69.8%) and had a mean age at pAPS diagnosis of 46years±14 and at neurological manifestation onset of 43years±14. The most frequent neurological manifestation was ischemic stroke (41.5%) and the least was chorea (3.8%). The neurological group was divided into t-pAPS (67.9%) and nt-APS (32.1%) subgroups. These subgroups were similar regarding sex, age at onset, titles of antiphospholipid antibodies, event recurrence and outcome after disease onset. Vascular risk factors (88.9% vs. 52.9%, p=0.011) and cognitive dysfunction (41.7% vs. 11.8%, p=0.029) were more prevalent in t-pAPS, while myelitis (8.3% vs. 41.2%, p=0.008) and ocular symptoms (5.6% vs. 47.1%, p=0.001) were more prevalent in nt-pAPS. Hypocoagulation rates were not significantly different between subgroups (69.4%vs.43.8%, p=0.079), but there is a tendency to start hypocoagulation more promptly in the t-pAPS.

Conclusion: In our cohort, patients with thrombotic vs. non-thrombotic p-APS with neurological manifestations had distinct features regarding frequency of vascular risk factors, cognitive dysfunction, myelitis, and ocular symptoms. The underlying pathophysiology of nt-pAPS events is yet to be fully elucidated. Even though no standard treatments are currently available for non-thrombotic manifestations, in clinical practice hypocoagulation is frequently used.

Disclosure: Nothing to disclose

Sunday, 17 June 2018

Cerebrovascular diseases 1

O201

Short and long-term risks of stroke after orthodox-definition transient ischaemic attack versus disqualified monosymptomatic events: Oxford vascular study

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Background and aims: Urgent medical treatment after Transient Ischaemic Attack (TIA) is highly effective in preventing early recurrent stroke. Diagnosis of TIA based on the National Institute of Neurological Disorders and Stroke (NINDS) criteria, disqualifies many monosymptomatic events with sudden-onset, non-progressive focal symptoms (e.g. diplopia, dysarthria). Patients with these NINDS-excluded events are often not investigated or treated, but reliable data on prognosis are lacking. We studied stroke risk after NINDS-TIAs, NINDS-excluded events and Minor Ischaemic Stroke (MIS).

Methods: Patients seeking medical attention after transient neurological symptoms or MIS were ascertained prospectively in a population of 92,728 in Oxfordshire, UK from 2002-14. Transient events were classified at baseline as NINDS-TIA, NINDS-excluded events, or other diagnosis. Patients with NINDS-TIA and MIS were treated strictly according to secondary prevention guidelines. NINDS-excluded events had treatment according to physician judgment. 90-day and 10-year risks of stroke were determined by face-to-face follow-up.

Results: Among 3116 patients (1002 MIS, 665 NINDS-TIA, 382 NINDS-excluded events and 1057 other diagnoses), NINDS-TIAs had a similar 90-day stroke risk to MIS (8.9%,6.7-11.1 vs 7.8%,6.0-9.6). Although the NINDS-excluded events had a lower 90-day risk (4.2%, 2.4-5.2) it was still 30 times higher than the expected background risk (p=0.0002), and the stroke risk from 90-days to 10-year follow-up was similar to that in NINDS-TIA (11.7%, 7.0-16.4 vs 10.9%, 7.4-14.4; p=0.84).

Conclusion: NINDS-excluded events account for over a third of all TIAs, have high short- and long-term risks of stroke, and require urgent medical treatment. Diagnostic criteria for TIA should be broadened to include these disqualified events.

Disclosure: The Oxford Vascular Study had support from the Wellcome Trust, National Institute for Health Research, Oxford Biomedical Research Centre, Medical Research Council, Dunhill Medical Trust and Stroke Association. Maria Tuna contribution to this research benefited from a scholarship awarded by the Calouste Gulbenkian Foundation.

O202

Idarucizumab in cerebral ischemia or intracranial hemorrhage under Dabigatran therapy in Germany – a nationwide case collection

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Background and aims: Reversal of anticoagulation by NOACs is a rare but sometimes urgently needed therapeutic demand. Idarucizumab is a monoclonal antibody fragment with high affinity for Dabigatran reversing its anticoagulant effects within minutes. It is indicated for patients on Dabigatran with life-threatening or uncontrolled bleeding and those requiring emergency intervention. Case reports and smaller case collections suggest a benefit for Dabigatran-treated patients suffering ischemic stroke to regain eligibility for rt-PA thrombolysis.

Methods: To provide insights into the clinical use of Idarucizumab in patients under effective Dabigatran anticoagulation presenting with signs of ischemic stroke or intracranial hemorrhage in clinical routine, we asked all German neurological/neurosurgical departments to contribute their retrospective data collected from administration of Idarucizumab following product launch in January 2016 to December 2017.

Results: In 51 responding stroke centers 95 patients presenting with signs of stroke received Idarucizumab. 60 patients treated with Dabigatran presented with ischemic stroke. In patients receiving rt-PA thrombolysis following idarucizumab, 78% had a benefit from i.v. thrombolysis with a median NIHSS improvement of 6 points. No symptomatic bleeding complications were observed.

A total of 35 patients had intracranial bleeding as reason for admission. In 24 patients presenting with intracerebral hemorrhage, hematoma growth with clinical worsening was documented in four. Outcome was favorable with a median NIHSS improvement of 3.5 points and mRS 0-3 in 63%. Overall, mortality was low with 6%.

Conclusion: In conclusion, Idarucizumab is a beneficial therapeutic option for patients under Dabigatran treatment presenting with ischemic stroke or intracranial hemorrhage in daily German stroke center routine.

Disclosure: CC Eschenfelder is an employee of Boehringer Ingelheim.

O203

Cerebral thrombi are heterogeneous and their composition correlates with the density of the occluded vessel on CT scan

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Background and aims: Recently, mechanical thrombectomy has been shown to be able to recanalyse large occluded vessels with benefit in terms of disability and mortality. Thus, the introduction of endovascular procedures has allowed the availability of human thrombus material for histopathologic analysis, with a wide range of possible applications.

We aimed to perform a systematic histological analysis of cerebral thrombi retrieved in ischemic stroke to unravel their composition and to detect possible correlations with imaging biomarkers.

Methods: Histological analysis of 27 human thrombi retrieved by angiography in acute stroke patients has been performed. We investigated the clot composition, in terms of structural components (fibrin, platelets, red blood cells, von Willebrand Factor), by means of aspecific stainings (Hematoxilin and Eosin, Masson's Trichrome) and immunohistochemistry (fibrinogen, CD61 for platelets, vWF).

Results: We found that cerebral thrombi are macroscopically heterogeneous in terms of consistence, dimensions, color, gross appearance (Fig. 1). Even in their structural composition, all clots presented a heterogeneous pattern of red blood cells, platelets, fibrin and vWF. Fibrin was the most represented component within the retrieved thrombi (Fig. 2). Moreover, we found that the "Hyperdensity Artery Sign" of the occluded vessel on the CT scan strongly correlated with the eritrocyte composition of the thrombus (Fig. 3).

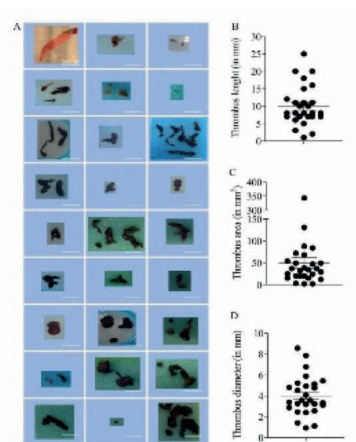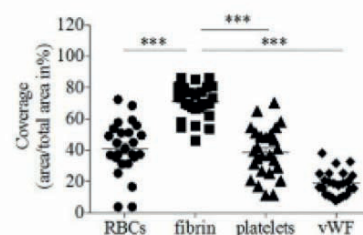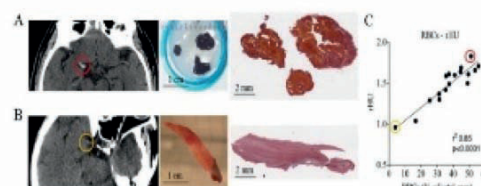Fig. 1

Fig. 2

Fig. 3

Conclusion: Arterial cerebral thrombi are widely hetereogenoeus and their composition correlate with the density of the occluded vessel on CT scan. Our pilote study supports the importance of the analysis of thrombus composition as a possible future tool for understanding the mechanisms underlying stroke and improve stroke care.

Disclosure: Nothing to disclose

O204

Effect and safety of Tenecteplase in stroke patients with atrial fibrillation

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Background and aims: The purpose of this post hoc analysis of the NOR-TEST study was to assess the effect and safety of TNK versus tPA in patients with acute ischemic stroke a AF and to assess the outcome in stroke patients with AF compared to patients with Sinus Rhythm (SR).

Methods: The Norwegian Tenecteplase Stroke Trial (NOR-TEST) was a multi-centre, prospective, randomized, open-label, blinded endpoint, phase 3 study. Patients with suspected ischemic stroke were randomized to receive either TNK at a dose of 0.4mg/kg or tPA at a dose of 0.9mg/kg. In this post-hoc analysis we assessed the effect and safety of TNK versus tPA in patients with AF.

Results: 183 patients (16.6%) in the NOR-TEST population (n=1100) were diagnosed with AF. Compared to patients with SR, the patients with AF were older and had more serious strokes. There were no major differences in outcome between the TNK and tPA group in the subgroup of patients with AF. Male sex, lower age and NIHSS was associated with better outcome. Patients with AF were older, had more serious strokes, lower functional outcome and higher mortality.

Conclusion: This is the first randomized controlled study to report the effect and safety of Tenecteplase in acute ischemic stroke in relation to AF. There were no major differences in outcome between the TNK and tPA group although female patients with AF had more serious strokes and tendency of less effect of TNK.

Disclosure: Nothing to disclose

O205

Characterisation of TRPM4-blocking antibody in ischaemic stroke

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Background and aims: Current treatment of Acute Ischaemic Stroke (AIS) is limited to achieving early reperfusion via the use of intravenous recombinant tissue plasminogen activator, which is associated with increased risk of intracranial haemorrhage beyond its therapeutic time window of 4.5 hours. Transient receptor potential melastatin 4 (TRPM4) channel has been identified as a potential target for AIS treatment. TRPM4 expression is increased in ischaemic stroke and inhibition post-ischaemia preserves cerebral vascular integrity. This study aims to delineate the role of a novel TRPM4-blocking antibody, M4P, in amelioration of neuroinflammation in AIS, and to study the expression of TRPM4 and inflammatory markers in human stroke brain.

Methods: Transient middle cerebral artery occlusion (tMCAO) rat models were generated and treated with M4P and control treatments prior to early stroke reperfusion. Behavioural analysis was performed using the rotarod apparatus. Rats were sacrificed 1-day and 7-days post-surgery. Brains were stained with 2,3,5-triphenyltetrazolium chloride (TTC) and infarct area quantified using ImageJ software. Expression of TRPM4 and inflammatory markers in rat and human stroke brains were evaluated by immunohistochemistry.

Results: TRPM4 inhibition reduced infarct area in 1 day and 7 days rat tMCAO models, with improved motor function recovery. Immunohistochemistry demonstrated decreased expression of myeloperoxidase (MPO) and OX-42, with increased CD68 expression in M4P-treated rat brains. There was increased expression of TRPM4, glial fibrillary acidic protein and MPO in human stroke brains as compared to control brains.

Conclusion: This study provides preliminary evidence supporting the therapeutic effects of M4P in AIS through reduction of neuroinflammation.

Disclosure: Nothing to disclose

O206

Mechanical thrombectomy for acute ischaemic stroke in the very old

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Background and aims: Mechanical Thrombectomy (MT) for large vessel occlusion of anterior Acute Ischaemic Stroke (AIS) improves functional outcome at 3 months. The aim of this study is to determine the effectiveness of MT for anterior circulation AIS in the very old population.

Methods: We reviewed patients with a pre-stroke mRS≤2 and anterior circulation AIS who underwent MT between November 2014 and June 2017 with a full completed register. Patients were divided into those <80-years-old (n=134) and those≥80 (n=74). Baseline characteristics, procedure data, and endpoints were compared.

Results: Hypertension and previous TIA were more frequent in the very old (p=0.05, and 0.005 respectively). There were no differences between both groups regarding admission NIHSS (16.6 vs. 16.2, p=0.65), previous intravenous thrombolysis (63.5% vs. 65.7%, p=0.76), revascularization time (267 vs. 254min, p=0,52) and haemorrhagic transformation (36.5% vs 34.3%, p=0,76). Age≥80years was associated with poor (mRS>2) 3-month functional outcome compared to younger patients (67.6% vs. 46.3%, p<0.01). 24 patients (32,4%)≥80years were functionally independent at 3 months. No difference in death was observed between the groups (p=0.08). On logistic regression, age (p<0.01) and admission NIHSS (p<0.01) were associated with a poor 3-month outcome.

Conclusion: In our series, MT for AIS in patients ≥80years with pre-stroke mRS≤2 was associated with a higher risk of a poor 3-month outcome compared to younger patients. However, one-third of the very old were functionally independent at 3 months. Further research is needed to identify factors associated with favorable outcome in this age cohort.

Disclosure: Nothing to disclose

Epilepsy

O207

Will this child have epilepsy? Development and validation of a prediction model to assess the risk of epilepsy after (a) paroxysmal event(s)

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Background and aims: Early and accurate diagnosis of paroxysmal events in children may be difficult. We aimed to develop and externally validate a model to predict the likelihood of the diagnosis of epilepsy based on data available after first consultation.

Methods: Data were retrospectively collected from a consecutive cohort of children who visited the 'first-seizure clinic', a program designed to evaluate children with paroxysmal events of (yet) unknown origin. Children were excluded if follow-up was less than one year. Diagnosis of epilepsy was made after clinical follow-up and, if considered necessary, additional investigations. Input data for model development consisted of clinical characteristics and results from electroencephalography (EEG). Backward selection of strongest predictors was applied. The final model was externally validated by Receiver Operating Curve (ROC) analysis.

Results: A total of 451 children (model development) and 187 children (model validation) were included. Included predictors were the child's sex, age at first event, event description (presence of automatisms, lateralizing symptoms, weakness/loss of muscle tone, bilateral jerking and cramping), medical history (neurological, metabolic or genetic syndrome, psychiatric) and EEG results. Model performance, as tested in the validation cohort, was excellent with an area under the curve (AUC) of 0.86 [95% CI: 0.80-0.92], a PPV of 0.93 [0.83-0.97] and a NPV of 0.76 [0.70-0.80]. Model performance in a sub-population of children with uncertain diagnosis after initial consultation was good: AUC was 0.73 [0.58-0.87].

Conclusion: This model can reliably predict eventual diagnosis of epilepsy, also in children for whom diagnosis is uncertain after first consultation.

Disclosure: Nothing to disclose

O208

Late-onset epilepsy of unknown origin and progression to dementia: two faces of beta amyloid pathology

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Background and aims: Despite recent evidence suggests that amyloid pathology plays a role in epilepsy, little is known about the relationship between beta amyloid and late-onset epilepsy. This study aimed to define beta amyloid status and progression to Alzheimer's Disease (AD) among patients with Late-Onset Epilepsy of Unknown Origin (LOEU).

Methods: We evaluated CSF AD core biomarkers and cognitive performance in 40 non-demented seizure-free patients diagnosed with LOEU versus age/sex matched controls (n=43); 3-year follow-up was performed to assess cognitive decline.

Results: Mean age was 70.0±6.4 years; mean MMSE score at baseline was 26.8. Despite baseline cognitive performance were similar to healthy controls, LOEU patients had significant CSF abnormalities. Indeed, 15/40 patients were found to have pathological Aβ1-42 (<500 pg/ml; 37.5%), 3 of them (7.5%) with an AD-like CSF pattern according to NIA-AA criteria. Patients with pathological Aβ1-42 had a 3.4 hazard ratio for progression to AD dementia at follow-up (Table 1, Figure 1 for survival analysis). Nevertheless, about half (53.8%) of the patients with pathological Aβ1-42 had stable cognitive performances after a 3-year follow-up.

	Progression to AD dementia		Progression to any dementia	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Gender (male)	0.810 (0.181-3.629)	ns	1.273 (0.340-4.764)	ns
Age (years)	1.066 (0.953-13.192)	ns	1.080 (0.981-1.189)	ns
EEG	1.222 (0.272-5.489)	ns	1.222 (0.272-5.489)	ns
Levetiracetam	1.652 (0.368-7.418)	ns	0.805 (0.200-3.238)	ns
Poly-therapy	1.054 (0.126-8.788)	ns	0.903 (0.111-7.362)	ns
Aβ1-42 (pg/mL)	0.996 (0.992-0.999)	0.019	0.998 (0.995-1.000)	0.040
t-tau (pg/mL)	1.005 (1.002-1.008)	0.002	1.004 (1.002-1.017)	0.002
p-tau (pg/mL)	1.005 (1.001-1.010)	0.003	1.005 (1.001-1.009)	0.025
Aβ1-42/t-Tau ratio	0.049 (0.006-0.364)	0.003	0.049 (0.006-0.364)	0.003
Aβ1-42/p-Tau ratio	0.735 (0.601-0.898)	0.003	0.843 (0.741-0.961)	0.010
Aβ1-42+	3.433 (0.665-17.73)	0.140	2.264 (0.635-8.076)	0.210

Table 1. Role of clinical and biochemical characteristics on progression to AD dementia and dementia of any type according to Cox regression model.
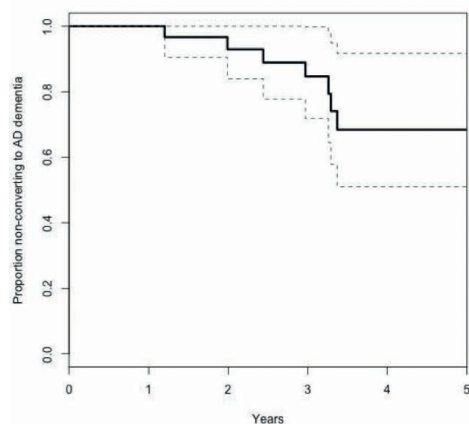
Figure 1. Survival curve for progression to AD dementia

Conclusion: The results of this study highlight a high prevalence of beta amyloid pathology among patients with LOEU, exposing them to higher risk of AD. Thus, LOEU patients should be screened for cognitive impairment to avoid late diagnosis. Moreover, the fact that half of LOEU patients with pathological Aβ1-42 experienced no cognitive decline suggests that beta amyloid might support epileptogenesis without impacting on cognition, pointing to an Aβ-mediated epilepsy.

Disclosure: Nothing to disclose

O209

Properties of epileptiform activity in the human hippocampus and temporal lobe intraoperatively recorded: preliminary results

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Background and aims: Pathophysiological mechanisms underlying generation of hippocampal spike is unknown. We analyzed interictal epileptiform activities intraoperatively recorded from the hippocampus and other temporal regions of adult patients with Temporal Lobe Epilepsy (TLE).

Methods: Five TLE adult patients with (N=2) or without (N=3) hippocampal sclerosis were included in this study. All of the patients underwent MR Imaging and video-EEG monitoring before the operation for localizing seizure onset and diagnosed as having unilateral mesial temporal lobe focus. After opening the anterior horn of lateral ventricle, recording was made under sevoflurane anesthesia using intrahippocampal multiple electrodes, hippocampal surface electrodes and temporobasal subdural electrodes.

Results: (1) Frequency of intrahippocampal spike was always higher than spikes from other areas.

(2) Intrahippocampal recording demonstrated that there was phase reversal in sclerotic hippocampi but there was not in nonsclerotic hippocampi.

(3) Even one transection perpendicular to the long axis desynchronized hippocampal spike.
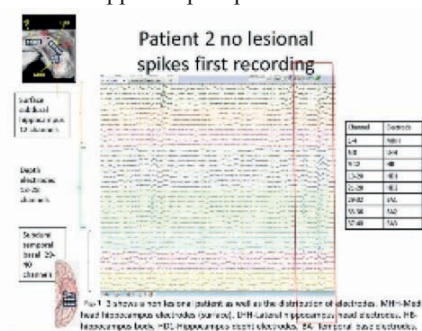

Fig.1 No lesional patient

Conclusion: - We speculate that the phase reversal occurred at the hippocampal sulcus and the subiculum was the spike generator in sclerotic hippocampus.

- Mechanisms underlying spike generation is likely to be different between sclerotic hippocampi and nonsclerotic hippocampi.

- Longitudinal synchronization may be essential for

generation of hippocampal spikes.

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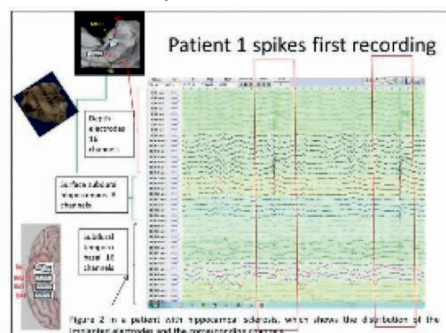

Fig. 2 Hipocampal sclerosis patient

Disclosure: Nothing to disclose

O210

MiR-134 serum expression in Mesial Temporal Lobe Epilepsy patients

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Background and aims: Several experimental and clinical studies have suggested that microRNAs (miRNAs) could be potential epilepsy biomarkers. Nowadays, research has been focused in miR-134, a brain-specific miRNA that plays important roles in dendritic spine development and neuronal structure regulation. An upregulation of miR-134 has been reported both in brain tissue of experimental models (Jimenez-Mateos 2012) and plasma from epileptic patients (Sun 2017). It has also been observed that some anti-seizure drugs down regulate mir-134 plasmatic levels (Sun 2017) highlighting the role of this miRNA in epileptogenesis. Our aim was to quantify miR-134 serum levels in a cohort of Mesial Temporal Lobe Epilepsy (MTLE) patients and correlate with clinical characteristics such as drug response.

Methods: MiR-134 expression levels were evaluated, by molecular biology techniques, in the serum of 46 MTLE-HS patients (26F, 43±12 years, age onset=13±11 years, 35 refractory to treatment) and 44 healthy individuals.

Results: We observed that miR-134 was higher in MTLE-HS (p=0.00002, Area Under the Curve=0.74), especially in those refractory to treatment, comparing to controls.

Conclusion: The results obtained in serum are in accordance with previous experimental and clinical studies, confirming that miR-134 may be a suitable epileptogenecis biomarker. These results also support the hypothesis that targeting miR-134 may be a novel therapy (Jimenez-Mateos 2015) that in conjunction with anti-seizure drugs could improve seizure control.

Disclosure: Partially, supported by a BICE Tecnifar Grant

O211

Laryngeal motor-evoked potentials as an indicator of vagus nerve activation

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Background and aims: In a preclinical study, we found that Vagus Nerve Stimulation(VNS)-induced Laryngeal Motor-Evoked Potentials (LMEPs) are reliable indicators of effective activation of cervical motor vagal fibers. In this study, we aimed to translate this technique to VNS-treated patients.
Methods: In five epilepsy patients (1M/4F), LMEPs were recorded at initiation of VNS therapy; in five (3M/2F) after one year of treatment; in 1/5 recordings at both time points were available. Six Ag/AgCl recording electrodes were cervically placed according to three perpendicular axes around the larynx. VNS parameters were programmed (pulse width: 130μs/250μs/500μs; frequency: 30Hz; duty cycle: 7s ON/18s OFF) and VNS output current was gradually ramped up (0.125mA/0.250mA steps) until individual tolerated thresholds.
Results: VNS-induced LMEPs could be recorded in all patients at both time points; axis 1A-1B was the best channel to reproducibly record LMEPs. VNS thresholds to evoke LMEPs ranged from 0.25-1.00mA. In the one patient tested twice, thresholds remained the same over time (0.25mA). Furthermore, VNS intensities to evoke LMEPs of half-maximum amplitude (x0) and slopes (b) were similar at start (x0=0.3134mA;b=0.0973μV/mA) and after one year (x0=0.3733mA;b=0.0855μV/mA).
Conclusion: VNS-induced LMEPs could be reproducibly, easily and non-invasively recorded in patients and LMEP characteristics seem to be similar at both time points. Furthermore, low output currents (0.25–1.00mA) are sufficient to activate vagal Aalpha-motor fibers. These LMEPs may help to more objectively optimize stimulation parameters using a correction factor in view of slightly higher thresholds for A- and B-fibers vs. low threshold Aalpha-motor fibers.
Disclosure: Charlotte Bouckaert is supported by an Aspirant grant from the "Fonds voor Wetenschappelijk Onderzoek (FWO) - Flanders".

O212

National surveillance of mortality in children with epilepsy in the UK and Ireland

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Background and aims: Patients with epilepsy are significantly more likely to die prematurely than the general population, with causes ranging from associated co-morbidities to Sudden Unexpected Death in Epilepsy (SUDEP). However, the epidemiology of paediatric epilepsy mortality, especially relating to SUDEP, is poorly defined; existing studies are limited to local case series, and national incidence estimates are lacking.
Methods: This was a prospective, population-based active surveillance study using the established British Paediatric Surveillance Unit methodology. The population under study were children aged under 16 years in the UK and Ireland, who died between November 2016 and November 2017, with a simultaneous diagnosis of epilepsy.
Results: Over 13 months surveillance, 129 deaths in children with epilepsy were reported. 70% of cases were male and of white ethnic group. Age at death ranged from 5 months to 16 years and causes of death included pneumonia, sepsis, SUDEP and underlying genetic condition. 54% had global developmental delay. In 55% of cases, a general paediatrician or a paediatrician with neurology interest was the primary care provider whilst 35% had a paediatric neurologist. 90% of patients were on AEDs at the time of death. The two most prescribed AEDs are sodium valproate and Levetiracetam.
Conclusion: In this study, SUDEP contributed to less than 10% of deaths, consistent with previous reports in the literature. There is a clear need to better understand and reduce the number of epilepsy deaths in children in the UK, and national surveillance of SUDEP is warranted to better understand this entity in the paediatric population.
Disclosure: Nothing to disclose.

Neuro-oncology

O213

Increased efficacy of carboplatin after blood-brain barrier opening using low intensity pulsed ultrasound in preclinical models of glioblastoma

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Background and aims: The Blood-Brain Barrier (BBB) limits the penetration and efficacy of therapeutic agents used for treatment of most neurological diseases, including glioblastoma (GBM). Carboplatin, a chemotherapy used as a 2nd or 3rd-line treatment against GBM, is effective in vitro; however, the efficacy is limited in vivo because of the poor passage through the BBB. Temporarily increasing the permeability of the BBB using low intensity pulsed ultrasound (LIPU) combined with microbubbles injected systemically improves the penetration of carboplatin in the brain of non-human primates. The objective of this study was to evaluate the therapeutic efficacy of LIPU-mediated BBB opening followed by carboplatin infusion in human GBM orthotopic xenograft models.
Methods: Carboplatin concentrations with or without BBB disruption were measured in healthy mice to assess the level of drug penetration. Four cohorts of immunocompromised mice bearing either orthotopic xenograft of U87MG-Luc cell line or patients-derived cell line (PDCL) were treated with: (i) vehicle, (ii) LIPU alone, (iii) carboplatin alone, (iv) carboplatin after LIPU-mediated BBB opening.
Results: Carboplatin brain penetration was increased by a factor of 4.2 fold on the whole brain by LIPU-induced BBB opening. In mice with either PDCL or U87 gliomas, tumor growth was delayed ($p < 0.05$) and survival was increased ($p < 0.05$) when mice were treated by carboplatin + BBB disruption.
Conclusion: Carboplatin concentrations was significantly enhanced in the brain after BBB disruption by LIPU. By increasing carboplatin concentrations locally in the brain, carboplatin have significantly enhanced efficacy against GBM. This approach is currently being tested in patients with recurrent GBM (NCT02253212).
Disclosure: Antonin Dréan, Guillaume Bouchoux, Michael Canney, Frédéric Sottilini and Alexandre Carpentier are part of CarThera SAS.

O214

Clinico-radiological, molecular, therapeutic and prognostic features of medulloblastoma of the adult: results from an institutional series

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Background and aims: Medulloblastoma is a highly malignant, embryonal and cerebellar tumor of the childhood. In adults it is rare and shows distinct clinical, histopathological and treatment response features.
Methods: We retrospectively identified 44 adults (17-48 years), with medulloblastoma and collected the demographic, diagnostic and therapeutic data. We calculated PFS (Progression-Free-Survival) and OS (Overall Survival) with Kaplan-Meier method and used the log-rank test for univariate and multivariate analysis.
Results: We observed a male prevalence, and a median age of 31 years at diagnosis. Symptoms at onset were headache (75%), cerebellar dysfunctions (72%), myeloradicular and/or cranial nerve involvement in 12%. Tumor site was cerebellum in 30 patients (16 vermian and 14 hemispheric), infratentorial in 8, disseminated at diagnosis in 6. Histological examination showed a classic variant in 73%, a desmoplastic/nodular variant in 23% and anaplastic variant in one patient. Molecular characterization was available in 22 patients with 15 SHH and 7 non-WNT/non-SHH: mOS was significantly higher in SHH (58.5 months) versus non-SHH (38.5 months) patients. All cases underwent a gross-total or subtotal resection, 43 received adjuvant craniospinal irradiation, followed in 20 patients by systemic chemotherapy (CCNU, cisplatin, vincristine). Five-year OS and PFS were 80% and 66%, respectively. Age, gender, histological variant and extent of surgery were not significantly associated with OS and PFS in both univariate and multivariable analysis. High risk classification and metastatic disease at diagnosis were predictor of a worse prognosis.
Conclusion: Future trials need to consider a stratification for molecular subgroups, and for SHH groups new targeted agents are on the way.
Disclosure: Nothing to disclose

O215

Associations of anticoagulant use with outcome in newly diagnosed glioblastoma

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Background and aims: Our objective was to test the hypothesis that, despite bleeding risk, anticoagulants improve outcome in glioblastoma because of reduced incidence of venous thromboembolic events and modulation of angiogenesis, infiltration and invasion.
Methods: We assessed survival associations of anticoagulant use from baseline up to start of temozolomide chemoradiotherapy (TMZ/RT) (period I) and from there to the start of maintenance TMZ chemotherapy (period II) by pooling data of three randomized clinical trials in newly diagnosed glioblastoma including 1,273 patients. Progression-Free Survival (PFS) and Overall Survival (OS) were compared between patients with: anticoagulant use versus no use; therapeutic versus prophylactic versus no use; different durations of anticoagulant use versus no use; anticoagulant use versus use of anti-platelet agents, versus neither nor. Cox regression models were stratified by trial and adjusted for baseline prognostic factors.
Results: Anticoagulant use was documented in 75 patients (5.9%) in period I and in 104 patients (10.2%) in period II. Anticoagulant use during period II, but not period I, was associated with inferior OS compared to no use on multivariate analysis (p=0.001, HR=1.52, 95% CI: 1.18-1.95). No decrease in OS became apparent when only patients with prophylactic anticoagulant use were considered. No survival association was established for anti-platelet agent use.
Conclusion: Anticoagulant use was not associated with improved OS. Our analysis does not support the notion that anticoagulants exert relevant anti-tumor properties in glioblastoma.
Disclosure: Nothing to disclose

O216

Stroke and "stroke-like" events after brain radiotherapy: a large series with long-term follow-up

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Background and aims: Patients with history of brain irradiation may develop acute "stroke-like" deficits independent of tumor progression. Diagnosis of these conditions may be challenging, as both cerebrovascular disorders and late-delayed paroxysmal syndromes – such as SMART, PIPG and ALERT – may present with acute focal deficits. The aim of this report is to provide a comprehensive description of the phenotypes associated with these conditions, highlighting the key elements to reach an accurate diagnosis.
Methods: Cases were collected among six different neuro-oncology departments in Italy and France. Ten patients were followed prospectively, while 15 other patients were identified by retrospective review of institutional databases.
Results: 25 patients with history of brain irradiation admitted for acute "stroke-like" deficits were included in the study. Four clinical-radiological subgroups were identified: - Group 1: severe encephalopathy and "stroke-like" deficits with multifocal enhancing white matter lesions or normal MRI (ALERT syndrome, 3 patients); - Group 2: "stroke-like" deficits and unilateral cortical-subcortical abnormalities on MRI (SMART syndrome and PIPG, 12 patients); - Group 3: long-lasting focal deficits and lacunar ischemic lesions on MRI (lacunar strokes, 6 patients); - Group 4: rapidly-transient focal deficits and normal MRI (TIA-like episodes, 4 patients). Despite treatment with antiepileptic drugs, high-dose steroids, and/or antiplatelets, 16 out of the 25 patients had relapses (median follow-up: 4 years).
Conclusion: Accurate diagnosis of the conditions in this spectrum is of utmost importance to distinguish patients with acute cerebrovascular disorders or ALERT syndrome, who would benefit from specific work-up and treatment. Brain MRI with diffusion-weighted imaging is essential for this purpose.
Disclosure: Nothing to disclose

O217

Long-term follow-up of Optic Pathway Gliomas in children with neurofibromatosis type-1: an oncology hospital experience

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Background and aims: Optic Pathway Gliomas (OPGs) are the most prevalent intracranial tumours in children with Neurofibromatosis type 1 (NF1). Although commonly indolent, OPGs may have an aggressive clinical course and their approach is often challenging. The aim of this study was to evaluate the outcome of OPGs diagnosed in patients with NF1 during pediatric age, followed up to 22 years.

Methods: Retrospective review of demographics, neurological and ophtalmological evaluations, neuroimaging and treatments applied to all children with OPGs and NF1 presenting to an oncology hospital, 1991-2017.

Results: Of 62 children (31 males, 31 females, median age at diagnosis 4,0 years), 27 (44%) were treated (based on clinical or imagiological progression), in 4 of whitch the initial decision had been watchful surveillance. Of the treated patients, all were submitted to chemotherapy, 4 underwent surgery, 1 radiotherapy. Visual acuity improved in 9, stabilized in 12 and worsened in 3. Complete response was obtained in 1 patient, partial response in 19 and disease stability in 6. One patient died. One patient is currently under treatment, the remaning 25 have stable disease. Patients who didn't undergo treatment remain neuro-ophtalmological stable, 2 had spontaneous tumour regression. Mean follow up time is 7.9 years.

Conclusion: Despite the complex management of patients with NF1 and OPGs, inherent to their variable natural history and difficulties in clearly defining neuro-ophtalmological progression and response to treatment in the pediatric population, our results suggest that careful surveillance is acceptable in most patients and that a majority of patients who undergo treatment benefit from it.

Disclosure: Nothing to disclose

O218

Association between kynurenine metabolism in peripheral blood mononuclear cells and cognition in lung cancer patients undergoing chemotherapy

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Background and aims: Kynurenine (L-KYN) pathway plays important role in immunosuppression, inflammation and neurodegeneration. The aim of the study was to evaluate kynurenine metabolism, expression of translocator protein 18kDa (TSPO-reflects microglia-line activation), G Protein-coupled Receptor (GPR35-KYNA receptor) and kynurenine aminotransferase II (KAT) in Peripheral Blood Mononuclear cells (PBMCs) in relation to cognition in lung cancer patients.

Methods: The study included 221 lung cancer patients hospitalized in Clinic of Oncology in Poznan. The expression of TSPO, GPR35, KAT in PBMCs was evaluated by means of ELISA. At baseline and after 6 months neurological examination, MiniMental State Examination (MMSE), Trail Making Test (TMT) A and B evaluations were performed.

Results: Down-regulation of TSPO expression in PBMCs was associated with better MMSE score (29.00; 28.0-29.0) than in patients with up-regulated TPSO (28.0; 26.0-28.7; P=0.016). TMT-A performance was better in patients with lowered TPSO (8.41±3.68s) than in subjects with up-regulated TPSO (12.92±7.30s; P=0.002). TSPO expression in PBMCs negatively correlated with MMSE score (Kendall's tau=-0.182; P=0.0178) and positively with TMT-A (Kendall's tau=0.168; P=0.0309) at baseline. Up-regulation of KAT expression in PBMCs was associated with improved MMSE 6 months after baseline (28.4±0.7) comparing to subjects with inhibited KAT (27.1±1.8). KAT and MMSE scoring correlated positively 6 months after baseline (Kendall's tau=0.308; P=0.0234).

Conclusion: The effective metabolism of kynurenines in PBMCs may play a protective role against cognitive decline, while stimulation of microglia cell-line can be considered as an independent pathomechanism leading to cognitive impairment in lung cancer patients.

Disclosure: The study was funded by National Science Center Poland (UMO-012/07/B/NZ7/04354)

Miscellaneous 1

O219

Predicting long-term neurological outcome after cardiac arrest with serum Neurofilament Light chain

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Background and aims: Serum biomarkers may improve prediction of neurological outcome after cardiac arrest. Neurofilament Light Chain protein (NFL) has shown promise as a marker of neuronal injury in other neurological diseases. We therefore hypothesized that serum NFL could be used to identify patients with poor neurological outcome after cardiac arrest.

Methods: Using an ultrasensitive immunoassay, we analyzed prospectively collected serum samples from 695 patients from the Target Temperature Management Trial. The serum NFL levels at 24h, 48h and 72h were correlated with poor neurological outcome (Cerebral Performance Category Scale 3-5; severe cerebral disability, coma, or brain death) at 6-month follow-up.
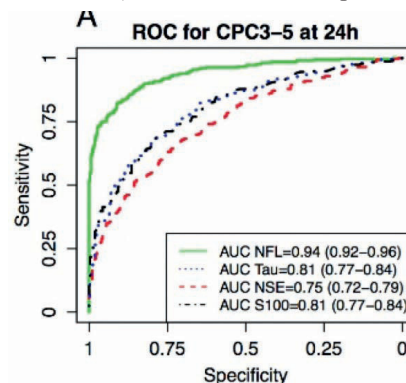

Fig 1 ROC-curve 24h biomarkers

Results: We found significantly increased levels of serum NFL in poor outcome patients (p<0.0001) at 24h-72h after cardiac arrest. NFL had significantly greater accuracy for poor outcome (AUC 0.94-0.95 at 24-72h) than the serum biomarkers tau, S-100 and neuron-specific enolase. Serum NFL had greater sensitivity and comparable specificity for predicting poor outcome compared to highly malignant patterns on EEG, generalized cerebral oedema on head computed tomography, bilaterally absent somatosensory evoked potentials and absent pupillary/corneal reflexes.

Conclusion: Serum NFL is a highly predictive marker of long-term poor neurological outcome from 24h after cardiac arrest and is a promising tool to complement neurological prognostication. Further studies are necessary to validate our results.

Disclosure: KB and HZ are co-founders of Brain Biomarker Solutions in Gothenburg AB, a GU Venture-based platform company at the University of Gothenburg. KB has served as a consultant or at advisory boards for Alzheon, BioArctic, Biogen, Eli Lilly, Fujirebio Europe, IBL International, Merck, Novartis, Pfizer, and Roche Diagnostics. All other authors declare no COI.

O220

Brain-computer interface technology for upper limb rehabilitation after stroke: a translational effort

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Background and aims: Evidence suggests that sensorimotor Brain-Computer Interface (BCI) systems can be beneficial for post-stroke motor recovery. Following a successful Randomized Controlled Trial (RCT) a translational effort was made at our instution with the implementation of the Promotœr, an EEG-based BCI training station (see Figure 1) which is currently employed to support upper limb Motor Imagery (MI) training in add-on to standard therapy.

The patient is seated on a wheelchair with arms resting on a pillow. A visual representation of forearms and hands is given on a dedicated screen, resembling the patient's own hands. The patient is asked to perform MI of affected hand and the therapist is provided with continuous feedback of the patient's EEG activity. (Figure 1)

Methods: Training setting is shown in Figure 1. Desynchronization occurring electrodes placed above the affected sensorimotor area at sensorimotor relevant frequencies is fed back to therapist and patient and reinforced along the training (2-3 weekly sessions of 40 minutes duration, for a minimum of a 1 month training). Before and after training patients undergo an EEG assessment to evaluate the expected reinforcement of MI-induced brain activation in the affected hemisphere (pre – post training).

Results: 25 patients underwent training with the Promotœr; 21 suffered from ischemic or haemorrhagic unilateral stroke, 4 had other type of acquired brain injury resulting in motor impairment of the upper limb; 12 patients were in the subacute phase (< 6 months from the event) while 13 where chronic. In total approximately 300 BCI training sessions were carried out. Two illustrative cases are presented in which a reinforcement of sensorimotor related activity on the affected hemisphere was observed (Figures 2, 3).
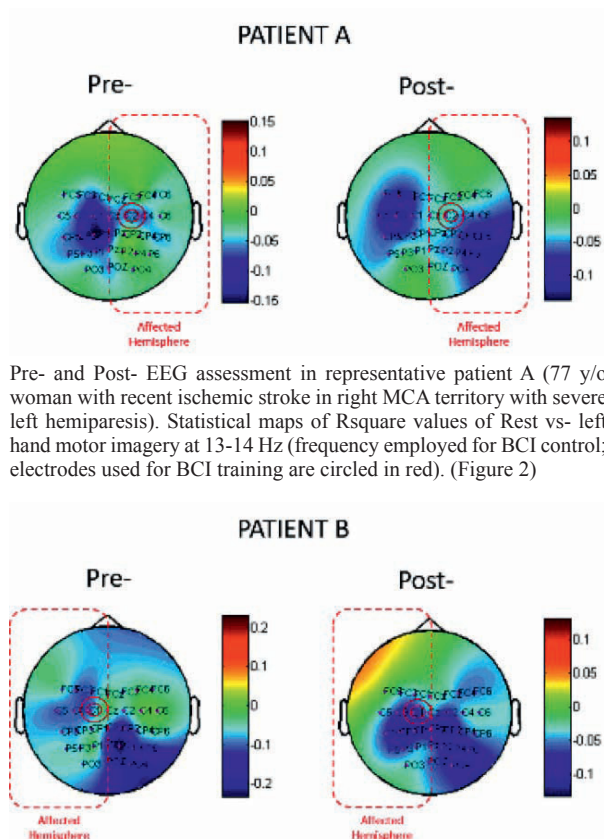
Pre- and Post- EEG assessment in representative patient A (77 y/o woman with recent ischemic stroke in right MCA territory with severe left hemiparesis). Statistical maps of Rsquare values of Rest vs- left hand motor imagery at 13-14 Hz (frequency employed for BCI control; electrodes used for BCI training are circled in red). (Figure 2)

Pre- and Post- training EEG assessment in representative patients B (20 y/o man with traumatic haemorrhage in the left hemisphere and severe right hemiparesis, 1 y from event). Statistical maps of Rsquare values of Rest vs- right hand motor imagery at 9-10 Hz (frequency employed for BCI control; electrodes used for BCI training are circled in red). (Figure 3)

Conclusion: The Promotœr represents a successful story of translational research in BCI for stroke rehabilitation. Results retrace those of a published RCT and support the feasibility of BCI training in the context of a real rehabilitation program.

Disclosure: Nothing to disclose

O221

Clinical features and risk factors in Metronidazole-induced encephalopathy: a systematic review of 121 patients

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Background and aims: Metronidazole, a commonly used antibiotic drug, can cause encephalopathy leading to diagnostic challenges. The condition is rare, and a detailed description of the phenotype is lacking. In this systematic review we investigated the clinical features and possible risk factors in Metronidazole-induced encephalopathy.

Methods: We performed a systematic literature search using PubMed to identify cases concerning Metronidazole-induced encephalopathy. Additionally, references were handsearched. Inclusion criteria were: available human case series or reports. Exclusion criteria were other languages than English. The following data were extracted: age, gender, country, comorbidities, indication for treatment, dose and duration, presenting symptoms, MRI findings at diagnosis and follow-up, and outcome.

Results: We found 641 publications of which 97 papers comprising 121 patients were included. Typical presentation included dysarthria, gait instability and cerebellar symptoms. Liver disease was the most common preexisting condition. MRI showed a characteristic pattern of reversible symmetrical hyperintensities on T2/FLAIR of the dentate nuclei in 90% of patients. Most patients improved significantly after discontinuation of Metronidazole. Poor outcome was associated with severe comorbidity and self-medication.

Conclusion: Metronidazole-induced encephalopathy should be considered in patients with newly initiated or prolonged Metronidazole treatment presenting with neurological symptoms and characteristic MRI changes. Patients with liver disease may be at increased risk. Prognosis is good if recognized early.

Disclosure: Nothing to disclose

O222

Predicting factors for quality of life following Traumatic Brain Injury: CROCFLAME catamnesis

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Background and aims: Predicting factors for long-term outcome in chronic Traumatic Brain Injury (TBI) are still insufficiently known and psychiatric long-term sequels are often not diagnosed, thereby restricting patients´ quality of life. This catamnesis survey was carried out to elucidate influencing factors on quality of life.

Methods: 439 out of 1266 patients suffering from mild, moderate or severe TBI and admitted to neurorehabilitation between 2005 to 2015 were contacted. Health-Related Quality of Life (HRQoL) was assessed (QOLIBRI: 0-100). A score below 60 indicates either an affective or anxiety disorder, a score below 40 both disorders. HRQoL was quantified (%; mean±SD) and correlated to TBI severity, etiology, age at TBI, age at survey, sex, decompressive craniectomy (DC), tracheostomy, shunt device using multivariate regression and stepwise forward selection.

Results: 43% was the overall and 72% the net survey response rate. 30% underwent DC, 44% tracheostomy, 58% received a shunt device. 64% indicated sufficient HRQoL with a QOLIBRI total score equal or greater 60 (65.50±22.57). 36% suffered at least from one psychiatric disorder, of which 16% suffered from an affective and anxiety disorder. Less pronounced TBI severity and DC (adjusted R2=0.068) slightly correlated with better HRQoL.

Conclusion: Most patients had a good HRQoL up to 10 years after TBI. TBI severity is not a strong predictor for HRQoL. Decompressive craniectomy has a slight positive impact on better HRQoL. 36% indicated insufficient HRQoL, most likely due to anxiety and/or depressive disorders. Hence, psychiatric disorders need enhanced attention to predict and improve HRQoL in chronic TBI patients.

Disclosure: Nothing to disclose

Monday, 18 June 2018

Ageing and dementia

O302

ABBV-8E12, a humanized anti-Tau monoclonal antibody for the treatment of Early Alzheimer's Disease and PSP: multiple dose, randomized, double-blind, placebo-controlled phase-2 studies

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Background and aims: ABBV-8E12 is a humanized anti-tau monoclonal antibody being developed for treatment of Early Alzheimer's Disease (AD) and Progressive Supranuclear Palsy (PSP). Results of a phase 1 study in PSP patients (NCT02494024) showed that when administered as a single dose up to 50mg/kg, ABBV-8E12 exhibited an acceptable safety/tolerability profile to support repeat-dose testing in patients with tauopathies. Here we present the designs of ongoing phase 2 studies in Early AD and PSP patients.

Methods: One phase 2, double-blind, placebo-controlled study assesses the 96-week efficacy and safety of ABBV-8E12 in Early AD patients (NCT02880956). A total of 400 male and female subjects, aged 55 to 85 years, will be enrolled at approximately 65 global study sites. A second phase 2, double-blind, placebo-controlled study assesses the 52- week efficacy and safety of ABBV-8E12 in PSP subjects (NCT02985879).

Results: Primary efficacy outcome in the Early AD study is the change in CDR – Sum of Boxes (CDR-SB) from baseline to Week 96. Primary efficacy outcome in the PSP study is the change in the PSP Rating Scale total score from baseline to Week 52. Adverse events will be monitored.

Conclusion: A significant unmet medical need exists for the development of disease-modifying drugs for AD and PSP which directly impact the biology of the diseases and reduce the associated burdens. ABBV-8E12 has shown an acceptable safety and tolerability profile in patients with PSP during phase 1 testing. The current studies are designed to evaluate the efficacy and safety of ABBV-8E12 in patients with Early AD and PSP.

Disclosure: This work was funded by AbbVie Inc. AbbVie participated in the study design, research, data collection, analysis and interpretation of data, writing, reviewing, and approving the publication.

O303

EEG microstates - association with cognitive impairment and Alzheimer's Disease CSF biomarkers

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Background and aims: Spontaneous mental activity is characterized by sub-second changes of quazi-stable brain states called functional microstates that are thought to represent crucial steps of information processing. Electroencephalography (EEG) reflects brain electrical activity at the level of synapses and has a high temporal resolution compatible to the resolution of human information processing. Since synaptic dysfunction is an early event and best correlate of cognitive decline in Alzheimer's Disease (AD), EEG microstates might serve as valuable early markers of AD. The present study investigated differences in EEG microstates parameters between a large number of healthy elderly and memory clinic patients and how they correlate to conventional Cerebrospinal Fluid (CSF) markers of AD in cognitively impaired individuals.

Methods: The EEG microstate analysis will be performed on resting state EEG data following well-established standard procedures in controls (n=308) and patients along AD continuum (subjective cognitive decline, n=210; mild cognitive impairment, n=230; AD, n=197) who underwent standard clinical investigation and CSF biomarker analysis (Aβ, t-tau and p-tau). The contribution, occurrence and duration of the four optimally fitted EEG microstate class topographies that presumably represent usage of different cognitive resources will be obtained since they are sufficient to explain most of the data and are comparable to the literature.

Results: The preliminary results of the ongoing large-scale EEG analysis showed significant, gradient-like correlation of EEG microstates parameters with cognitive status and conventional CSF biomarkers of AD.

Conclusion: Novel functional EEG markers of brain synchronous activity contribute to understanding and detecting early disruption of neurocognitive networks in AD.

Disclosure: Nothing to disclose

O304

Added value of multimodal structural MRI to the clinical diagnosis of primary progressive aphasia variants

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Background and aims: To determine the added value of multimodal Magnetic Resonance Imaging (MRI) to language assessment for the differential diagnosis of primary progressive aphasia (PPA) variants.

Methods: 59 patients [29 nonfluent (nfvPPA), 15 semantic (svPPA), 15 logopenic (lvPPA) variants] and 38 healthy controls underwent a comprehensive language assessment, 3DT1-weighted and diffusion tensor (DT)-MRI. Cortical thickness (CT) and DT-MR indices from the white matter tracts were obtained. A random forest analysis identified MRI features associated with each clinical syndrome. Finally, using ROC curve analysis, the individual patient classification was performed using the language features alone ('language model') and by adding to this model the contribution of multimodal MRI, i.e. the combination of CT and DT-MRI measures.

Results: The language model alone was able to differentiate svPPA from both nfvPPA and lvPPA patients with high accuracy (AUC 0.88-1.00 and 0.97-1.00, respectively). When CT of the left inferior parietal lobe, DT-MRI metrics of genu of the corpus callosum and of left frontal aslant tract were added to the language model, the discriminatory ability of nfvPPA relative to lvPPA significantly increased from AUC 0.77 ('language model' only) to 0.94 ('language+MRI model').

Conclusion: Language features alone are able to distinguish svPPA from the other two PPA variants with very high accuracy. On the contrary, multimodal MRI may improve the differential diagnosis of nfvPPA and lvPPA and can reflect their different underneath pathology.

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O305

Enrichment of clinical trials in prodromal AD using ventricular volume to identify individuals at increased risk of rapid disease progression

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Background and aims: Neurodegeneration detected on MRI has been applied for trial enrichment. The goal of this study is to investigate enrichment strategies based on MRI structural biomarkers to identify prodromal MCI patients with fast cognitive decline.

Methods: 81 Aβ42/P-tau positive amnestic MCI patients (Aβ42/P-tau ratio<7.8 for APOE4 non-carriers, <15.2 for carriers) were selected from the WP5 of PharmaCog (E-ADNI). Patients performed cognitive (ADAScog13) and MRI assessments every 6 months for 2 years. Linear Mixed Model was conducted with baseline structural biomarker, time and biomarkerXtime interaction as factors to predict longitudinal changes in ADAS-cog13. Biomarker cut-offs extraction was settled by applying the mixture model. Sample size was calculated to detect a reduction of 30% of the outcome slope in a 2-year clinical trial.

Results: The analysis of the proportion of variability in ADAScog13 over time reported a significant biomarkerXtime interaction for lateral ventricle volume (LVV, P-value=0.003, standardized β=0.287, η2=0.29). LVV mixture model derived cut-off (14330 mm3) was applied to distinguish patients with large and small LVV. Without LVV enrichment, hippocampal and dentate gyrus

volumes were the biomarkers requiring the lowest sample size (52, 55 subjects vs 294 for ADAScog13). By selecting the subgroup with large LVV, the sample size in a clinical trial could be reduced of 30% for hippocampal volume, 25% for dentate gyrus volume and 40% for Adascog13.

Conclusion: These results demonstrate the utility in using the baseline lateral ventricle volume as enrichment strategy for prodromal AD trials.

Disclosure: Pharmacog is funded by the EU-FP7 for the Innovative Medicine Initiative (grant n°115009).

O306

Metabolic correlates of reserve and resilience in MCI due to Alzheimer's Disease (AD)

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Background and aims: We explored reserve and resilience in late-converter MCI-AD and in slowly-progressing amyloid-positive MCI patients (AMY+MCI) by assessing both topography and extent of neurodegeneration on FDG-PET, also stratifying as per educational level.

Methods: We analyzed 94 MCI-AD patients later converted to AD-dementia and 46 AMY+MCI. Using a data-driven approach based on conversion time, MCI-AD patients were divided into 'typical AD' and late-converter subgroups. Based on the MMSE annual rate reduction, AMY+MCI were divided into tertiles, thus obtaining smoldering (first tertile) and aggressive (third tertile) subgroups. Finally, the whole group of MCI-AD and AMY+MCI was divided into quartiles according to their education. FDG-PET of typical-AD, late converters, aggressive and smoldering AMY+MCI subgroups as well as education-based subgroups were compared to controls with SPM8. Late-converter and smoldering AMY+MCI subgroups were also compared with 'typical AD' and aggressive AMY+MCI subgroups, respectively.

Results: Late converters showed relatively preserved metabolism in right middle temporal gyrus and left orbitofrontal cortex with respect to typical-AD. Given expected higher reserve, when compared to CTR High-EDUC subgroup demonstrated a more extended bilateral hypometabolism in posterior parietal cortex, posterior cingulate/precuneus than Low-EDUC. Instead, Except-EDUC patients showed less extended cluster of hypometabolism and a post-hoc analysis demonstrated that metabolism in middle and inferior temporal gyri was relatively spared in this subgroup with respect to the other MCI patients.

Conclusion: Middle and inferior temporal gyri seem to be sites of resilience (when relatively preserved) rather than a hallmark of a more aggressive pattern (when hypometabolic). Education may affect brain metabolism through both reserve and resilience mechanisms.

Disclosure: Nothing to disclose

Peripheral nerve disorders 2

O307

Peripheral neuropathy in the context of systemic vasculitis and other autoimmune diseases: the importance of etiologic characterization

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Background and aims: Peripheral neuropathies may present in the context of systemic vasculitis and other autoimmune diseases. Their treatment and prognosis depend on etiologic characterization.

Methods: Diagnostic evaluation and follow-up of four cases of CHEDV Neuromuscular Clinic.

Results: Case 1: A 57-year-old male was admitted with bilateral lower limb weakness and hypoesthesia in the left ulnar nerve territory. Blood panel: high ESR, proteinuria, ANA, anti-MPO and anti-SSA/B positive. EMG/NCS: sensitive axonal polyneuropathy. Skin biopsy: microscopic polyangiitis. Under azathioprine.

Case 2: A 53-year-old male was admitted with bilateral lower limb sensorimotor deficit and hypoesthesia in the right median nerve territory. Blood panel: elevated liver enzymes and positive serology for HBV. EMG/NCS: asymmetric sensorimotor axonal polyneuropathy. Nerve biopsy: possible vascular/vasculitic etiology. The diagnosis of polyarteritis nodosa was established. Under tenofovir.

Case 3: A 54-year-old female, previously diagnosed with Churgh-Strauss vasculitis, was admitted with bilateral lower limb sensorimotor deficit, dysesthesia and right hand paresis. Blood panel: eosinophilia, high IgE and positive anti-MPO. Chest CT scan: chronic eosinophilic pneumonia. EMG/NCS: sensorimotor axonal polyneuropathy with active denervation. Nerve biopsy: possible vasculitic process. Under cyclophosphamide.

Case 4: A 34-year-old female was admitted with sensory complaints of left sural and right median nerve territories. Blood panel: diminished complement levels. EMG/NCS: multifocal axonal impairment. Nerve biopsy: possible vascular/vasculitic process. The cause of vasculitis remains unknown. No medication.
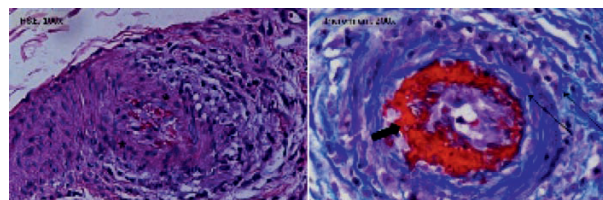
Skin biopsy revealing an inflammatory infiltration in arteriole wall with disruption of internal elastic lamina and fibrinoid necrosis, allowing the diagnosis of leukocytoclastic vasculitis.
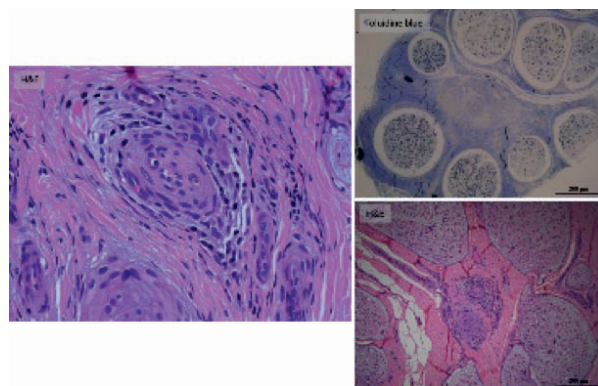
Nerve biopsy revealing a perivascular inflammatory cell infiltration, in a perineural blood vessel, and an asymmetric involvement of nerve fascicles, fulfilling criteria of probable vasculitic neuropathy.
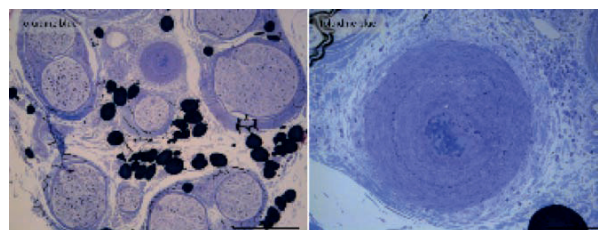
Nerve biopsy showing an asymmetric involvement of nerve fascicles and a vessel with fragmentation of internal elastic lamina reflecting a cicatricial process and suggesting a vascular/vasculitic process.

Conclusion: This series reveal the etiologic and phenotypic diversity of peripheral neuropathies related with systemic vasculitis and other autoimmune diseases. The therapeutic approach and prognosis was distinct in each patient, emphasizing the importance of a prompt diagnosis.

Disclosure: Nothing to disclose

O308

Mutations in MME cause autosomal recessive late-onset CMT type-2 disease

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Background and aims: Mutations in the metalloendopeptidase gene (MME) gene were initially identified as causative for autosomal recessive CMT2. Subsequently, other authors published variants in MME linked to late-onset autosomal dominant polyneuropathies. Our goal is to deepen the phenotype of our patients with changes in MME and try to delineate the pattern of inheritance.

Methods: We screened 197 index case subjects with hereditary neuropathy Charcot-Marie-Tooth (CMT)/Distal hereditary motor neuropathy (DHMN) and 10 patients with familial Amyotrophic Lateral Sclerosis (fALS) by a custom panel of 119 genes. Beyond the index case subjects, we included additional affected and unaffected family members for segregation analysis. All patients were examined by experienced neurologists in their respective centers.

Results: We found 18 variants of MME in a total of 20 index cases; 9 families (13 cases) had bi-allelic MME mutations (3 homozygosis and 6 compound heterozygosis) and 11 showed a heterozygous variant. All patients with bi-allelic variants had similar phenotype consistent with late-onset axonal neuropathy. Segregation analysis in patients with heterozygous variants did not show positive results; the phenotype of these patients showed a wide spectrum including CMT1, CMT2, DHMN and familial ALS.

Conclusion: MME mutations segregating as an autosomal recessive pattern showed late-onset CMT2 phenotype. We couldn't demonstrate that variants in heterozygosis in MME were the cause of neuropathy in our cases. Our results highlight the need for deeply investigating the mode of inheritance not only for academic interest but also especially for genetic counseling.

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O309

Validity and reliability of the Transthyretin Amyloidosis Neuropathy Score (TTR-ANS): a new outcome measure designed specifically for Familial Amyloid Polyneuropathy (TTR-FAP)

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Background and aims: The systemic Transthyretin (TTR) amyloidoses are a group of clinically heterogeneous, devastating diseases for which a remarkable development of new therapies has occurred. An axonal length-dependent neuropathy with variable involvement of other organs is one of the phenotypes associated with these diseases, frequently referred to as Familial Amyloid Polyneuropathy (TTR-FAP). Herein we report the development, construct validity and reliability of a clinical scale specifically for TTR-FAP (TTR-ANS).

Methods: We used our experience as a reference center for hereditary TTR Amyloidosis to develop TTR-ANS. We performed a cross-sectional study using electronic clinical registries of 60 patients representing mild, moderate and severe disease stages. TTR-ANS was independently applied by two observers. Correlations with existing clinical scales – Neuropathy Impairment Score (NIS; including Total and Lower Limbs, NIS-LL), Norfolk, Karnofsky, Polyneuropathy Disability Score (PND), time from symptom onset, disease stages and neurophysiology measurements were analyzed.

Results: TTR-ANS includes three major sub-scores: small fiber sensory neuropathy (subjective sensory neuropathy and objective pain sensitivity assessment), autonomic neuropathy (gastrointestinal, genitourinary and cardiovascular manifestations) and large fiber neuropathy (reflexes, touch and vibration sensitivity and motor function). Smaller sub-scores evaluating kidney, heart, eye and central nervous system functions are also included. As expected, total TTR-ANS correlates highly with disease stages, time from disease onset and NIS/NIS-LL, with the two scales diverging predominantly in the autonomic neuropathy sub-score.

Conclusion: In a single center retrospective study, TTR-ANS has shown construct validity and reliability. Future validity prospective studies and studies of TTR-ANS responsiveness to therapy are ongoing.

Disclosure: Nothing to disclose

O310

Statins and cryptogenic axonal polyneuropathy: a literature review and case-control study

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Background and aims: Polyneuropathy is one of the most common neurological disorders (prevalence 2-4%). In approximately 25% no cause is found and the diagnosis Cryptogenic Axonal Polyneuropathy (CAP) is made. Nerve biopsies in these patients are suggestive of microvascular etiology. This is supported by studies showing an association between CAP and metabolic syndrome. However, this association might be confounded by statin use. Case reports have presented patients with suspected statin induced polyneuropathy, but outcomes from larger studies have been conflicting. With an increasing number of patients using statins, it is very important to know whether a real relationship between statin use and polyneuropathy exists. To answer this question we present our findings from our prospective case-control study and systematic review.

Methods: We conducted a prospective case control study comparing exposition to cholesterol lowering drugs between CAP patients and controls before index date (onset of symptoms or firs visit for controls). We calculated odds ratio's both for statins and cholesterol lowering drugs seperately and corrected for possible confounders such as lipid spectrum, cardiovascular diseases and risk factors.

Results: 340 CAP patients and 289 controls were included. We found a negative association between ever use of cholesterol lowering drugs and statins before index date and CAP. Results were similar for current use. There was no difference in dosage or exposition duration between groups. We found no evidence of a positive association between statins and CAP in current literature.

Conclusion: There is no evidence of sufficient quality supporting an assocition between statin use and CAP.

Disclosure: This study was funded by the Prinses Beatrix Spierfonds, the Netherlands.

Cerebrovascular diseases 2

O311

### Predicting intracerebral haemorrhage expansion with non-contrast CT: the BAT Score

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Background and aims: While the CT angiography spot sign performs well as a biomarker for Hematoma Expansion (HE), CT angiography is not routinely performed in the emergency setting. We developed and validated a score to predict HE based on non-contrast CT (NCCT) findings in acute intracerebral haemorrhage (ICH).

Methods: After developing the score in a single center cohort of ICH patients (n=344), we validated it in a large clinical trial population (n=954) and in a multicenter ICH cohort (n=241). The following NCCTmarkers of HE were analysed: hypodensities, blend sign, hematoma shape and density, and fluid level. HE was defined as hematoma growth>6 mL or >33%. The score was created using the estimates from multivariable logistic regression after final predictors were selected from bootstrap samples.

Results: Presence of blend sign (odds ratio (OR) 3.09,p=0.002), any intrahematoma hypodensity (OR 4.54, p<0.0001) and time from onset to NCCT<2.5 h (OR 3.73, p=0.0002) were predictors of HE. A 5–point score was created (BAT score:1 point for Blend sign, 2 points for Any hypodensity and 2 points for Timing of NCCT<2.5h). The c statistic was 0.77 in the development population,0.65 and 0.70 in the validation cohorts. A dichotomised score (BAT score>3) predicted HE with 0.50 sensitivity, 0.89 specificity and 0.82 accuracy.
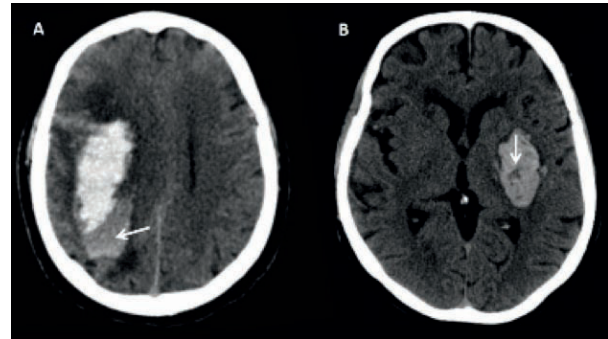
Illustrative example of blend sign (A, arrow) and intrahematoma hypodensity (B, arrow) on admission non-contrast computed tomography.

Conclusion: An easy to use 5-point prediction score can identify subjects at high risk of HE. This tool requires just a baseline NCCT scan and may help select ICH patients for anti-expansion clinical trials.

O312

Direct oral anticoagulants versus Vitamin K antagonists after a recent ischaemic stroke: a pooled individual patient data analysis

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Background and aims: We compared the clinical benefit of Direct Oral Anticoagulants (DOAC) and Vitamin-K antagonists (VKA) in patients having Atrial Fibrillation (AF) with a recent ischemic stroke or TIA.

Methods: We conducted an individual patient data analysis of 7 prospective studies and analyzed the association between type of anticoagulation (DOAC vs. VKA) with a composite endpoint (recurrent ischemic stroke (AIS), intracerebral hemorrhage (ICH) or mortality) using mixed effects Cox proportional hazards regression models and calculating adjusted hazard ratios (HRadj) with 95% confidence intervals (95% CI).

Results: Of 4912 patients [median age 78years (IQR71-84); 2331 (47.5%) female; 4739 (96.5%) ischemic stroke as index event, median NIHSS-at-onset 5 (IQR2-12)], 2256 (45.9%) patients received VKA and 2656 (54.1%) received DOAC after the index stroke. The median time from index stroke to start of oral anticoagulation was 5days (IQR2-14) for VKA and 5days (IQR2-11) for DOAC (p=0.53). There were 262 AIS (4.4%/year), 71 ICH (1.2%/year) and 439 deaths (7.4%/year) during the total follow-up of 5970 patient years. DOAC treatment reduced the risk of the composite endpoint (HRadj 0.78, CI95% 0.64-0.94, p=0.01). In a secondary analysis, DOAC reduced the risk of ICH (HRadj 0.34, CI95% 0.16-0.71, p=0.01) and mortality (HRadj 0.71, CI95% 0.56-0.90, p<0.01) while the risk of recurrent AIS did not differ between DOAC and VKA treatment (HRadj 0.98, 95%CI 0.72-1.35, p=0.91).

Conclusion: In patients with AF, DOACs commenced in a median of 5 days after stroke seem to have a clinical benefit compared to treatment with VKA, mainly due to a lower risk for ICH and mortality.

Disclosure: The research presented in this abstract is investigator-driven.

O313

Cerebrovascular lesions during normal aging: a neuropathological study with 7.0-tesla magnetic resonance imaging

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Background and aims: Successful aging is associated with regional brain shrinkage and an increased cerebrovascular risk. The present post-mortem study investigates whether the increase of small cerebrovascular lesions is more frequent in normal elderly persons compared to adult ones.

Methods: 34 persons with normal cognition and without a stroke history underwent an autopsy. The incidence and the severity of cerebrovascular lesions in post-mortem brains of 20 adult (average age: 43±12 years) and 14 elderly (average age: 75±8 years) brains were examined. The neuropathological examination included a T2 and T2* 7.0-tesla MRI on three coronal sections.

Results: The neuropathological examination revealed more severe White Matter Changes (WMCs) and an increase of Cortical Micro-Bleeds (CoMBs) in the elderly compared to the adult brains. No differences were observed concerning Cortical Micro-Infarcts (CoMIs). Similar findings were observed on MRI examination: increased severity of WMCs and incidence of CoMBs were found to the same extend in the frontal, the central and the occipital section of the elderly brains. CoMIs were on the other hand more or less similarly low and distributed in the three sections of the adult and elderly brains.

Conclusion: During the aging process only increased severity of WMCs and of the incidence of CoMBs are observed. CoMIs, which are the most specific cerebrovascular lesions, are not amplified by getting older. The brain changes during normal aging are not due to the increased impact of cerebrovascular disease but rather the consequence of the age-related neuronal degeneration.

Disclosure: Nothing to disclose.

O314

Correlates of pontine small vessel disease: a post-mortem study

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Background and aims: The pons has not been included in most Small Vessel Disease (SVD) pathology scores. We aim to investigate the relationship of pontine SVD and SVD in other brain areas, and extracranial and intracranial artery atheromatous disease.

Methods: A semi-quantitative score was applied to assess the extent of atheroma in aorta, coronary, cervical and intracranial arteries in a human post-mortem control cohort. SVD scores (1 point for each: arteriolosclerosis, perivascular space enlargement, microbleeds/large and lacunar infarcts, fibrinoid necrosis) were obtained from pons, frontal WM (FWM), occipital WM(OWM) and basal ganglia(BG). A multivariate model was used to explain the pons SVD score taking into account age, gender, aorta+coronary, cervical and intracranial artery atheroma, and heart weight.

Results: A total of 36 cases were studied (mean age 58.7 ± 13.15 years, 58.3% females). SVD changes were found in 52.8% (N=19) of the cases, only >2 in 2 cases. Pons SVD score (0.75 ± 0.87) was slightly lower (p=0.01) than SVD scores in FWM (1.42 ± 1.2), OWM (1.4 ± 1.4) and BG (1.6 ± 1.2). Pons SVD was weakly correlated with FWM SVD (r=0.37, p=0.026) and OWM (r=0.349, p=0.04) and did not correlate with BG SVD. In multivariate analysis only intracranial artery atheroma associated with pons SVD (b=0.44, p=0.014).

Conclusion: Pons SVD was relatively independent from SVD in other brain regions. However, Pons SVD was closely related to intracranial artery atheroma which is consistent with limited imaging data.

Disclosure: Nothing to disclose

O315

Atrial fibrillation in cryptogenic stroke: the Nordic Atrial Fibrillation and Stroke Study (NOR-FIB)

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Background and aims: The optimal duration and timing of cardiac rhythm monitoring after cryptogenic stroke is unknown. Identification of reliable biomarkers indicating AF will be valuable in the selection of patients for prolonged cardiac rhythm monitoring. The purpose of the study is to assess the incidence of AF detection using implantable cardiac monitors (Reveal LINQ®) in patients with cryptogenic stroke or TIA and to identify biomarkers that can be used as predictors of incident AF.

Methods: Our study is a multi-center prospective observational study of the occurrence of AF in cryptogenic stroke/TIA patients with implantable cardiac monitors for 12 months. Blood samples measuring biomarkers are taken in the acute phase and at 12 months´ follow-up. Estimated number of patients to be included in the study is 500.

Results: By January 2018, the total number of patients included in 7 out of 18 participating centres, is 45. Out of 45 included patients, AF has been detected in 7 patients, resulting in detection rate of 15,5%. Treatment with anticoagulants has been initiated in all patients with AF. The pilot study has identified biomarkers that seem to be useful for the detection of AF in cryptogenic stroke/TIA.

Conclusion: Updated interim analysis of included patients will be presented as well as new results from extended analyses of biomarkers.

Disclosure: Nothing to disclose

O316

Integrity of the Circle of Willis as an important predictor of early catastrophic outcome after endovascular thrombectomy in middle cerebral artery occlusion stroke

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Background and aims: To evaluate whether proximal collaterome influences early catastrophic outcome (defined as hospital death) in patients treated with Endovascular thrombectomy (ET) due to middle cerebral artery occlusion stroke.

Methods: We consecutively included stroke patients with acute occlusion of the M1 portion of Middle Cerebral Artery (MCA) who underwent ET either as a standalone treatment or with intravenous thrombolysis. We recorded demographics, National Institutes of Health Stroke Scale (NIHSS) scores, baseline clinical and radiographic characteristics, and in-hospital death. Incomplete Circle of Willis (iCW) was defined as absence of crossflow through anterior communicating artery and absence of posterior communicating artery ipsilateral to the affected side on the CT angiography.

Results: In total, 152 patients were studied [median age 73 (interquartile range [IQR] 59-80), median admission NIHSS score 17 (IQR 12-21)]. In-hospital death rate following the intervention was 14.5% (n=22). The survivors were younger [median age 73(58-79) vs 81(69-86)], had lower NIHSS [17(12-20) vs 20(17-26)], and lower rates of anticoagulant medication intake [12.3% vs 36.4%], all $p<0.01$. In a logistic regression analysis adjusted for age, NIHSS, anticoagulation, infarct volume, symptomatic hemorrhage, in-hospital death was strongly associated iCW [OR 8.3(CI 1.2-56.8)].

Conclusion: iCW is associated with early catastrophic outcome after ET in patients with MCA occlusion. Development of strategies to augment proximal collaterome in this critical group of patients is urgently needed.

Disclosure: Nothing to disclose

Motor neurone diseases

O317

AVXS-101 phase-1 gene replacement therapy clinical trial in SMA type-1: continued event free survival and achievement of developmental milestones

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Background and aims: Spinal Muscular Atrophy is a devastating, monogenic neurodegenerative disease. Children with SMA1 will never sit unassisted or maintain head control or achieve CHOP-INTEND score of >40. Moreover, a natural history study reported that 75% die or require permanent ventilation by 13.6 months. This trial explores safety and efficacy of a gene replacement therapy. AVXS-101 delivers the SMN gene in a one-time intravenous dose.

Methods: In this Phase 1 trial, 15 patients with SMA1 confirmed by genetic testing (with 2xSMN2 copies) were enrolled. Patients received low-dose AVXS-101 (Cohort 1, n=3) or proposed therapeutic dose (Cohort 2, n=12). The primary objective was safety and secondary objectives included survival (avoidance of death/permanent ventilation) and ability to sit unassisted (video confirmed by external independent reviewer). CHOP-INTEND scores and other motor milestones were additional objectives.

Results: AVXS-101 appeared to have a favorable safety profile and to improve survival at data cut-off (20January2017). All patients reached 13.6 months free of permanent ventilation and none have died (3 live >30 months). Cohort 2 patients demonstrated improvement in motor function: 11/12 achieved head control and sat with support, and 9/12 sat unassisted. Two patients stood and walked independently.

Conclusion: In contrast with the natural history, a one-time intravenous administration of AVXS-101 appeared to demonstrate a positive impact on the survival of both cohorts and a dramatic, sustained impact on motor function of Cohort 2: 11/12 patients achieved CHOP-INTEND scores and motor milestones rarely/never seen in this population. A clinical update will be given at the time of presentation.

Disclosure: This clinical trial is sponsored by AveXis, Inc.

O318

Integrated miRNAs analysis of ALS iPSCs and iPSCs-derived motor neurons towards the development of a molecular therapy for ALS

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Background and aims: Amyotrophic Lateral Sclerosis (ALS) is characterized by progressive degeneration of Motor Neurons (MNs). The mechanisms underlying the disease are almost unknown, even if dysregulation in RNA metabolism, including microRNAs (miRNAs) processing, has been increasingly recognized. Since miRNAs are highly expressed in central nervous system and are required for MNs survival, they may play important roles in the aetiology or progression of neurodegenerative diseases such as ALS.

We aim to analyze miRNAs profiling in human induced Pluripotent Stem Cells (iPSCs) and iPSC-derived spinal MNs from ALS subjects compared to healthy controls.

Methods: We reprogrammed patient and control fibroblasts in iPSCs and subsequently we differentiated them into spinal MNs. Then, we isolated miRNAs contained in extracellular vesicles from iPSCs and MNs culture media. Finally, we performed Next Generation Sequencing (NGS) analysis on our lines.

Results: We obtained a transcriptome analysis of human iPSCs, MNs, and exosomes in ALS. Among miRNAs deregulated in ALS MNs, we found miRNAs involved in MNs survival and p53 pathways and, interestingly, relevant targets of these miRNAs, including apoptotic factors, were aberrantly increased in ALS MNs. Moreover, two other altered miRNAs were implicated in synapsis and neurogenesis. Finally, we silenced selected miRNAs targets with morpholino antisense oligonucleotides in the SOD1G93A murine model evaluating survival, neuromuscular function and neuropathology.

Conclusion: The identification of specific miRNAs relevant to ALS pathology can lead to the discovery of new disease biomarkers and potential therapeutic targets. This approach can increase the chances of modifying complex diseases by modulating entire gene networks through a specific miRNAs subset.

Disclosure: Nothing to disclose

O319
RNA-Sequencing and motif analysis of Human Motor Neurons implicates selective role of SMN/SYNCRIP complex and Motif 7 in Spinal Muscular Atrophy

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Background and aims: Spinal Muscular Atrophy (SMA) is a neuromuscular disorder that represents the leading cause of genetic death during childhood. SMA is caused by mutations in Survival Motor Neuron (SMN) gene resulting in a loss of function of the SMN protein, which plays a crucial role in pre-mRNA processing. The exact pathogenetic mechanisms and the reasons of selective motor neurons (MNs) vulnerability are still not completely understood.

Methods: To address this question, we generated MNs from control and SMA patient-derived induced pluripotent stem cells (iPSCs) and performed deep RNA sequencing and bioinformatic analyses.

Results: We detected SMA-specific molecular changes in MNs, including alterations in axonal and synaptic genes that involved Synaptotagmin 13, a key component of the synaptic machinery, and neurexin2 (NRXN2), a protein essential for MN survival and function. The overexpression of NRXN2 could extend human SMA-MN survival and increase axon length. Motif enrichment analysis of differentially expressed/spliced genes revealed a common Motif-7, which is a target for SYNCRIP. SYNCRIP is an RNA binding protein and a splicing modulator of SMN that promotes the inclusion of exon 7 in SMN2. Interestingly, it interacts only with full-length SMN and not with the Δ7 truncated form. SYNCRIP overexpression rescued SMA-MNs phenotype, thanks to the consequent increase of SMN and of their down-stream target NRXN2, through a positive loop mechanism.

Conclusion: The study of complementary pathways disrupted in human SMA is important to identify alternative therapeutic targets besides direct SMN increase. This finding represents a crucial step towards the discovery of efficacious therapies for all SMA subtypes.

Disclosure: The study was supported by a Cariplo grant awarded to Stefania Corti.

O320
Structural connectivity alterations in Amyotrophic Lateral Sclerosis are modulated by the topology of the anatomical brain connectome

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Background and aims: To test whether the spatial patterning of structural brain alterations in Amyotrophic Lateral Sclerosis (ALS) is modulated by the topology of the anatomical brain network using connectomics.

Methods: 58 ALS patients and 34 controls underwent T1-weighted and Diffusion Tensor MRI. Graph analysis and connectomics were used to define the "healthy" connectome in controls and assessed global and local topological network properties in ALS patients. Regions of subsequent stages of ALS pathology were defined according to the Braak pathological propagation pattern.

Results: ALS patients showed reduced local efficiency and nodal strength of the sensorimotor network relative to controls. At the regional network level, ALS patients compared to controls showed alterations involving sensorimotor network and connections linking motor to basal ganglia and frontal regions. In the healthy subject connectome, brain regions of subsequent stages of ALS pathology are shown to be more closely interconnected with the primary motor cortex (ALS-epicenter) than regions of more distant stages. The topological distance between the epicenter and brain nodes of subsequent stages of pathology in controls correlated with the structural connectivity between the same regions in ALS patients, such that more closely connected regions in controls exhibited more severe alterations of structural connectivity in ALS patients.

Conclusion: In ALS, graph analysis and connectomics represent a powerful approach to detect upper motor neuron degeneration, extra-motor brain changes and network disorganization associated with the disease. Altered structural connectivity was greater between closely connected regions. Axonal connections may influence the spatial spreading of pathology in ALS.

Disclosure: Study supported by: Italian Ministry of Health (#RF-2011-02351193).

O321
Amyotrophic Lateral Sclerosis (ALS) spatial epidemiology in the Mount Etna region, Italy: further evidences for a pathogenetic role of volcanogenic metals

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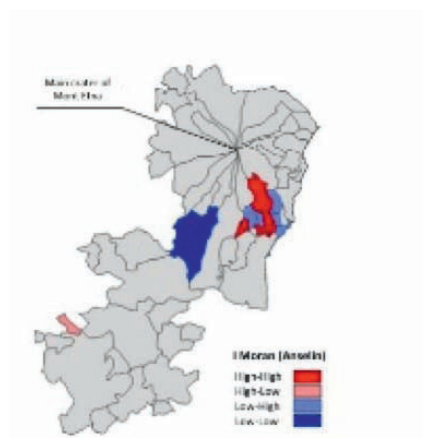
Fig. 2. Moran's Index in the Mount Etna region. Moran's Index studies spatial correlation by quantifying the similarity in incidence between neighbor areas.

Background and aims: Spatial epidemiology could give important clues on environmental causes of a disease. Previously, we described a higher incidence of Amyotrophic Lateral Sclerosis (ALS) in the eastern flank of the Mount Etna when compared to the western one and volcanogenic metals have been proposed as a possible explanation.
We aimed to perform a cluster analysis of ALS cases in the Mount Etna region.

Methods: ALS cases residents in the province of Catania and who had experienced the onset of symptoms during the 2005-2015 period were included. Address at the moment of onset was considered for each case. Cluster analysis was performed using both Kulldorff's spatial scan statistic and Moran's Index.

Results: A total of 193 ALS cases have been identified. The mean annual crude incidence rate was 1.63/100 000 person-years (95% CI 1.40-1.86). Kulldorff's statistics identified a spatiotemporal cluster including 13 communities in the eastern flank of the mount Etna. Here, 12.73 cases were expected and 33 were observed (SIR 2.59; 95% CI 1.78-3.64, p-value 0.003) (Fig. 1). Moran's Index confirmed a positive spatial autocorrelation in the same area (Fig. 2).

Fig. 1. Spatiotemporal cluster identified by Kulldorff's spatial scan statistics in the Mount Etna region.

Conclusion: Our study showed a higher ALS incidence cluster in the eastern flank of Mount Etna. Despite the retrospective nature of the study, the adoption of two proper spatial analyses independents from an a priori hypothesis strengthen the validity of our results. These findings further suggest the possible role of volcanogenic metals in ALS pathogenesis.

Disclosure: Nothing to disclose

Cognitive neurology/neuropsychology

O322

Locus coeruleus atrophy assessed with 3T MRI in typical and atypical Alzheimer's Disease and correlations to neuropsychological data

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Background and aims: The Locus Coeruleus (LC), a noradrenergic nucleus, shows early alteration in Alzheimer's Disease (AD). This involvement has been poorly studied in vivo while it could constitute a therapeutic target. The objectives were to investigate the LC signal in typical and atypical AD using 3T MRI and to evaluate the impact of LC involvement on neuropsychological data.

Methods: Three groups of subjects matched for age were studied: controls, patients with typical AD, and patients with atypical AD (logopenic primary progressive aphasia) defined by clinical-biological criteria, with CSF biomarkers. All subjects had a standardized neuropsychological assessment and a 3 Tesla MRI including a sequence designed to quantify the LC neuromelanin signal. Treatments were comparable in both AD groups.

Results: 8 controls, 17 typical and 9 atypical AD patients were included. The LC signal was significantly lower in the typical and atypical AD groups compared to controls (p=0.002 and p=0.013, respectively). In patients with typical AD, the episodic memory scores (free and total recall) were positively correlated with the LC signal (Figure 2: p=0.023, p=0.028, respectively).
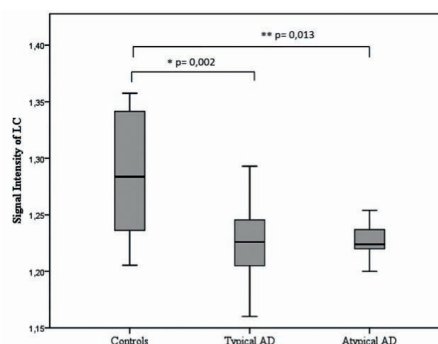
Figure 1: Box plot of the LC signal intensity in controls and patients with typical and atypical Alzheimer's disease. Plots indicate median, the boxes indicate the upper and lower quartiles. Whiskers are defined as the lowest/highest values still within the 1.5 interquartile range from the box. AD=patients with Alzheimer's disease.
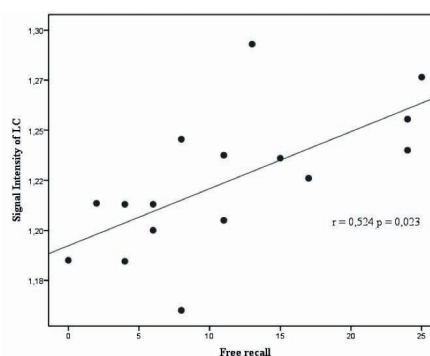

Figure 2: Correlation between LC signal intensity and verbal episodic memory test (free recall) in typical Alzheimer's disease patients. AD=patients with Alzheimer's disease.

Conclusion: We found a clear decrease of LC signal assessed by 3T MRI in typical and atypical AD, independently of the clinical presentation. The positive correlations with the episodic memory scores suggest that the LC plays a crucial role in maintaining cognitive function, probably via the norepinephrine system. AD patients may thus benefit from innovative therapeutic approaches targeting the noradrenergic system.

Disclosure: Public fundings

O323

Reduced dynamism of functional connectivity is associated with cognitive impairment in Multiple Sclerosis patients: a dynamic functional connectivity study in a multi-center setting

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O. Ciccarelli[7], C. Enzinger[8], G. Tedeschi[3],
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Background and aims: To investigate the relationship between Multiple Sclerosis (MS)-related Cognitive Impairment (CI) and time-varying Functional Connectivity (FC) using a dynamic Resting State (RS) FC approach.

Methods: RS fMRI scans from 62 MS patients and 65 healthy controls (HC) were obtained at seven European sites. MS patients underwent clinical/cognitive evaluation. Independent component analysis was used to identify 43 relevant intrinsic FC components. Between-group differences of network FC were evaluated using a dynamic approach and then grouping FC correlation matrices into recurrent states of transient FC. Summary dynamism measures were computed for each group.

Results: 23 MS patients (37%) were cognitively impaired (CI) (> two abnormal neuropsychological tests). Dynamic FC analysis revealed, in HC and MS, 3 recurrent FC states: two states characterized by strong inter-network connectivity and one characterized by weak inter-network connectivity. CI-MS patients had lower dwell time in the high-connectivity State2 compared to cognitively preserved (CP)-MS ($p=0.05$). Compared to CP-MS, CI-MS patients exhibited lower dynamic fluidity (less switches between states) ($p=0.01$) and operated over a restricted dynamic range ($p=0.01$). Between-group comparison of connectivity strengths revealed lower FC in MS vs HC between cortical-

subcortical networks. In connectivity State3, CI vs CP-MS patients showed reduced FC between cortical-subcortical networks.

Conclusion: In both HC and MS patients, dynamic RS FC analysis was able to detect recurrent patterns of strong and weak inter-network RS FC. Time-varying RS FC patterns were less dynamic in CI than in CP-MS patients and HC, suggesting that slow inter-network connectivity is associated with worse cognition in MS.

Disclosure: Nothing to disclose

O324

Association between neuropsychiatric symptoms, cognitive functioning and structural brain changes in Clinically Isolated Syndrome

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Background and aims: Neuropsychiatric symptoms and impairment of cognitive functioning are present in patients with multiple sclerosis and are associated with structural brain changes, but have been less studied in Clinically Isolated Syndrome (CIS).

Objective: To characterize neuropsychiatric symptoms (depressive symptoms, anxiety, apathy and fatigue), cognitive functioning and disability and their associations with structural brain changes in CIS.

Methods: Patients with CIS (n=67) and demographically matched healthy controls (n=46) underwent neurological (using Expanded Disability Status Scale - EDSS) and neuropsychological examination including questionnaires of neuropsychiatric symptoms and subjective cognitive functioning using Multiple Sclerosis Neuropsychological Screening Questionnaire (MSNQ). Next, both groups underwent MRI (magnetic resonance imaging) of brain with measurement of global, regional and lesion load volume.

Results: The CIS group had more depressive and anxiety symptoms ($p \leq 0.026$). The groups did not differ in apathy, fatigue and MSNQ score. There was no correlation of the EDSS score with neuropsychiatric symptoms. Cognitive functioning unlike clinical disability was associated with depressive symptoms and anxiety ($p \leq 0.001$). Higher depressive symptoms correlated with higher lesion load in the right temporal lobe ($p=0.013$). Higher apathy was associated with higher lesion load in the right and left insulas and right occipital lobe ($p \leq 0.026$). Higher anxiety correlated with lower white matter volume ($p=0.045$).

Conclusion: We demonstrated that increased depressive symptoms and anxiety are present in patients witch CIS unlike impaired cognitive functioning. Next, neuropsychiatric symptoms are associared to cognitive

functioning an are the result of structural brain changes in specific brain regions unlike disability.

Disclosure: Nothing to disclose

O325

Transcranial Direct Current Stimulation (tDCS) over lateral parietal cortex facilitates object-location and face-word associative memory

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Background and aims: Management of memory impairments presents one of the most challenging issues in cognitive neurology and neurorehabilitation. Anodal tDCS was shown to increase activation in the targeted cortical area and related subcortical structures. The current study explores whether physiological modulation of the putative hippocampus - lateral parietal cortex neural loop can bring enhancement in associative memory performance.

Methods: Two double-blind, cross-over sham-controlled experiments were conducted. In both experiments, in two separate sessions, either anodal tDCS or sham were delivered over lateral parietal cortex (Figure 1). In Experiment 1 left-sided stimulation and face-word associative memory task were used, while in Experiment 2 right-sided stimulation and object-location task were used (Figure 2). Two distinct groups of 20 healthy subjects participated in each of the experiments.
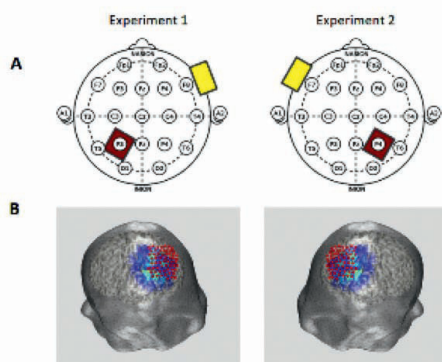
Figure 1. A. Position of the electrodes in two experiments - anode (red) was over lateral parietal cortex while cathode (yellow) was over contralateral cheek. B. Simulation of the induced electric fields under anode (Comets Toolbox, Lee at al. Journal of Neuroscience Methods, 2017, 277: 56–62).
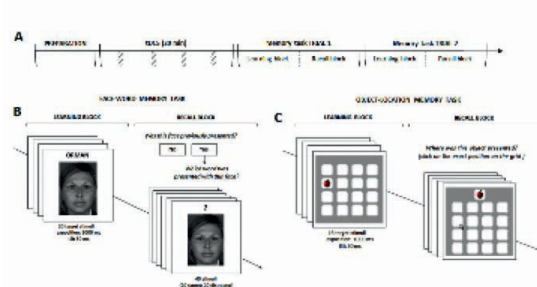
Figure 2. A. Study design. B. Face-word memory task (Experiment 1). C. Object-location memory task (Experiment 2).

Results: The 2x2 repeated measures ANOVA for face-word task showed main effects of stimulation condition [$F(1,19)=7.908$, $p=.011$] and of between-trials learning [$F(1,19)=6.357$, $p=.021$], but no interaction effect [$F(1,19)=0.223$, $p=.642$]. Similar results were for object-location task, i.e. main effects of stimulation condition [$F(1,19)=5.400$, $p=.031$] and learning [$F(1,19)=23.840$, $p<.001$], but no interaction effect [$F(1,19)=0.444$, $p=.531$].
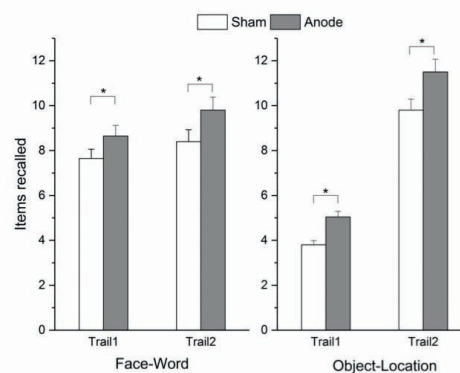

Figure 3. Results (group mean and standard error) from both experiments. Significant difference between conditions (i.e. active vs. sham) is indicated with asterix.

Conclusion: Results suggest that anodal tDCS over lateral parietal cortex is able to facilitate performance in associative memory tasks regardless of the modality of the associations. The tDCS-induced improvement does not interfere with, but acts as add-on to the repetition-induced improvement. Noninvasive neuromodulation seems as a promising new tool for memory enhancement.

Disclosure: The study was supported by project grant (#175012) from the Ministry for Education, Science and Technological Development of Republic of Serbia. Authors have nothing else to disclose.

O326

Assessment of auditory localisation in patients with disorders of consciousness

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Background and aims: Visual pursuit and pain localisation are both considered as signs of consciousness but auditory localisation is not. The objectives of this study are to assess the frequency of auditory localisation in patients with disorders of consciousness and to compare brain metabolism of unresponsive patients with and without auditory localisation in order to determine if this behaviour could be considered as a sign of consciousness.

Methods: We considered retrospectively 228 patients with severe brain injury. We looked at how many of these patients presented auditory localisation. We then measured cerebral metabolism using Fluorodeoxyglucose Positron Emission Tomography (FDG-PET) in a subset of patients in an unresponsive wakefulness syndrome who showed auditory localisation and compared it to unresponsive patients who did not show such behaviour.

Results: Auditory localisation was observed in 10% of unresponsive patients, in 43% of minimally conscious state minus, in 62% of MCS plus (i.e., language processing preserved) and in 76% of patients who emerged from the MCS. FDG-PET results showed brain metabolism differences between unresponsive patients with and without localisation in auditory and consciousness related brain regions.

Conclusion: Our results indicate a relationship between the presence of auditory localisation and the level of consciousness in patients with disorders of consciousness. UWS patients with auditory localisation also showed more preserved brain metabolism than UWS without localisation. These findings suggest that auditory localisation could be considered as a sign of consciousness.

Disclosure: Nothing to disclose

O327

Persistent allocentric navigation deficits indicate hippocampal damage in Transient Global Amnesia

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Background and aims: Although TGA is defined as a temporary loss of working memory, recent studies indicate more persistent deficits in episodic/spatial memory. In the present study, real-space orientation was investigated longitudinally in TGA as a surrogate marker of hippocampal function.

Methods: 18 TGA patients and 14 age-matched controls had to find target items in a realistic spatial environment. Throughout the experiment subjects wore a gaze-controlled, head-fixed camera that recorded their visual exploration behaviour. In 8 patients [18F]-fluorodeoxyglucose was injected during the acute stage at the beginning of the task, to detect navigation-induced brain activations. DWI lesions were recorded by MRI and mapped to the hippocampus in TGA patients.

Results: After 3d of symptom onset, patients with TGA navigated significantly worse and had a higher error rate than controls in allocentric (p=0.002) but not egocentric route planning (p=0.16), despite recovery of non-spatial working memory. Spatial disorientation increased with age, TGA duration, and hippocampal DWI lesion size. Navigation-induced brain activation was increased in the right anterior hippocampus, retrosplenial/parietal/mesiofrontal cortex and dentate nucleus bilaterally compared to controls. Allocentic navigation deficits improved slightly within 3m after TGA onset, but were still significant compared to controls (p=0.05). Patients above age 65 had a worse course of recovery. The navigation strategy of TGA patients was severely altered in the acute stage and during follow-up: they used fewer shortcuts and stayed longer at crossings.

Conclusion: TGA patients show persistent deficits in allocentric real-space navigation indicating enduring microstructural hippocampal damage. PET imaging indicates a recruitment of extrahippocampal hubs of the cerebral navigation network.

Disclosure: The study was performed as a project of the German Center for Vertigo and Balance Disorders (DSGZ) (grant number 01 EO 0901) with support of the German Federal Ministry of Education and Health (BMBF).

MS and related disorders 2

O328

Efficacy of Ozanimod versus Interferon beta-1a by DMT treatment experience and EDSS categorisation from a multicenter, randomised, double-blind, phase-3 study of relapsing Multiple Sclerosis

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Background and aims: Ozanimod is an oral, once-daily immunomodulator selectively targeting sphingosine 1-phosphate receptors 1 and 5. Annualised Relapse Rate (ARR) was evaluated by pre-specified baseline subgroups that included prior Disease-Modifying Treatment (DMT) status, Expanded Disability Status Scale (EDSS; ≤3.5 or >3.5), sex, age (≤40 or >40 years), and presence of GdE lesions.

Methods: Patients with Relapsing Multiple Sclerosis (RMS) in the RADIANCE Part B (NCT02047734) study received ozanimod HCl 1 or 0.5 mg vs Interferon (IFN) beta-1a 30 µg for 24 months.

Results: In 1313 patients, ARR over 24 months was significantly reduced for Ozanimod 1mg (0.172, P<0.0001) and 0.5mg (0.218, P=0.0167) compared with IFN beta-1a (0.276). ARR was lower with Ozanimod 1mg (0.157) and 0.5mg (0.228) vs IFN beta-1a (0.246) among DMT-naïve patients (71% of population) as well as lower for Ozanimod 1mg (0.205) and 0.5mg (0.191) vs IFN beta-1a (0.357) among DMT-experienced patients (see Table). ARR was lower with Ozanimod 1mg (0.146) and 0.5mg (0.183) than with IFN beta-1a (0.237) in patients with baseline EDSS ≤3.5 (85% of population), with similar effects for EDSS >3.5.

Conclusion: Ozanimod had significantly lower ARR than IFN for both doses; in addition, Ozanimod showed reduced ARR across a broad range of subgroups, with 1mg generally having better rate ratios than 0.5mg, supporting the potential of Ozanimod as an effective oral treatment in a broad spectrum of patients with RMS.

Disclosure: Nothing to disclose

O329

Multiple Sclerosis Impact Scale and brain volume are independent predictors of cognitive impairment in Secondary Progressive Multiple Sclerosis

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Background and aims: Cognitive deficits in Multiple Sclerosis (MS) affect up to 70% of patients with progressive MS. We investigate the associations between the disease specific Multiple Sclerosis Impact Scale psychological subscale (MSIS-29v2-PSYCH), Magnetic Resonance Image (MRI) normalised brain volume and cognitive impairment in people with Secondary Progressive MS

(SPMS).

Methods: A group of SPMS patients were recruited at baseline from a randomised phase 2 clinical trial(MS-SMART). Patients were assessed using a cognitive test battery to define cognitive status based on conservative criteria (standard deviation of z-score of -1.96 on ≥2 tests), and completed the MSIS-29v2 questionnaire. Normalised brain volume(NBV) was measured using the geodesic information flow and SIENAX algorithms. We analysed associations of cognitive impairment with MSIS-29v2-PSYCH subscale and brain volume using binary logistic regression.

Results: 60 subjects were analysed with baseline characteristics. We find NBV and MSIS-29v2-PSYCH to be independent predictors of cognitive impairment after adjusting for age, gender and years of education. There is a significant negative association between NBV and cognitive impairment (OR: 0.45; 95% CI: 0.21-0.84; p=0.0191) and a significant positive association between MSIS-29v2-PSYCH and cognitive impairment (OR: 1.89; 95% CI: 1.03-3.72; p=0.0491).

Conclusion: MSIS-29v2-PSYCH is therefore useful predictor of cognitive impairment in a SPMS patients, but in our logistic regression methodology may be confounded by NBV. Longitudinal data will confirm MSIS-29v2-PSYCH as a marker of MS future cognitive status.

Disclosure: The MS-SMART (NCT01910259) trial is a project funded by the Efficacy and Mechanism Evaluation (EME) Programme, an MRC and NIHR partnership. It is also supported by the UK and National Multiple Sclerosis Society; the National Institute for Health Research University College London Hospitals Biomedical Research Centre and University College London; NIHR Leeds CRF (DenTCRU). CJW and RP were supported in this work by NHS Lothian via the ECTU. The remaining authors declare no conflict of interests with respect to this work.

O330

Siponimod affects disability progression in SPMS patients independent of relapse activity: results from the phase III EXPAND study

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Background and aims: In the EXPAND study, Siponimod reduced the risk of Confirmed Disability Progression (CDP) in patients with Secondary Progressive Multiple Sclerosis (SPMS). We assessed the impact of Siponimod on CDP in patients with/without relapses to uncouple the treatment effect on CDP from the effect of relapses.

Methods: We analysed the impact of Siponimod on CDP by: (a) subgroup analysis using the Cox model on time to 3 month- (m)/6m-CDP in patients with/without relapses in 1- and 2-years before study; (b) principal stratum analysis to estimate the effect in patients who would not have relapsed on-study by m12, m18 and m24, regardless of treatment; (c) Cox model on time to 3m/6m-CDP in the overall population, censoring at time of first relapse.

Results: For non-relapsing patients in 1- and 2-years before study, risk reductions were 18% (HR, 0.82 [CI:0.66;1.02]) and 13% (0.87 [0.68;1.11]) for 3m-CDP and 25% (0.75 [0.59;0.96]) and 18% (0.82 [0.62;1.08]) for 6m-CDP, respectively. For relapsing patients in 1- and 2-years before study, risk reductions were 33%/33% (3m-CDP) and 30%/37% (6m-CDP), respectively. In the principal stratum estimate, siponimod reduced 3m-CDP by 14–20% and 6m-CDP by 29–33% in non-relapsing patients across the 3 intervals, suggesting that these patients can achieve a large portion of the effect on overall population. Cox model censoring at relapses confirmed beneficial effect reaching nominal statistical significance (6m-CDP: HR 0.77 [0.62;0.96]).

Conclusion: Siponimod reduces the risk of CDP in SPMS patients with/without relapses; our analyses indicate that its effect on disability is largely independent from its effect on relapses.

O331

Phase-2 multicenter study results of Ublituximab, a novel glycoengineered antiCD20 monoclonal Antibody (mAb), in patients with Relapsing Multiple Sclerosis (RMS)

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Background and aims: Ublituximab, a novel chimeric mAb targeting a unique epitope on the CD20 antigen, is glycoengineered to enhance affinity for all variants of FcγRIIIa receptors, demonstrating greater Antibody-Dependent Cellular Cytotoxicity Activity (ADCC) than Rituximab. This enhanced ADCC potency may offer benefits over currently available anti-CD20s in terms of lower doses and shorter infusion times. This Phase-2 study examines Ublituximab's effect on B-cell depletion and key clinical measures in RMS patients.
Methods: TG1101-RMS201 is a 52-week, Phase-2, placebo-controlled, multicenter study designed to assess the optimal dose and infusion time of Ublituximab in RMS subjects. All subjects, including placebo subjects (post-placebo phase), receive 3 Ublituximab infusions on Days 1, 15, and Week 24.
Results: All subjects (24/24) exceeded the target level of 95% B-cell depletion within 4 weeks of Ublituximab treatment. To date, 11 of 24 subjects have completed all assessments in the 52-week trial, where 87% remain relapse-free and 81% are confirmed free of disability progression. There was 100% reduction of T1 Gd-enhancing lesions at 52 weeks. Common adverse event (AE) was IRRs (all grade 1 or 2, in 17% of subjects). No severe AEs were associated with Ublituximab treatment. Faster infusion time (as low as 1 hour) did not correlate with an increased IRR frequency.
Conclusion: The Phase-2 results suggests Ublituximab, with infusion times as low as one hour, is safe and well tolerated, with favorable clinical and MRI outcomes at Week 52. We will be reporting the immunological and clinical data set for all subjects at the date of presentation.
Disclosure: This Phase-2 study was supported by TG Therapeutics, Inc.

O332

Measuring disease activity in Multiple Sclerosis: do we need spinal cord MRI?

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Background and aims: Magnetic Resonance Imaging (MRI) of the Spinal Cord (SC) is recommended during diagnostic process in suspected Multiple Sclerosis (MS), while its role in monitoring disease evolution or as a surrogate marker in clinical trials, is still controversial. We hypothesise that using brain MRI only might fail in detecting inflammation in a proportion of patients. Thus we aimed to study the frequency of SC acute inflammatory activity and whether it occurs independently from brain activity.
Methods: From MS registry, we selected patients fulfilling the following criteria: 1) diagnosis of MS; 2) having received at least two different MRI (brain and SC) scan at two time point (at least 30 days apart); 3) MRI reports available. Inflammatory activity was defined as the presence of at least one Gd enhancing lesion according to its location (brain/SC-both).
Results: Demographical and clinical data are listed in Table 1. A total of 5717 scans were reviewed, 4537 (79,3%) did not present Gd enhancement. Of the 1180 scans left, 651 (55,2%) showed brain Gd enhancing lesions only, 232 (19,7%) a concomitant presence of brain and SC Gd enhancing lesions, while 297 (25,2%) showed SC Gd enhancing lesions exclusively

Table 1. Demographical and clinical characteristics of patients included in the study

Number of Patients in the original MS registry	1332
Number of patients selected	828
Proportion Female/Male	572/256
*Medium age (SD)	34.7 (9.7)
*Median Expanded Disability Status Scale (EDSS) [range]	2.0 [0-8]
*Medium Disease Duration (SD)	5.8 (6.3)
Medium scans for patient (SD)	7 (2)
* Calculated according to the first scan date	

Demographical and clinical characteristics of patients included in the study

Conclusion: Our study demonstrates that inflammatory activity can be detected frequently in SC and occurs in approximately 25% alone. Limiting MRI monitoring to brain, underestimates inflammatory activity thus requiring a larger sample in clinical trials. MRI monitoring of SC in clinical practice will allow neurologists to switch treatment to more powerful drugs in a larger number of patients
Disclosure: Nothing to disclose

O333

A neurometabolic profile of SPMS: the relationship between brain metabolites and clinical disability

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Background and aims: Neurometabolite concentrations measured using magnetic resonance spectroscopy imaging (1H-MRSI) could be potential biomarkers of progression in Secondary Progressive Multiple Sclerosis (SPMS). Here we explore the neurometabolic characteristics of a SPMS cohort and investigate their associations with clinical disability.

Methods: A baseline cross sectional analysis of 52 patients was performed from a trial of neuroprotection in SPMS (MS-SMART NCT01910259). Subjects underwent a standardised 1H-MRSI protocol (2D-PRESS TE=35ms) to measure neurometabolites. Spectra were then analysed using LCmodel to obtain absolute values for neurometabolites including total N-acetyl aspartate (tNAA) and myo-Inositol (mIns). Subjects underwent the Paced Auditory Serial Addition Test (PASAT), Symbol Digit Modalities Test (SDMT) and Expanded Disability Status Scale (EDSS) as part of a clinical assessment.

Kendall's tau-b correlation coefficients followed by multivariable linear regression analysis adjusted for age, gender, disease duration, EDSS and T2 lesion volume, were used to investigate the association between clinical outcome measures and neurometabolites.

Results: Table 1 reports the demographics and clinical characteristics of the cohort. Significant correlations were seen between tNAA, and PASAT (t=0.315,p=0.001) and SDMT scores (t=0.315, p=0.001). tNAA/tmIns showed significant correlation with PASAT (t=0.336,p=.001) and SDMT (t=0.306,p=0.002). Regression analysis showed that tNAA and tNaa/tmIns statistically significantly predicted SDMT and PASAT scores.

Baseline demographics and clinical characteristics

Conclusion: We have shown tNAA and tNAA/mIns, markers for neurodegeneration and gliosis, correlate with measures of cognition and can predict the presence of cognitive deficits in SPMS, making them strong candidates for biomarkers of cognitive impairment in MS.

Sleep disorders

O334

Sleep microstructure in Parkinson's Disease: Cycling Alternating Pattern (CAP) as a sensitive marker of early NREM sleep instability.

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Background and aims: Sleep disorders are frequent in Parkinson's Disease (PD). Apart from the occurrence of REM behavior disorders, in the early phase of disease standard sleep macrostructure evaluation was inconclusive. We analyzed NREM sleep microstructure (CAP) in a group of PD patients, in order to provide an objective measure of sleep disruption.

Methods: We recruited 31 PD patients (mean age 59.5±12.4 years; mean Hoehn-Yahr (H-Y) stage: 3.4±1.8) and 34 age-matched non-parkinsonian subjects (mean age 61.5±15.2 years) as control group. All patients underwent a full-night laboratory polysomnography (PSG). Conventional sleep macro/microstructure analysis were performed. Patients were then divided into two groups: group 1 (H-Y stage≤2) and group 2 (H-Y stage≥3).

Results: In group 2 of PD patients alterations of both sleep macrostructure and microstructure were found, compared to controls. More interestingly, PD subgroup with milder disease (group 1) presented sleep macrostructure, movements and respiratory parameters not significantly different from controls, while CAP rate was significantly higher and proportion of A1 phase of CAP was reduced. Multivariate logistic regression showed that disease duration, disease severity and arousal index emerged as independent predictive factors for CAP rate ³ 55% (Table 1) and A1 phase of CAP £ 40% (Table 2).

	Exp (B)	C.I.	p
Age	1.02	0.3 - 1.3	NS
H&Y: 3-4	10.7	1.4-14.2	0.002*
Disease duration	7.8	1.2-11.5	0.01*
% REM	0.4	0.1-3.9	NS
Sleep efficiency	0.8	0.2-2.4	NS
RBD	0.3	0.1-4.8	NS
PLM index	1.3	0.5-2.8	NS
Arousal index	2,1	0.9-5.1	0.05*

Table 1. Independent predictive factors for CAP rate>55%

	Exp (B)	C.I.	p
Age	1.12	0.2 - 1.5	NS
H&Y: 3-4	5.1	1.8-16.2	0.04*
Disease duration	8.7	2.3-11.5	0.001*
% REM	0.7	0.1-5.2	NS
Sleep efficiency	0.5	0.2-2.1	NS
RBD	0.6	0.2-3.5	NS
PLM index	1.7	0.3-3.2	NS
Arousal index	3.1	0.7-7.2	NS

Table 2. Independent predictive factors for A1 proportion<40%

Conclusion: The main result of our study consists in the disclosure of altered NREM sleep microstructure in PD, even at an earlier stage of the disease, so suggesting early alteration of the central pathways involved in the NREM sleep building-up and stability.

Disclosure: Nothing to disclose

O335

Reliability of a standardized test to document cataplexy to identify hypocretin deficiency

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Background and aims: Type 1 narcolepsy (NT1) diagnosis requires the evidence of cerebrospinal hypocretin deficiency (biological disease fingerprint) or the presence of neurophysiological criteria coupled with definite history of cataplexy. We recently standardized a laboratory test to video document cataplexy under emotional stimulation, and the current study aimed at testing its predictive value towards hypocretin deficiency in consecutive drug-free patients.

Methods: We analyzed in a population of 151 consecutive patients (101 with NT1, 28 with other hypersomnias of central origin, and 22 with subjective sleepiness complaint) the diagnostic potential of our standardized test for cataplexy documentation against the evidence of hypocretin deficiency with ROC curve analysis. Video recordings were analyzed by a technician blind to clinical suspicion, and occurrence of possible hypotonic phenomena were subjectively confirmed by patients (positive test).

Results: Positive test results had an area under the ROC curve of 0.805 ± 0.043 ($p<0.0001$) against the biological disease marker of NT1. The most useful parameters at semi-quantitative blind assessment were ptosis (area=0.732 ± 0.048, $p<0.0001$), head drop (area=0.682 ± 0.051, $p=0.001$), and mouth opening (area=0.674 ± 0.051, $p=0.002$) under emotional stimulation, while trunk dyscontrol and assessments in baseline conditions did not provide any significant result.

Conclusion: Video documentation of suspected cataplexy may help to identify NT1. Further studies should evaluate the potential diagnostic value of automatic hypotonia detection from video recordings of facial expression during emotionally triggered laughter.

Disclosure: Nothing to disclose

O336

Effects of acute exposure to high altitude on RLS symptoms and PLMS: a bilateral study

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Background and aims: Peripheral tissue hypoxia has been associated with restless legs syndrome (RLS) symptoms and is correlated with RLS severity. A higher RLS prevalence was reported at high altitude compared to coastal regions. Aim of this study was to investigate the influence of acute exposure to high altitude on Periodic Leg Movements during Sleep (PLMS) in patients with RLS and matched controls.

Methods: 20 patients with RLS and 13 healthy sex- and age-matched controls were investigated in a altitude chamber in randomised order: one night in a simulated altitude environment with normobaric hypoxia corresponding to 3000m above sea level, and a control night at Innsbruck local altitude (574m). Before each night, a Suggested Immobilisation Test (SIT) was performed in the same environment. Polysomnography and PLMS scoring were performed according to AASM criteria.

Results: Median age of participants was 49 (range 40-52) years. Median IRLS in the patient group was 16 (range 13-28). Motor symptoms during SIT and during the whole night were more severe at 3000m as compared to Innsbruck local altitude in the patient group. In subgroup analysis, this was confirmed for untreated patients and for patients under dopaminergic therapy. PLMS index showed no difference between the two nights ($p>0.05$)

Conclusion: We found a trend towards more severe RLS symptoms at high altitude. RLS therapy may modulate the effects of hypoxia on RLS symptoms and PLM. In RLS pathogenesis, peripheral hypoxia may represent a downstream secondary alteration, due e.g. to iron dysregulation or dopaminergic dysfunction. Further studies with larger sample sizes are needed.

Disclosure: We are thankful to Sten Sevborn and the Swedish RLS Foundation for supporting the participation of patients from Sweden in this study.

O337

Actigraphy ultradiam and circadian rhythmicity in disorders of consciousnes

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Background and aims: The Unresponsive Wakefulness Syndrome and Minimally Conscious State (UWS; MCS) are characterized by the absence or the presence but severe disordered signs of consciousness in spite of the presence of preserved sleep-wake cycles. Spectral entropy has used to find periodicity on EEG signals of DOC (disorders of consciousness) patients. Circadian and ultradian are fisiological rhythmits found in all living organisms.

Methods: We used data from 126 patients (controls, EMCS, LIS, MCS, MCS+, MCS-, MCS*, and UWS). We recorded the movements on the wrist for 7 consecutive days, then we use average 5 complete days in 24 hours to compute the circadian rhythmicity and in 120 min to compute the ultradian rhythmicity. Spectral entropy is used to compute to find the signficant diffference inthe amplitude of the movements and its periodicity (spectral amplitude) is used to find the rhythmicity.

Results: We have found a circadian rhythmicity in DOC patients within 18 hours in average and and ultradiam rhythmicity between 40 to 80 min.

Conclusion: The actigraphy can give useful information about the circadian and ultradian rhytmicity in DOC patients.

Disclosure: Nothing to disclose

O338

Autoreactive T-cells in narcolepsy patients target multiple antigens of hypocretin-producing neurons

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Background and aims: Narcolepsy is an orphan chronic neurological disorder caused by the selective loss of neuronal cells of the lateral hypothalamus that produce the neuropeptide hypocretin (HCRT). There is increasing evidence that narcolepsy is an immune-mediated, T cell-mediated disorder that manifests in genetically (HLA-DQB1*06:02) predisposed individuals upon exposure to environmental factors, such as infection. However, unambiguous identification of HCRT-specific T cells in narcolepsy patients is still lacking.

Methods: Assessment of narcolepsy patients and controls included clinical, sleep laboratory and laboratory (CSF, blood) data. In order to characterize memory T cells, we combined antigenic stimulation, T cell cloning, and TCR deep sequencing.

Results: We isolated autoreactive CD4+ and (occasionally) CD8+ T cell clones specific for HCRT and other self-antigens expressed by HCRT-producing neurons (e.g. TRIB2) from 80% of patients (n=18), including those lacking the HLA-DQB1*06:02 allele, but were found in only 20% of healthy HLA-DQB1*06:02 donors. The CD4+ T cell response was polyclonal, and directed against multiple epitopes. Autoreactive T cell clones recognized exogenous peptides but failed to respond to whole proteins, suggesting that the epitopes recognized are generated by extracellular processing. TCR sequencing of CSF T cells identified clonotypes present in blood of the same and also in some cases of different patients.

Conclusion: Our data demonstrate the existence of autoreactive CD4+ and CD8+ T cells that target different neuronal antigens in narcolepsy patients. These data have potential implications for the (early) diagnosis and (causal) treatment of narcolepsy and its borderland.

Disclosure: Nothing to disclose

O339

Differential diagnosis in excessive daytime sleepiness based on sleep- and vigilance tests: a preliminary analysis of the Bern sleep database

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Background and aims: After excluding the most frequent causes of excessive daytime sleepiness, e.g. sleep apnoea, a few ambiguous diagnoses remain, and their differential diagnosis is still challenging. Sleep and vigilance tests are used as additional and supportive tools in the process of diagnosing. This study aimed to determine the extent to which these tests can help to differentiate between Narcolepsy with Cataplexy (NC), without Cataplexy (N), Idiopathic Hypersomnia (IH), Non-Organic (psychiatric) Hypersomnia (NOH), and psychiatric Fatigue Syndromes (FS).

Methods: The Bern sleep database contains >17,000 sleep and vigilance tests. We retrospectively analysed those 102 NC, 63 N, 86 IH, 155 NOH, and 167 FS patients who underwent ≥1 MSLT and ≥1 additional sleep or vigilance test. The patient groups were compared with each other (=10 pairs) for each test (ANOVA, post-hoc Bonferroni; significance level $p < 0.05$).

Results: Mean values differed significantly in 8/10 diagnoses-pairs in both the maintenance of wakefulness test (MWT) and the multiple sleep latency test (MSLT), and in the other tests: Epworth sleepiness scale (7/10), Steer Clear test (6/10), pupillary unrest index (5/10), psychomotor vigilance test (4/10), actigraphy inactivity index and sleep efficacy in polysomnography (2/10).

Conclusion: The MWT and the MSLT are the most valuable diagnostic tests to differentiate between N-NC-IH-NOH-FS. This is relevant if tests must be limited to a low number. However, single sleep and vigilance tests have a rather poor differentiating power and combining a higher number of tests to accurately diagnose patients suffering from excessive daytime sleepiness may be favourable.

Disclosure: Nothing to disclose

Tuesday, 19 June 2018

Headache and pain

O401

Cluster Headache is more than the extreme pain attack: a prospective diary study of 500 Cluster Headache attacks

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Background and aims: In contrast to the premonitory and resolution phases of migraine, only little is known about the pre-ictal and post-ictal phase of a Cluster Headache (CH) attack. We aimed to describe the nature, prevalence and duration of symptoms in the pre-ictal, ictal and post-ictal phases of CH attacks.
Methods: 57 patients with episodic CH (eCH) or chronic CH (cCH) participated in this prospective observational study. Patients reported presence and duration of 34 CH and migraine related symptoms in the pre-ictal, ictal and post-ictal phases of up to 10 CH attacks/patient. Symptoms were grouped in 3 categories: Local and painful; Local and painless (including autonomic symptoms) and general symptoms. Duration of symptoms presented as medians.
Results: In total 500 CH attack descriptions were obtained. Pre-ictally local and painful symptoms, occurring 10 minutes before the attack, were reported in 54.4% of attack; Local and painless symptoms occurring 10 minutes before, occurred in 35.0% of attacks; and general symptoms, occurring 20 minutes before 46.0% of attacks. Post-ictally local and painful symptoms, lasting 30 minutes were reported after 43.6% of attacks; local and painless symptoms lasting 20 minutes, after 40.8% of attacks; and general symptoms, lasting 37.5 minutes after 66.4% of attacks.
Conclusion: Pre-ictal and post-ictal symptoms are very frequent in CH indicating that a CH attack is not restricted to the pain-phase alone. Since the origin of CH attacks is unresolved, studies of pre- and post-ictal symptoms could contribute to the understanding of CH-pathophysiology and potentially early abortive treatment strategies.
Disclosure: Nothing to disclose

O402

Increased preictal beta-ERD-response of primary sensorimotor cortex during brief hand movements with sensory stimulation in migraine

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Background and aims: Different neurophysiological modalities have shown cyclic alterations in the migraine brain. In the present blinded longitudinal study we aimed to evaluate if neurophysiological properties of sensorimotor cortex changed before the migraine attack. We applied low-beta (12 – 19 Hz) Event Related Desynchronization (ERD) because it is thought to represent cortical activity of afferent inputs during movement tasks.
Methods: Thirty-three migraine patients and thirty-one healthy controls underwent three consecutive EEG-examinations. Participants executed repeated movement tasks with and without sensory discrimination, and we analyzed ERD from sensorimotor cortex 1 – 3 seconds after movement onset. We chose a cutoff of 36 hours before each headache attack to define the preictal phase, and twelve migraine patients were available for the interictal – preictal paired analysis.
Results: A significant ERD-response was seen during the combined sensorimotor task. There were no differences between migraine patients in the interictal phase and healthy controls. However, in the preictal period the migraine patients had a significant increase in lower beta-ERD compared to the interictal phase in the contralateral sensorimotor cortex for both tests (Paired student's t-test, sensorimotor p=0.038; motor p=0.049).
Conclusion: Neurophysiological function of the sensorimotor cortex measured as lower beta-ERD changed from normal interictal values to increased ERD-responses preictally in migraine patients. We interpret the findings as alterations in cortical processing of sensory input before the migraine attack. Increased ERD suggests that a cortical or thalamo-cortical hyperactivity is present even before the onset of headache.
Disclosure: Nothing to disclose

O403

Identifying natural subgroups of migraine based on profiles of Comorbidities and Concomitant Conditions: results of the Chronic Migraine Epidemiology and Outcomes (CaMEO) Study

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Background and aims: Migraine is a complex disease. Identifying natural subgroups (endophenotypes) may facilitate biological and genetic characterization and individualization of treatment. We sought to identify natural subgroups of migraine based on profiles of Comorbidities and Concomitant Conditions (CCCs).

Methods: The CaMEO Study is a prospective web-based survey study designed to characterize the course of migraine and related comorbidities in a systematic US sample of people meeting modified ICHD-2 criteria. Respondents were asked if they ever had a specific condition/symptom and, if present, if the symptom/condition was confirmed/ diagnosed by a "doctor"; 62 CCCs were available for analysis. Latent Class Analysis (LCA) modeled the optimal number of classes and a parsimonious set of CCCs

Results: Of the 12,810 respondents, 11,837 reported ≥ 1 CCC and were included in this analysis. An 8-class model was empirically selected containing 22 comorbidities/ variables. Each class had a distinct CCC pattern, characterized as follows: Class 1, many CCCs; Class 2, respiratory/psychiatric; Class 3, respiratory/pain; Class 4, respiratory; Class 5, psychiatric; Class 6, cardiovascular; Class 7, pain; Class 8, few CCCs. The distribution of individuals across models was variable with one-third of respondents in Class 8 (few CCCs) and <10% in Class 1 (many CCCs). Demographic and clinical characteristics varied across classes.

Conclusion: LCA modelling identified 8 underlying patterns of comorbid health problems among people with migraine. These classes show differences in headache features and treatment patterns not used to form the classes. Subsequent research will assess prognostic differences among the classes.

Disclosure: The funding source for this study is Allergan plc (Dublin, Ireland)

O404

The long-term efficacy and safety of OnabotulinumtoxinA for the prevention of chronic migraine in patients with medication overuse: results of the COMPEL study

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Background and aims: This sub-analysis of COMPEL Study data evaluates long-term efficacy and safety of OnabotulinumtoxinA in those with acute pain Medication Overuse (MO).

Methods: The 108-week, multicentre, open-label COMPEL Study enrolled adults with CM receiving OnabotulinumtoxinA 155U for 9 treatments. Patients completed a daily diary recording headache days; Migraine Disability Assessment (MIDAS) was collected via patient-completed questionnaires. Adverse events were monitored. MO was defined as those using acute pain medication at baseline on ≥ 5 diary days/week and then ≥ 2 days/week with the additional requirements for simple analgesics ≥ 15 days/ month or for ergotamines, triptans, opioids or combination analgesics, ≥ 10 days/month. Observed data are reported.

Results: Of the 716 enrolled patients, 639 patients (89.2%) used acute pain medication; with 456 patients (63.7%) classified as having MO. Compared to patients without MO, those with MO were slightly older (44.1 [10.9] vs 41.1 [11.7] years), and more likely to be Caucasian (84.9% vs 74.9%). Mean (SD) headache day frequency at week 108 significantly decreased from baseline in the analysis population: 22 (4.8) to 11.3 (7.4) days (P<0.0001). In the subgroup analysis, the effect of onabotulinumtoxinA was similar in patients with and without MO on reduction in headache days (−11.4 [7.2] vs −12.5 [7.5] days), and MIDAS scores (−41.8 [48.0] vs −48.7 [59.6], P<0.0001. OnabotulinumtoxinA was well tolerated in the MO population, with no new safety concerns.

Conclusion: Results suggest that OnabotulinumtoxinA reduces headache day frequency and improves disability and is well tolerated in the MO population.

Disclosure: The funding source for this study is Allergan plc (Dublin, Ireland)

O405

Phase-3 study (SPARTAN) of Lasmiditan compared to placebo for acute treatment of migraine

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Background and aims: Investigated Lasmiditan in a double-blind, phase-3 study (SPARTAN; NCT02605174) on headache pain and the patient-centric measure of most bothersome symptom (MBS; nausea, phonophobia, or photophobia) at 2 hours post-dose.

Methods: Patients with a Migraine Disability Assessment Score >11 were randomised 1:1:1:1 to Lasmiditan (200mg, 100mg, or 50mg) or placebo. Patients took first dose within 4 hours of a migraine attack and, if needed, took a randomly assigned second dose. Primary and key secondary analyses compared patients in the lasmiditan 200-mg group with placebo who were headache pain-free and MBS-free at 2 hours post-first dose, respectively.

Results: Proportion of patients headache pain-free and MBS-free at 2 hours post-first dose was significantly greater with Lasmiditan 200mg (38.8%, 48.7%; p<.001 both), 100mg (31.4%, 44.2%; p<.001 both), and 50mg (28.6%, 40.8%; p<.01 both) than placebo (21.3%, 33.5%). In lasmiditan 200mg, 100mg, 50mg or placebo groups, 29.1%, 34.5%, 40.3%, and 48.1% took a second dose, respectively. Proportion of patients who experienced a TEAE after the first dose of lasmiditan 200mg, 100mg, 50 mg or placebo were 39.0%, 36.1%, 25.4%, and 11.6%, respectively and most frequently reported dizziness, paresthesia, and somnolence.

Conclusion: SPARTAN met the primary and key secondary endpoint of pain-free and MBS-free at 2 hours for Lasmiditan 200mg. Lasmiditan 100mg and 50mg were also significant on the same endpoints compared to placebo. Safety was consistent with a previous Lasmiditan trial, with dizziness reported as the most frequent TEAE.

Disclosure: Sponsored by Eli Lilly and Company and/or one of its subsidiaries.

O406

Field testing the diagnostic criteria for headache attributed to Transient Ischemic Attacks

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Background and aims: The International Classification of Headache Disorders diagnostic criteria for Headache Attributed to Transient Ischemic Attacks and many other secondary headaches are based primarily on the opinion of experts. Here we formally analyze, for the first time, the diagnostic criteria for headache attributed to Transient Ischemic Attacks.

Methods: Consecutive patients with Transient Ischemic Attacks were extensively interviewed soon after admission. Eligible patients had focal brain or retinal ischemia with resolution of symptoms within 24 hours without presence of new infarction on magnetic resonance imaging with diffusion weighted imaging (n=112) or computed tomography (n=8). Data were collected on previous headaches, headaches around the time of Transient Ischemic Attacks and characteristics of Transient Ischemic Attacks using validated neurologist conducted semi-structured interview forms.

Results: 120 patients with Transient Ischemic Attacks were included. A new type of headache occurred within 24 hours of Transient Ischemic Attacks in 13%, a preexisting type of headache with altered characteristics in 7.5% and without altered characteristics in 6.6%. The risk of headache was much greater with posterior circulation Transient Ischemic Attacks than with anterior. Only 24% of the headaches fulfilled the criteria of the International Classification of Headache Disorders. We propose new criteria fulfilled by 94% of the headaches and argue that specificity remains good.

Conclusion: Existing diagnostic criteria for headache attributed to Transient Ischemic Attacks are too insensitive. We suggest new diagnostic criteria with high sensitivity and argue why they are still valid.

Disclosure: Nothing to disclose

Miscellaneous 2

O407

Reduced pupillary modulation in patients with relapsing-remitting Multiple Sclerosis is associated with longer disease duration and higher disease severity

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Background and aims: Pupillary dysfunction is common in patients with Relapsing-Remitting Multiple Sclerosis (RRMS) and may be due to central MS lesions. So far, it is unclear whether the degree of pupillary autonomic dysfunction is associated with disease-duration and severity. Therefore, we aimed at evaluating correlations between pupillary autonomic modulation and disease-duration and severity in RRMS-patients.

Methods: In 85 RRMS-patients (mean age 37.4 ± 10.4 years, 58 women, disease-duration 91.1 ± 81.0 months), we performed light reflex pupillography using a CIP 9.08TM pupillometer (45-min dark-adaptation, 1.25-ft candles background illumination; 200ms light stimulation at 104 cd brightness). We determined pupil-diameter, early and late re-dilatation velocities as sympathetic parameters, light-reflex-latency, reflex-amplitude, and constriction-velocity as parasympathetic pupillary indices. MS-severity was assessed by the Expanded-Disability-Status-Scale (EDSS) and the Multiple-Sclerosis-Functional-Composite (MSFC). The Spearman signed rank test was used to determine correlations between pupillary parameters and disease-duration, EDSS- and MSFC-scores. Significance was set at $p<0.05$.

Results: EDSS-scores were 2.5 [1.5-3.5] (median; interquartile range), MSFC-scores were -0.11 ± 0.80. Pupil-diameter correlated negatively with age, disease-duration and EDSS-scores. Early re-dilatation velocity correlated negatively with age, disease-duration and EDSS-scores and positively with MSFC-scores. Reflex-latency correlated positively with age, disease-duration and EDSS-scores, and negatively with MSFC-scores. Reflex-amplitude correlated negatively with age, disease-duration, and positively with MSFC-scores. Constriction-velocity correlated negatively with age, EDSS-scores and positively with MSFC-scores.

Conclusion: In our RRMS-patients, the decrease in sympathetic and parasympathetic pupillary autonomic modulation was associated with longer disease-duration and higher disease-severity. These additional markers of MS severity and progression may be easily assessed by the non-invasive light reflex pupillography.

Disclosure: Nothing to disclose

O408

Early hemodynamic profile in tilt-induced vasovagal syncope

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Background and aims: Little is known about whether asystole during syncope is reflected in the hemodynamic pattern of Vasovagal Syncope (VVS) during Tilt Table Testing (TTT) in the 10 minutes before syncope.

Methods: TTT data were gathered from the database of our tertiary Syncope Unit. Inclusion criteria were probable VVS, based on a clinical history and syncope during TTT, established using continuous Blood Pressure (BP), Heart Rate (HR), EEG and video data. Exclusion criteria were additional diagnoses or incomplete data. We sampled BP, HR, Cardiac Output (CO), Stroke Volume (SV) and Total Peripheral Resistance (TPR) every second of 10 minutes before syncope and compared their course over time using vectors from singular value decomposition. We first analysed these variables for all cases and then compared groups with and without asystole.

Results: Over all 154 patients, BP started to decline ~6 minutes before syncope after which the decrease accelerated. The mechanism behind low BP is likely the consistent decrease in SV, not sufficiently countered by an increase in HR or TPR, so CO fell. In patients with asystole BP decreased later but much more steeply then in those without asystole ($p=<0.01$).

Conclusion: We confirm that the main factor explaining low BP in tilt-induced VVS is a decrease in SV, probably due to an inability to prevent venous pooling. Asystole during syncope is reflected in a specific hemodynamic pattern well before syncope.

Disclosure: Nothing to disclose

O409

'JUMP', an innovative trans-pathology transitional care program for young adults with chronic neurological disease

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Background and aims: The "JUMP program" is a trans-pathology multi-disciplinary transitional program developed at the Pitie-Salpêtrière Hospital, Paris which optimises the transition of young adults with chronic neurologic conditions into adult services while addressing adolescent-health related challenges. The JUMP team comprises of two coordination nurse specialists, 13 neurology sub-specialists and a dedicated team of medical specialists and allied health-care professionals.

Methods: Demographic and clinical details of patients in the JUMP program were collected. Two satisfaction outcome measures were sent to patients and their parents; an 18-item On Your Own Feet Transfer Experience Scale (OYOF-TES) rated on a five-item Likert scale (total score=90) and a 10-point visual analogue scale.

Results: A total of 133 patients were referred to the JUMP program. The median age at inclusion to the JUMP program was 19.7 years (range: 14.6 – 36.1 years), 73 patients (54.9%) were female. All patients met the coordination nurse specialists who tailored the transition process to address the current life concerns of each patient. In addition to their neurologist of referral, 67% saw an allied-health professional. The mean transfer experience, as assessed by the visual analogue scale, was 9.19 (range, 6 - 10, SD 1.13). The mean score of the OYOF-TES for patients was 75.2 (SD=7.5; range, 62 - 89) and 63 (SD=9.5; range, 58 – 90) for parents.

Conclusion: The JUMP program, which is rooted in a multi-disciplinary and coordinated approach to transitional neurology care, demonstrated high levels of satisfaction on satisfaction outcome measures completed by patients and their parents.

Disclosure: Nothing to disclose

O410

Characterization of a Listeria monocytogenes meningitis mouse model

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Background and aims: L.monocytogenes is the third most common cause of bacterial meningitis in adults. Further understanding of the pathophysiology of listeria meningitis is needed to improve the prognosis. We describe the development of the listeria meningitis mouse model.

Methods: C57BL/6 mice were inoculated in the cisterna magna (1µl) with increasing doses (105-109CFU/ml) of L.monocytogenes strain ST1 in a non-treatment survival study. In a time-point study mice were inoculated with 108 CFU/ml and euthanized after 6 and 24 hours. Cerebrospinal fluid, blood, brain, liver, lung and spleen were collected to analyse bacterial counting and inflammatory markers. In a treatment-survival study mice were inoculated with 109 CFU/ml and treated with 50-200mg/kg/24hours Amoxicillin intraperitoneally. Effect of increasing frequency of treatment per 12 hours or adding Gentamicine (20mg/kg/24hours) were analysed. In the treatment-survival time-point study mice were euthanized after 16 ad 24 hours.

Results: A 20% survival rate was reached in the non-treatment-model in 48 hours (105 CFU/µl). In the treatment-model a 50% survival rate was reached after 72 hours(100mg/kg/24h amoxicillin). Increasing the dosage, frequency or adding Gentamicin did not improve clinical outcome. Time-point experiments showed increase of bacterial outgrowth in blood, CSF and all organs between 6 and 24 hour. In the treatment model, the bacterial outgrowth decreased after i.p. treatment with Amoxicillin (16 vs. 24hours).

Conclusion: We developed a Listeria meningitis mouse model, which can be used for future studies to analyse the pathophysiology, the host's immune response, new (adjunctive) treatment options and bacterial genetic factors to improve outcome.

Disclosure: Nothing to disclose

O411

Cerebral lesion localization in patients with acute pure vestibular and ocular motor strokes: results from the prospective EMVERT trial

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Background and aims: To prospectively investigate cerebral lesion localization in patients with acute isolated rotational vertigo, dizziness or double vision due to acute unilateral stroke.

Methods: 342 adult patients submitted to the ER with acute vertigo, dizziness or double vision of unclear etiology were enrolled prospectively in the EMVERT trial and underwent a standardized protocol of clinical, video-oculographic and posturographic measurements as well as a MRI within 7d after symptom onset. The MRI protocol included DWI-/ FLAIR-/T2-/T2*-/3D-T1-weighted sequences and a TOF-angiography. MRIs with acute DWI lesions were further processed using SPM-based algorithms for lesion mapping.

Results: In 47 of the patients the MRI indicated acute stroke (13.6%). The most frequent chief complaint in these patients was dizziness (44.7%), followed by vertigo (38.3%) and double vision (17.0%). In patients with the chief complaint dizziness the lesions were found mostly in the lateral PICA and SCA territories (involving the flocculus/ superior vermis), and the pontomesencephalic brainstem tegmentum (involving the ocular motor centers for the pitch and role plane). Patients with vertigo frequently had lesions in the medial PICA territory (including the vermis/nodulus/ uvula), the pontomedullary brainstem (involving the vestibular nuclei) and the insular cortex (parieto-insular vestibular cortex). Patients with double vision had pontomesencephalic and meso-diencephalic lesions.

Conclusion: Prospective evaluation of lesion localization in acute vertigo and dizziness showed that mostly the cerebellum was affected by strokes, with some preference towards the medial cerebellar structures accociated with vertigo and lateral hemispherical structures accociated with dizziness. In the brainstem pontomedullary lesions induced vertigo, pontomesencephalic rather dizziness.

Muscle and neuromuscular junction disease

O412

Molecular mechanisms of mitochondrial DNA disease: pathological and genetic studies in patients with Mendelian disorders of mtDNA maintenance

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Background and aims: The underlying genetic defect in patients with cPEO is either a primary mutation of the mtDNA or recessively and dominantly-inherited mutations in nuclear genes leading multiple mtDNA deletions in muscle.

Methods: Muscle biopsies of 16 patients with genetically- and clinically-characterized mitochondrial disease of nuclear origin (9 POLG, 4 TWNK, 2 RRM2B, 1 SLC25A4) and 4 controls were analysed using quadruple OXPHOS immunohistochemistry, quantifying the biochemical phenotype in individual muscle fibres. Further studies on 6/17 patients included the correlation of biochemical deficiency with the mtDNA abnormality in individual cells, following laser microcapture and determination of size and level of clonally-expanded mtDNA deletion within fibres by real-time PCR, long-range PCR and sequencing of breakpoints.

Results: The data from quadruple immunocytochemical studies show a distinct biochemical phenotype in patients with multiple mtDNA deletions, however, there was no difference between genotypes. Real-time PCR showed, that the level of deletion is increasing with the biochemical defect. In all patients, the levels of deletion of ND4/D Loop and ND4/ND1 are significantly increasing with the MRC profile. However, in all groups of fibres there seem to be very low levels of ND1 deletions.

Conclusion: It has already been shown, that patients harbouring multiple deletions have a distinct muscle respiratory chain profile. Three different groups of fibres were found in these patients: cells without deficiency, cells with isolated complex I deficiency and cells with combined complex I and complex IV deficiency. The correlation of biochemical deficiency with level of deletion is arguing against any point mutations as cause of the deficiency.

Disclosure: Nothing to disclose

O413

A phase 1/2 Golodirsen trial developed by the SKIP-NMD consortium to identify potential treatments for Duchenne Muscular Dystrophy: study design and patient characteristics

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Background and aims: Duchenne Muscular Dystrophy (DMD) is a rare, X-linked, recessive disorder causing progressive muscle loss and early death. The SKIP-Neuromuscular Disease (SKIP-NMD) consortium of academic, commercial, and advocacy partners formed and secured an EUFP7 grant to develop and evaluate Golodirsen, a phosphorodiamidate morpholino oligomer designed to skip exon 53 of the dystrophin gene.

Methods: Part 1 of this first-in-human phase 1/2 study of once-weekly intravenous Golodirsen was a double-blind dose titration study that enrolled males aged 6-15 years with DMD and genetic mutations amenable to exon 53 skipping, baseline 6-minute walk test (6MWT) distance $>=250$ m, and North Star Ambulatory Assessment (NSAA) total score $>17/34$ or rise (Gowers') time <7 seconds. Part 2 was open label and included assessments of change in motor function and strength, using traditional tools (6MWT, NSAA), newer outcomes (Performance of Upper Limb test, ActiMyo), dystrophin expression and disease-related biomarkers, pulmonary function, and lower limb pathology using magnetic resonance imaging and spectroscopy.

Results: Part 1 randomised patients to Golodirsen (n=8) or placebo (n=4). In part 2, all 12 patients from part 1 and 13 newly enrolled patients received Golodirsen. Baseline characteristics of all treated patients are summarised in the Table. Analysis of Week 48 muscle biopsies demonstrated dystrophin restoration in treated patients; full study results, including clinical outcomes, are expected in late 2019.

Table. Patient Demographic and Baseline Characteristics

Variable	All Golodirsen-Treated Patients (N = 25)
Age, years	
Mean (SD)	8.2 (2.16)
Range	6–13
Baseline weight, kg	
Mean (SD)	28.20 (9.14)
Range	17.1–49.0
Baseline 6MWT distance, m	
Mean (SD)	403.74 (56.66)
Range	290.0–512.0

6MWT, 6-minute walk test; SD, standard deviation.

Conclusion: The SKIP-NMD collaboration produced the successful design and initiation of a Golodirsen trial with unique, clinically relevant inclusion criteria and outcome measures, providing valuable advancement of DMD research on the effects of potential exon-skipping therapies.
Disclosure: This study was sponsored by Sarepta Therapeutics. Francesco Muntoni: Consultant to Sarepta Therapeutics. Volker Straub: Scientific advisory board member for Sarepta Therapeutics. Diane Frank: Employee of Sarepta Therapeutics, Inc. Andreea Seferian: Nothing to disclose. George Dickson: Inventor on related patent. Michela Guglieri: Nothing to disclose. Joana Domingos: Nothing to disclose. Laurent Servais: Nothing to disclose. Eugenio Mercuri: Nothing to disclose.

O414

Quantifying muscle amyloid content in inclusion body myositis using [18f] florbetapir positron emission tomography

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Background and aims: Inclusion Body Myositis (IBM) shares some histopathological features with Polymyositis (PM) but does not respond to conventional immunosuppressive treatments. Current investigations have low sensitivity for identification of amyloid deposits that are characteristic of IBM, contributing to frequent misdiagnosis.
We performed a prospective case control study comparing muscle amyloid content, quantified using a novel Positron Emission Tomography (PET) technique, in IBM and PM.
Methods: Ten cases with IBM and six controls with PM underwent clinical review, [18F]florbetapir PET/computed tomography, and magnetic resonance imaging (MRI) of whole-body skeletal musculature.
[18F]florbetapir standardised uptake value ratios (SUVRs, reference=lumbar fat pad) in skeletal muscle were compared between cases and controls. The relationship in IBM of [18F]florbetapir SUVRs to clinical and MRI-derived measures of disease severity were also investigated.
Results: [18F]florbetapir SUVRs were significantly higher in those with IBM for all muscle regions assessed (total SUVR 1.45 [IQR 1.28-2.05] versus 1.01 [IQR 0.80-1.22], p=0.005) (Figure 1).
Strong negative correlation between MRI-derived muscle inflammation levels and [18F]florbetapir SUVRs were observed only in calf muscles bilaterally (right -0.73, p=0.02; left -0.68, p=0.03). No significant relationship between [18F]florbetapir SUVRs and clinical measures of disease severity were identified.
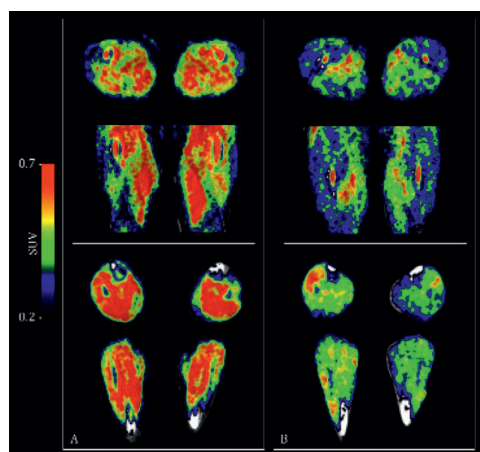
Figure 1: Differences in [18F]florbetapir positron emission tomography (PET) derived standardised uptake values (before reference tissue normalisation) between a case with inclusion body myositis (A) and a control with polymyositis (B)

Conclusion: Muscle amyloid imaging using [18F] florbetapir PET may be useful in the diagnostic workup of IBM, particularly when differentiating from PM. The observed correlation between inflammation and muscle amyloid content may provide clues to pathways of amyloidogenesis in IBM.

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O415

Cardiorespiratory function in Duchenne Muscular Dystrophy in a UK large tertiary care centre: longitudinal progression and the role of steroid treatment

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Background and aims: Duchenne Muscular Dystrophy (DMD) is the most common muscular dystrophy of childhood. The implementation of current standards of care has had a dramatic impact on motor performance and life expectancy. We aimed to characterise the current progression of cardiorespiratory function in face of these changes.

Methods: A retrospective longitudinal study including all patients with DMD followed up at the Dubowitz Neuromuscular Centre between 2000 and 2017. Clinical data was collected, including respiratory (forced vital capacity, FVC, and percentage predicted FVC) and cardiac function (fractional shortening, FS). We fitted average longitudinal models for each outcome. We performed time-to-event analysis for relevant thresholds.

Results: 312 patients were included with a mean age at baseline of 6 +/- 2.3 years old. We observed an increase in FVC up to age 13 years followed by relative stability.% FVC declined on average 6% per year after the age of 9 years old. At the age of 16 years, 5 out of 51 patients on steroids were on NIV versus 3 out of 5 steroid naïve patients. Overall%FS decreased by 0.6% per year. The median age at cardiomyopathy diagnosis was 15.4 years. However, stratifying by steroid treatment showed: for steroid naïve patients median age was 13.9 years and for those on steroids it was above 15 years of age.

Conclusion: We present the longitudinal progression for cardiorespiratory function in DMD. Our data indicate a benefit of steroid treatment in delaying the time to reach important not only respiratory but also cardiac milestones.

Disclosure: Nothing to disclose

O416

Vacuolated PAS-positive lymphocytes as screening tool and a possible therapeutic biomarker in late-onset Pompe disease (LOPD)

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Background and aims: To investigate the diagnostic value of PAS-positive vacuolated lymphocytes on blood smear (BSE) and their role as possible biomarker in LOPD patients

Methods: We examined blood smear of 26 LOPD patients, 10 treated and 16 untreated . Among the latter group, 7 patients initiated ERT and were tested again 6 months after ERT start. Blood smear was also evaluated from 82 controls and 19 patients with other Muscle Glycogenoses (MGSDs). PAS staining was used to t presence of lymphocytes with glycogen-filled vacuoles, 2) quantification of vacuolated lymphocytes

Results: PAS-positive lymphocytes were significantly higher in LOPD patients than in controls or other MGSDs (p<0.05 and p<0.001, respectively). ROC curve for discriminating between untreated LOPD patients and controls yielded an AUC of 1.00 (95%CI 1.00-1.00; P<0.0001). A PAS-positive lymphocyte cutoff level of >10 yielded a sensitivity of 100% (95%CI 78%-100%), a specificity of 100% (95%CI 96%-100%), and a positive predictive value of 100%. Patients studied before and after ERT showed a dramatic decrease of the number of PAS-positive lymphocytes (P<0.0001). In other MGSDs, PAS-positive lymphocytes were significantly lower that untreated LOPD patients, but higher than controls

Conclusion: Our data suggest that the BSE for PAS-positive lymphocytes quantification in peripheral blood films could be used as a simple and quick screening test to shorten diagnosis time in suspected Pompe patients. The quantification of vacuolated lymphocytes appears to be also a valuable tool for detecting and monitoring the therapeutic effects of drugs.

Disclosure: Nothing to disclose

O417

Statin-induced myopathies: beyond immuno-mediated necrotizing myopathies

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Background and aims: Statins are involved in the genesis of myopathies that persist after its withdrawal. Mostly immuno-mediated mechanisms but also degenerative mechanisms have been implicated in its pathogenesis.
To study patients with permanent myopathy following statin exposure that persist after discontinuing statins.

Methods: Prospective study of patients with statin-induced myopathy in a Neuromuscular Unit between 2008 and 2017. Demographic, clinical, laboratory, electromyographic, muscle MRI and biopsy data were collected.

Results: 46 patients, 56.5% woman and 43.5% men, mean age: 64 years. The course of the myopathy was mainly subacute (66%), but also chronic (27%) and acute (7%). Muscle weakness was predominantly proximal (96%) and involved axial muscles in 35%. Other symptoms: myalgias (52%), fatigue (25%), dysphagia (21%), exercise intolerance (18%), dysphonia (11%), dyspnea (7%) and cramps (4%). 65% of the patients were on atorvastatin (mean exposure time: 42 months). HyperCKemia was detected in 90% (425-5108 IU/L). Anti-HMGCR antibodies determined in 30 patients were positive in 11 (37%). EMG was myopathic in 88% and spontaneous activity was present in half of them. Muscle MRI detected muscle involvement in 94%of patients and STIR sequences hyperintensity suggestive of edema in 19. Muscle biopsy was performed in all patients: inflammatory myopathy (73%) (immune-mediated necrotizing in 37%) and other myopathies in 27% (mitochondrial, necrotizing, other primary myopathies).

Conclusion: Statin-induced myopathies constitute a heterogeneous group of disorders in which autoimmune necrotizing forms predominate, although other types of inflammatory myopathy and other non-inflammatory myopathies are frequent. Detection of anti-HMGCR antibodies can be useful although its pathogenic implication is unknown.

Disclosure: Nothing to disclose

Movement disorders 2

O418

Non-invasive intervention for motor signs of Parkinson's Disease: the effect of vibratory stimuli

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Background and aims: It has been proposed that in healthy individuals the down weighting of sensory afferents prior to and during active movement is an essential step in initiating movement. This is realised by increasing the uncertainty on the estimate of the somatosensory signal. Here we tested the hypothesis that motor signs (bradykinesia and tremor) in Parkinson's disease can be ameliorated by non-invasive interventions (peripheral tactile vibration) that increase somatosensory uncertainty.

Methods: We assessed motor performance in a group of 16 right-handed Parkinson's Disease patients (ON medication; 10 out of 16 were also tested OFF medication) using three tasks: the nine-hole peg test and three drawing tasks. We recorded tremor with two accelerometers.

Each task was repeated three times and under three conditions: with no external stimulus; and when a vibratory stimulus was applied to the dominant wrist at a frequency of 200Hz with either a 20bpm or 60bpm modulating frequency.

Results: Parkinson's Disease patients showed a significant improvement in motor performance when a 200Hz vibratory stimulus with 60bpm trials was applied compared to 20bpm trials ($p<0.05$) and in absence of vibration. There was no significant difference in motor performance following no vibration and 20bpm trials ($p>0.5$).

Conclusion: These preliminary data are consistent with a novel the idea that vibrotactile stimulation results in less slowing and decrement in amplitude of a repetitive hand movement and less tremor compared to baseline measures in PD patients. Further work is required now to establish this finding and investigate further.

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O419

The Nocebo effect in Parkinson's Disease

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Background and aims: The placebo effect is well recognized in Parkinson's Disease (PD) and is thought to be at least partially mediated by an increase in dopaminergic neurotransmission. Its counterpart, the nocebo effect, remains ill-characterized. This study aims to estimate and characterize the nocebo response in PD.

Methods: Databases were searched up to February 2017. Randomized, parallel-designed, placebo-controlled trials of patients with PD were included. Nocebo response was defined as the proportion of participants experiencing adverse events in the placebo arm. It was further characterized as the proportion of withdrawals, withdrawals due to AE and deaths in the placebo arm. Random-effects meta-analysis was used to pool data, with statistical heterogeneity being assessed with the I2 statistic. The same analyses were repeated with data from the intervention arm to provide a term of comparison.

Results: 239 randomized controlled trials (47,797 participants) were included. Pooled nocebo response was 55,8% (95% CI 51,5%–60,1%, 149 trials; I2=97.5%). 13,9% (95% CI 12,4%–15,4%, 229 trials; I2=90,54%) patients withdrew from trials, 5,7% (95% CI 5,0%–6,4%, 222 trials; I2=72,44%) did it because of AE and 0,6% (95% CI 0,5%–0,7%, 231 trials; I2=0%) died during follow up. Similar proportions were identified in patients in intervention arms.

Conclusion: The magnitude of the nocebo response in parallel-designed randomized clinical trials in PD is substantial. This information should be integrated in the evaluation, planning and designing of future clinical trials.

Disclosure: Nothing to disclose

O420

Generation and characterisation of iPSC-derived oligodendrocytes of patients with Multiple System Atrophy

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Background and aims: Multiple System Atrophy (MSA) is a fatal disease characterized by alpha-synuclein inclusions in oligodendrocytes and neuronal loss in the striatonigral pathway, cerebellum and autonomic system. However, the origin of aggregates and the molecular connection between oligondendrocytic alpha-synuclein accumulation and neurodegeneration are still unclear. In this project, we exploit the potential of induced Pluripotent Stem Cells (iPSCs) to address these challenges. The aim of this study is to generate and characterise iPSC-derived oligodendrocytes of MSA patients.

Methods: Fibroblasts obtained from skin biopsies of patients with MSA, alpha-synuclein gene (SNCA) duplication, and controls were reprogrammed to iPSCs using CytoTune-iPS 2.0-Sendai Reprogramming Kit (Life Technologies) based on viral transduction of factors Oct4, Sox2, Klf4 and c-Myc. Method by Douvaras and Fossati (2015) was applied to derive myelinating oligodendrocytes.

Results: iPSCs of two patients with MSA, one patient with SNCA duplication and two controls were differentiated into Olig2+, Nkx2.1+ oligodendrocyte precursors cells, then specified into myelinating oligodendrocytes expressing lineage-specific markers (O4, MBP). Morphological evaluation at different stages of maturation demonstrated typical oligodendrocytic changes, confirmed by immunocytochemistry and RT-PCR. Analysis of alpha-synuclein expression in patient and control lines showed that mRNA and protein are produced by progenitors, but decrease markedly in mature oligodendrocytes, with perinuclear localization suggesting the degradation of the protein. Conversely, myelinating oligodendrocytes with SNCA duplication displayed increased alpha-synuclein content.

Conclusion: IPSC-derived oligodendrocytes represent an effective tool to investigate MSA pathogenesis. Our results support the hypothesis that alpha-synuclein in MSA glial inclusions is not primarily produced in oligodendrocytes and accumulation does not result from endogenous overexpression.

Disclosure: Nothing to disclose

O421

Spastic-ataxia in a Portuguese cohort of hereditary ataxias

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Background and aims: Hereditary Spastic-Ataxias (HSA) are a heterogeneous group of disorders combining overt spasticity and ataxia. SACS, SPG7 and FXN are the genes most frequently associated. Our aim was to describe the clinical features and genes of HSA patients in our cohort of Hereditary Ataxias (HA).

Methods: Patients were identified from a clinical-epidemiological database. Information collected according to specific protocol.

Results: In 77 HA patients, 16 had HSA: six ARSACS, two SPG46, one SPG7, one SPG78, one SPG15, one L-2-hydroxyglutarate dehydrogenase (L2HGDH); four had no mutation identified. Onset was in early-childhood (<2y) in five (three ARSACS, one SPG15, one L2HGDH); late-childhood/adolescence (6-15y) in five (two ARSACS, two SPG46, one unknown mutation); during adulthood (20-52y) in six (one ARSACS, one SPG7, one SPG78, three unknown mutation). Presenting symptom was spastic gait (nine), disequilibrium (four), dysarthria, upper limbs dysmetria or cognitive delay (one each). After variable disease progression, all presented dysmetria, predominantly in upper limbs, and spasticity in lower limbs. Non-cerebellar/pyramidal symptoms included: neuropathy in six ARSACS, two SPG46, two SPG7, one SPG15, one unknown mutation; dystonia in ARSACS, SPG46 and L2HGDH (one each); seizures in ARSACS and unknown mutation (one each); Parkinsonism in SPG7 and SPG78 (one each). Five ARSACS, one SPG15, one unknown mutation were wheelchair-bound by their 30s-40s.

Conclusion: In our cohort, HSA represented a genetically diverse group of patients. As expected, many were ARSACS, but variants in SPG7, GBA2 (SPG46), ATP13A2 (SPG78), ZFYVE26 (SPG15), L2HGDH were also

identified. Phenotypical overlap among pathogenic variants in various genes poses a great challenge for genetic diagnosis.

Disclosure: Nothing to disclose

O422

Evaluation of gait and posture in essential tremor before and after unilateral Gamma Knife Thalamotomy

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Background and aims: Despite its high frequency, Essential Tremor (ET) pathophysiology remains poorly understood and few data about the existence of gait disorders in this affection are available. Our aim is to describe specific features of gait disorders and postural instability in patients with ET, and to evaluate the effect on motor skills of a unilateral Gamma Knife Thalamotomy (GKT).

Methods: 72 patients with severe ET underwent GKT (mean age :73 years). Targeting of the ventral intermediate nucleus (Vim) was achieved with Leksell Gamma Knife with a single shot through a 4-mm collimator helmet. The prescription dose was 130 Gy.
Severity of ET (Fahn-Tolosa-Marin Tremor Rating Scale), cognitive function, activities of daily living (Bain's functional scale for activities of daily living), gait and postural control were assessed before and 1 year after radiosurgery.

Results: The comparison between ET patients before surgery and control subjects showed poorer gait performances in the patients group.
All tremor components (rest, postural, and intention) of the rating scale and activities of daily living were improved after GKT. Cognitive functions like gait and postural control remained unchanged after GKT.

Conclusion: This study showed postural instability and gait impairment in ET, which may be related to a dysfunction of cerebello-thalamo-cortical pathway. Moreover, our work showed no deleterious effect of unilateral GKT on posture and gait skills. The unilateral and progressive nature of GKT could explain the absence of degradation of gait and posture. Unilateral GKT is a safe and efficient procedure for severe medically refractory tremor.

Disclosure: This study was supported by "APTES", the french association for patients with essential tremor

O423

Functional brain connectome architecture in a large cohort of Parkinson's Disease patients

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Background and aims: To investigate the functional network organization in patients with Parkinson's Disease (PD).

Methods: 134 PD patients (82 early PD [Hoehn and Yahr {HY} 1-1.5] and 52 mild-to-severe PD [HY 2-4]) and 99 controls performed clinical evaluation and resting state functional MRI. Graph analysis and connectomics assessed global and local topological network properties and regional functional connectivity (FC).

Results: Compared with controls, PD patients showed altered functional topological features (lower mean nodal strength and longer mean path length) of the sensorimotor and parietal areas relative to controls, with mild-to-severe cases showing the greatest alterations. Mild-to-severe PD patients had a reduced mean nodal strength in the temporal lobe relative to early PD patients. At the regional network level, compared to controls, PD groups showed decreased FC within basal ganglia/sensorimotor network, parietal regions such as posterior cingulate and precuneus bilaterally, and bilateral superior frontal and middle temporal areas. Compared to early PD cases, mild-to-severe PD patients were characterized by a greater involvement of basal ganglia/sensorimotor connections linking putamen, caudate and postcentral gyri bilaterally, parietal network involving posterior cingulate, precuneus and supramarginal bilaterally, and pathways to the bilateral hippocampus.

Conclusion: This study showed widespread motor and extra-motor functional network degeneration in PD patients at different disease stage. Network-based advanced MRI analyses might represent a powerful approach to understand the pathophysiological process across different stages of the disease and hold the promise to provide an objective in vivo marker of disease-related pathological changes.

Disclosure: Supported by: Ministry of Education and Science Republic of Serbia (Grant #175090).

ePoster Sessions

Saturday, 16 June 2018

Ageing and Dementia

EPO1001

Impact of White Matter Hyperintensities on progression in Alzheimer's disease

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Background and aims: Cerebral white matter hyperintensities (WMH) have been suggested to contribute to progression in Alzheimer's disease (AD). Quantification of WMH in patients can be performed both manually, where WMH is categorized according to the Fazekas scale, and automatically using software which calculates WMH based on a FLAIR MRI sequence. The aim of this study was to investigate to which extent the WMH-burden affects progression in a mixed population of clinical AD and prodromal AD. Furthermore, we assessed whether manual rating and automatic segmentation of WMH provide equal information on progression.

Methods: Patients with clinical diagnosis of AD and MCI patients suspected of having early AD were included. Evaluation of progression was performed by an experienced clinician at a 12-month follow-up visit. Manual evaluation (Fazekas scale) of WMH was performed by an experienced neuroradiologist and automatic segmentation was performed as previously described (Koikkalainen et al, 2016, Neuroimage). Patients were examined for the association between WMH-burden at baseline and progression in disease after 12 months and stratified by diagnosis of AD without CVD and AD with CVD.

Results: There was no significant difference between WMH-burden and progression status in either AD without CVD (p=0.122) or AD with CVD (p=0.159). However, there was a trend for a higher WMH-burden in progressed vs. stable patients diagnosed with AD with CVD.

	AD without CVD	AD with CVD
n	139	31
progressed: *n*, (WMH mean)	85 (4,33 ml)	16 (23,02 ml)
Stable: *n*, (WMH mean)	54 (6,69 ml)	15 (14,82 ml)
p-value, WMH-burden (stable vs. Progressed)	p = 0,122	p = 0,159

Conclusion: WMH-burden seems to have an impact on progression in AD only when present in large amounts. We are currently investigating the prognostic value of manual and automatic WMH-burden measurements.

Disclosure: Nothing to disclose

EPO1002

Comparison of Amyloid Biomarkers in Alzheimer's Disease – a Monocentric Study

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Background and aims: According to international criteria, amyloid-biomarkers are diagnostic elements for Alzheimer's disease (AD). Controversies about their accuracy for early and differential diagnosis may be explained by distinct pathological processes or by between-center variability in amyloid-markers. We pretended to compare the agreement between amyloid CSF-biomarkers, [11C]-Pittsburgh Compound Positron Emission Tomography (PIB-PET) and Florbetapir (18F) and the accuracy of these biomarkers for AD diagnosis.

Methods: 96 patients with at least two amyloid markers were included. The clinical course was considered the diagnostic gold standard. We used locally established cut-offs of amyloid CSF-AD biomarkers–$A\beta42<610pg/mL$; $A\beta42/A\beta40$ ratio<0.068. PIB-PET and 18F were evaluated qualitatively.

Results: There was entire agreement between PIB-PET and 18F. Amyloid Imaging Markers (AIM) agreed with $A\beta42$ in 77% cases and with $A\beta42/A\beta40$ ratio in 74%. Discrepancies were found in 10 clinically non-AD patients (9 with CSF-AD profile and negative AIM; 1 with positive AIM and a non-AD CSF profile) and 12 AD patients (11 with non-AD CSF and positive AIM; 1 with CSF-AD profile and negative AIM). CSF $A\beta42$ had, in this cohort, a sensitivity of 71% and a specificity of 66% for the diagnosis of AD and MCI-AD, with an overall diagnostic accuracy of 69%. AIM achieved a sensitivity of 85%, a specificity of 92%, with 88% diagnostic accuracy.

Conclusion: Agreement between CSF amyloid and AIM indicates that these measures are not fully equivalent as surrogates of AD-pathology. CSF amyloid seems to have a moderate sensitivity and specificity for AD-related pathologies, while AIM achieves a higher diagnostic accuracy. These results deserve a neuropathological confirmation.

Disclosure: Nothing to disclose

EPO1003

Activation and connectivity of attention networks are preserved in mild AD patients performing a short term memory task

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Background and aims: Alzheimer's disease (AD) has been described as a disconnection syndrome. Network dysfunction has frequently been related to memory impairment, but the involvement of other functional networks in early AD remains a matter of debate.

Objective: The study aimed to explore the effects of early clinical AD on dorsal and ventral attention networks (DAN and VAN) using an activation fMRI protocol.

Methods: Patients with AD and healthy elder controls performed a fMRI short term memory (STM) task. Variation in load (5 versus 2 items) allowed studying DAN and VAN activity and their interaction.

Results: At the behavioral level, STM performance decreased and reaction times increased with increasing task load in both groups. AD patients had poorer performance and were slower than controls, suggesting decreased STM capacities. Imaging revealed common DAN activation for high load in both groups. There was neither significant between group difference nor common activation for low compared to high load condition, even if post-hoc analysis revealed VAN activation for low load in the elder group only. Psycho-physiological interaction analysis showed that there was a negative relationship between DAN and VAN for high versus low load condition in AD patients.

Conclusion: Dorsal attention network remains activated and connected to ventral attention network in early AD patients during (impaired) performance of short term memory tasks. Accordingly, when patients succeed in doing the tasks, they are slower than controls, but this is neither explained by loss of DAN activity nor by disconnection between DAN and VAN in early stage AD.

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EPO1004

The role of a cued recall memory test in the prediction of Mild Cognitive Impairment conversion to Alzheimer's disease

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Background and aims: Mild Cognitive Impairment (MCI) due to Alzheimer's disease (AD) requires evidence of episodic memory impairment. Semantic cued recall tests, like the Free and Cued Selective Reminding Test (FCSRT) seem to be a good tool in the early detection of AD. We intend to evaluate how FCSRT, compared with Mini-Mental State Examination (MMSE), CSF biomarkers, Apolipoprotein E (ApoE) genotyping and hippocampal volumetric measures predict the conversion of MCI patients to AD.

Methods: A group of 56 MCI patients with a follow-up≥2 years were included. Memory was assessed using the MMSE and the FCSRT–Immediate Recall (IR) and Delayed Recall (DR). CSF Aβ42, Aβ40, total tau (t-Tau) and phosphorylated-tau (p-Tau) were determined by sandwich ELISA. Patients were genotyped for ApoE status.T1-weighted MRI scans were acquired in a 3T scanner and processed with the FreeSurfer software. Hippocampal volumes were obtained and corrected accordingly to total intracranial volume.

Results: During follow-up 30 patients converted to AD (MCI-AD) while 26 remained stable (MCI-St). A CSF-AD biomarker profile was strongly associated with conversion to AD (p<0.001; overall accuracy=82%), followed by an abnormal FCSRT score (p<0.001; overall accuracy=80%), ApoE-ε4 genotype (p<0.001; overall accuracy=75%) and abnormal MMSE (p<0.001; overall accuracy=73%). Hippocampus volume failed to reach a significant difference between MCI-AD and MCI-St. A regression logistic model identified FCSRT-IR score, t-Tau and ApoE as the best predictors of MCI conversion to AD.

Conclusion: We conclude that FCSRT, along with t-tau and ApoE, are good predictors of the conversion to AD in MCI patients.

Disclosure: Nothing to disclose

EPO1005

Incidence of Cancer in Patients with Alzheimer's Disease: A 11-Year Nationwide Population-Based Study

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Background and aims: Alzheimer`s disease (AD) increases with age and is characterized by the premature progressive loss of neuronal cell. In contrast, cancer cells have inappropriate cell proliferation and resistance to cell death. We evaluated the association between cancer and AD and also examined the specific types of cancer.

Methods: This retrospective, nationwide, longitudinal study used National Health Insurance Service–Senior cohort (NHIS-Senior) 2002-2013, which was released by the KNHIS in 2016, comprising 550,000 random subjects who were selected from over than 60. The study included a cohort of 4,408 patients who were first diagnoses as AD between 2003 and 2005. To match each dementia patient, 19,150 subjects were selected from the database by Propensity Score Matching.

Results: We enrolled 4,790 patients for analysis in this cohort and the prevalence of AD was higher in female (19.29%) than in male (17.71%). A higher prevalence of AD was observed in the 70-84 year age group and in the higher income status group. A total of 540 cancers occurred within the observation interval. Overall cancer was less frequent in those with AD (12.25%) than in the control (18.46%), with HR 0.704 (95% Confidence Intervals (CIs)=0.0.64-0.775, p-Value<0.0001).

Conclusion: Our data showed a decreased incidence of overall cancers in patients with AD similar to previous studies. Patients with AD had a significantly decreased risk of colon & rectum, lung and stomach cancer. This finding lower than but consistent with Western countries. We need further investigation of genetic evidence linking AD to cancer.

Disclosure: Nothing to disclose

EPO1006

Cerebellar white matter disruption in AD patients: a Diffusion Tensor Imaging study

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Background and aims: Diffusion tensor imaging (DTI) is an MRI technique sensitive to microscopic changes occurring within the white matter throughout the course of Alzheimer's disease (AD). Given the recent recognition of cerebellar involvement in cognitive functions, the aim of our work is to investigate the DTI microstructural fiber integrity of the cerebellar WM tracts in AD patients compared to healthy controls (HS).

Methods: We enrolled 75 participants, 50 patients with probable AD and 25 age-matched healthy controls. All subjects underwent MRI at 3 T, with the collection of TSE, FLAIR, MDEFT and DTI scans. DTI data were analysed to yield maps of fractional anisotropy (FA), axial diffusivity (Dax), radial diffusivity (RD) and mean diffusivity (MD), and to reconstruct the middle cerebellar peduncle (MCP), and the left and right superior cerebellar peduncles (SCPL and SCPR).
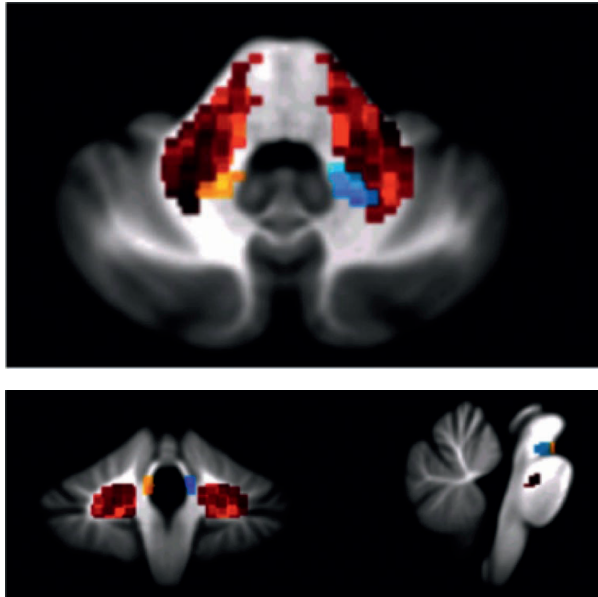
Results: AD patients showed a lower FA and a higher RD compared to HS in MCP, SCPL and SCPR. Moreover, a higher Dax and MD were found in SCPL and SCPR.
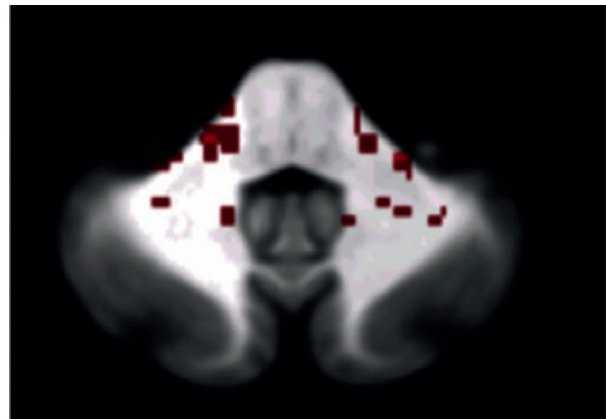
Conclusion: This study confirms the pivotal role of WM tracts impairment in AD patients, which could be traced not only in brain regions that are traditionally regarded as highly affected in AD patients, but also in the cerebellum, a yet underestimated cognitively relevant brain region.

Disclosure: Nothing to disclose

EPO1007

Assessement of early cognitive impairment induced by microbleed in male and female mice by Touchscreen automated task

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Background and aims: Cerebral microbleeds (CMBs) could contribute to cognitive impairment in the general population and in patients with dementia. We previously presented a novel murine model to induce CMB by stereotaxic surgery. In this study, we aimed to identify an early impact of CMB on the cognitive impairment by object location paired associates learning, which was known to be hippocampus dependant task in rodents.

Methods: Male and female C57Bl6/J mice were stereo-tactically administered collagenase ($0.8 \ \mu U/\mu l$) to induce cortical lesion. CMB-mice received atorvastatin (5 mg/kg/day) over the follow-up period. At 6 weeks post-surgery, the visuo-spatial memory was evaluated by the Paired Associates Learning in the Touchscreen test, during 30 daily-sessions. For each trial type, only one visual stimulus was presented in its correct location. Mice were also evaluated for the motor activity and the anxiety level.
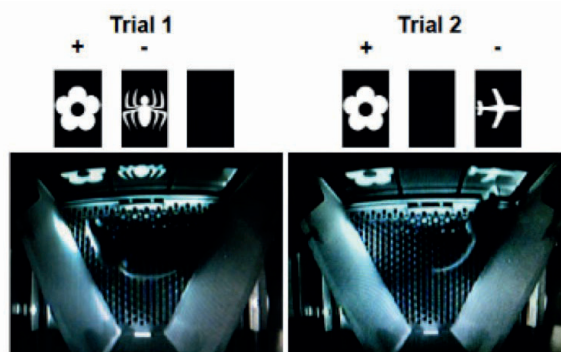
The touchscreen automated dPAL task: illustration with two possible trial types. For each trial type, only one visual stimulus was presented in its correct location (denoted '+'); the second visual stimulus was presented in one of its two incorrect locations (denoted '-'), and the third location remained blank.

Results: At 6 weeks, different results were observed in male and female mice in the Touchscreen test. Male CMB-mice expressed a decline of the visuospatial memory, restored by the administration of atorvastatin. For female CMB-mice, the visuospatial memory was even better than sham-mice. Atorvastatin also improved the visuaospatial memory. There was no difference in motor activity. A slight reduce of anxiety level was observed in male CMB-mice.

Conclusion: The Touchscreen test is less biased than other behavioral tests, and is interesting in its translational approach. We validated in a prospective manner that CMB affected the cognitive performance differently in male and female mice. We will apply the same model with transgenic mice of Alzheimer's disease.

EPO1008

Neuropsychiatric symptoms in Mild Cognitive Impairment: biological determinants and prediction of conversion

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Background and aims: Mild Cognitive Impairment (MCI) is accepted as prodromal stage of Alzheimer's disease (AD). Neuropsychiatric symptoms (NPS) are frequent in MCI patients, but their impact in prognosis and biological determinants are not fully established.

Aims: To investigate the relationship of NPS with clinical and CSF biomarkers as well as to establish their prognostic impact, in a prospective cohort of MCI patients.

Methods: Data collected besides demographics and rate of conversion at 3 years: cognitive assessment (MMSE and MoCA); staging scales as Blessed and Clinical-Dementia-Rating (CDR); psychopathological assessment, namely Geriatric-Depression-Scale (GDS), Hamilton-Anxiety-Scale and Neuropsychiatric-Inventory (NPI); CSF biomarkers (Aβ42, tau and p-tau); Apolipoprotein E. A univariate, followed by a multivariate analysis for independent predictors of conversion were performed; statistical significance was considered when $p < 0.05$.

Results: We studied 129 patients with MCI, 50 males (38.8%) and a mean age was 68.9 ($\pm$ 10.9). At 3 years of follow up to 44 (34.1%) patients had converted to AD-dementia. In univariate analysis, GDS and Hamilton were significantly correlated with CSF p-tau and GDS with Aβ42. Conversion was associated with age of onset, NPI-caregiver-burden, Blessed, MoCA, tau and p-tau. In multivariate analysis, Aβ42 was associated with GDS (β=15.435, 95%CI=[5.258, 25.611],p=0.003) and Hamilton with p-tau (β=2.811, 95%CI=[1.111, 4.511],p=0.001). NPI-caregiver-burden was an independent predictor for conversion (OR: 1.093;95%IC;1.007 to 1.186, p=0.033).

Conclusion: Our study demonstrates that in prodromal AD (MCI), NPS are related to cognitive, functional and biological biomarkers and NPI-caregiver-burden emerged as an independent predictor of progression to dementia.

Disclosure: Nothing to disclose

EPO1009

Genomic studies in early onset Alzheimer's disease (EOAD) in Hungary

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Background and aims: The major Alzheimer's disease (AD) associated genes support the merit of the traditional amyloid cascade hypothesis, since the genes APP, PSEN1, and PSEN2 all directly affect amyloid production or cleavage. Mutation of these genes are mainly responsible for early onset forms of AD (EOAD). The aim of this study was to characterize genotype-phenotype association in the Hungarian patients with EOAD.

Methods: 93 patients diagnosed with EOAD were examined with Sanger sequencing in the case of the coding exons of the PSEN1, PSEN2 and APP genes were investigated. Predisposing genetic factors such as APOE genotypes, MTHFR C677T and TREM2 G140A alterations were analysed. The genetic risk factors were detected in 100 old healthy persons as well.

Results: Five presumed pathogenic mutations (two PSEN1, two PSEN2, one APP) were identified, including one newly detected heterozygous mutation: PSEN1 (c.265 G>C;Val89Leu) which was supposed to be likely pathogenic based on the result of prediction scores and segregation analysis. APOE E4 homozygous, TREM2 heterozygous and MTHFR homozygous status were presented in 7.4%, 5.9% and 13.2%, respectively.

Conclusion: In the EOAD Hungarian cohort likely pathogenic mutations were detected in the three examined genes, with 5.2% frequency. The prevalence of the predisposing genetic risk factors were higher than in the normal population. Our results were suggested that even in the EOAD group the monogenic form was relatively rare. In conclusion, we are hypothesized that in the prevalence of EOAD other gene-gene interactions and relevant genetic and environmental risk factors might be contributing to disease development.

Disclosure: Hungarian Brain Research Program

EPO1010

Role of quantitative MRI measures in prognostic assessment of Mild Cognitive Impairment patients and correlation with Cerebrospinal Fluid biomarkers

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Background and aims: Patients with mild cognitive impairment (MCI) are at greater risk of developing dementia, namely Alzheimer's disease (AD). Limbic atrophy is an early finding of AD and several structures of interest have been investigated as disease biomarkers. The aim of this study was to compare MRI biomarkers between MCI subjects who progressed to AD (MCI-P) and non-progressors (MCI-NP) and to investigate possible correlations with Cerebrospinal Fluid (CSF) biomarkers.

Methods: 78 MCI patients were identified and divided into MCI-NP and MCI-P (53.8%) at a minimum 2-year follow-up. At baseline, hippocampal volume (HV) and cortical thickness of para-hippocampal (PH) and entorhinal (ER) cortices were automatically calculated with FreeSurfer software using T1-weighted volumetric imaging, compared between groups and correlated with CSF total tau (t-Tau), phosphorylated tau (p-Tau) and amyloid-beta1-42 (Aß42) levels.

Results: Significant statistical difference was found for HV and ER, but not for PH between groups (Table 1). Significant correlations were found between ER-[Aß42 (right hemisphere), t-Tau and p-Tau], PH-Aß42, and HV-[p-Tau (right hemisphere) and Aß42] (Table 2). Exploratory receiver operating characteristic curve (ROC) analysis yielded a specificity of 70% and sensitivity of 72% for ER to predict progression to AD.

Conclusion: According to previous studies, these findings suggest that baseline ER could predict progression to AD. Also, variations in HV, ER and PH measures could reflect differences in CSF biomarkers. It would be interesting to further investigate whether the combination of ER measure and Aß42/p-Tau ratio would increase the predictive power to AD progression.

Disclosure: Nothing to disclose

Cerebrovascular diseases 1

EPO1012

Evaluation of platelet-derived microvesicles in patients after thrombotic stroke

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Background and aims: Platelet-derived microvesicles (pMV) are involved in the development of atherosclerotic lesions and are increased in ischemic stroke. The aim of the study was a comparison of pMV in patients after ischemic stroke secondary to large-artery atherosclerosis (LAA) and small vessels occlusion (SVO).

Methods: We recruited patients after ischemic stroke secondary to LAA and SVO. Stroke subtype was determined based on the TOAST classification criteria. pMV were isolated from citrated blood by centrifugation, incubated with the following antibodies: CD61/PerCP (platelet gating Ab), Annexin V/PE (Ab against phosphatidylserine), CD62P/PE-Cy5 (Ab against P selectin), PAC-1/FITC (Ab against active form of GPIIb/IIIa), and CD154/APC (Ab against CD40L) then analysed with an Apogee A50-Micro flow cytometer.

Results: We included 49 stroke patients (mean age 67±9 years): 29 patients (59%) with LAA and 20 patients (41%) with SVO subtype. There was no significant difference in concentration of pMV subtypes between LAA and SVO: CD61+ [1352 (840-1544) n/µl vs 1411 (1048-1945) n/µl, p=0,56], CD61+/AnV+ [174 (118-251) n/µl vs 180 (130-335) n/µl, p=0,77], CD61+/CD62P+ [8 (6-13) n/µl vs 8 (5-12) n/µl, p=0,27], CD61+/PAC-1+ [8 (6-13) n/µl vs 7 (4-12) n/µl, p=0,29], CD61+/CD154+ [6 (5-11) n/µl vs 6 (4-11) n/µl, p=0,88].

Conclusion: We demonstrated that there is no significant difference in the concentration of pMVs or their subtypes determined as an expression of GPIIb/IIIa, PS, P-selectin or CD40L between the thrombotic subtypes of stroke, LAA and SVO.

Disclosure: This study was supported financially by the governmental research grant National Science Centre 2014/15/B/NZ4/00736

EPO1013

Factors associated with short-term mortality after ischemic stroke in Conakry Teaching Hospital

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Background and aims: Stroke is the most debilitating disease in adults and the third leading cause of death worldwide
The aim of this work was to identify the factors associated with mortality in ischemic stroke patients in the neurology department of Conakry Teaching Hospital

Methods: We conducted a prospective study during one year, from January 1st to December 31st, 2016. We included all patients admitted for ischemic stroke in neurology department of Ignace Deen teaching hospital. Clinical, paraclinical and prognostic data were recorded. We compared the characteristics of alive and deceased patients. Data were analyzed using SPSS 20 software. Any p-value less than 0.05 was considered statistically significant

Results: We collected 156 patients hospitalized for ischemic stroke. A total of 43 patients died with a frequency of 28%. The average age was 61±13.5 years. The average NIHSS at reception was 12±4.6. Factors associated with mortality were urinary tract infection (p Value=0.01), sepsis (p-Value=0.01), heart disease (p Value=0.02) and hyperglycemia (p Value=0.01). Half of the deaths (50%) occurred in the first 30 days

Conclusion: Heart disease, hyperglycemia, sepsis are associated with high mortality in ischemic stroke. Better management of these factors could significantly reduce this mortality

Disclosure: Nothing to disclose

EPO1014

Contribution of blood biomarkers to the diagnosis of cardioembolic stroke

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Background and aims: Cardioembolic strokes might be effectively prevented by anticoagulation. Blood biomarkers helping to suggest cardioembolic etiology and to steer the complex diagnostic work-up would therefore be of great advantage. This study addresses the possible contribution of biomarkers associated with thromboembolism (NT-proBNP and D-dimer) to the diagnosis of cardioembolic stroke.

Methods: Over a 7-month period, we prospectively investigated all ischemic stroke patients admitted to our Stroke Unit. All patients underwent a complete stroke work-up including cerebral imaging (CT and/or MRI), neurosonography, electrocardiography, cardiac rhythm monitoring (for at least 24 hours) and echocardiography. Blood to determine NT-proBNP and D-dimer levels was drawn immediately after admission.

Results: Of 188 ischemic stroke patients (age: 69±14 years, female: 38%), 67 had cardioembolic (36%), 73 non-cardioembolic (39%) and 48 cryptogenic strokes (25%), based on extensive work-up. NT-proBNP and D-dimer levels were significantly higher in cardioembolic vs. non-cardioembolic strokes (2543 vs. 707 pg/ml, p<0.001; 2.4 vs. 1.4 μg/ml, p<0.001). The area under the curve (AUC) of NT-proBNP obtained for the diagnosis of cardioembolic stroke was 0.81. The cut-off point with the highest sensitivity and specificity was set at 525 pg/ml (sensitivity: 82%, specificity: 77%). The AUC of D-dimer in cardioembolic stroke was 0.69, with a cut-off set at 0.75 μg/ml (sensitivity: 67%, specificity: 69%).

Conclusion: In concordance with previous studies, NT-proBNP has reasonable diagnostic accuracy for stroke related to cardiac embolism. Nevertheless, sensitivity and specificity are too low to essentially improve the diagnostic work-up. The contribution of D-dimer levels is even more limited.

Disclosure: Nothing to disclose

EPO1015

"Monocular double vision" – central or peripheral?

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Background and aims: The monocular diplopia usually implies a peripheral etiology related with intraocular pathology. More uncommon are the central nervous system causes that included visual illusory phenomenon, epileptic disorder or aura of migraine. We described a case of central monocular diplopia related with visual illusory phenomenon named polyopia.

Methods: Case report.

Results: A 39-year-old right-handed woman presented to the emergency department with complaints of double vision as seeing separated or overlapping images and vertigo sensation that began abruptly. She was smoker. She had no history of headaches, epilepsy or stroke. On admission, she was afebrile, her blood pressure was 157/114 mmHg. The neurological examination disclosed a horizontal diplopia, in all directions of gaze, maximal on the right gaze. The diplopia persisted when she closes only one eye, both right or left. The ophthalmologic examination was normal. She had no pupillary involvement, nystagmus, cranial nerve palsy, visual campimetry deficits or visual extinction. She had a right algic hypoesthesia. Brain MRI shows an acute ischaemic left parietal lesion.

Conclusion: This case shows the clinical challenge of localizing a subjective complaint of double vision, which can localize to the eyes, oculomotor systems, visual pathways, and as in our patient, central structures of visual perceptual processes. A careful history and examination were the key. The patients, often have associated other signs of occipital or parietooccipital region lesion, such as homonymous hemianopia or visual agnosia. In our patient these signs were absent, and the sensitive loss was the clue to consider a central cause for her monocular diplopia.

Disclosure: Nothing to disclose

EPO1016

Is it possible to identify acute ischemic stroke patients with large-vessel occlusions using clinical screening scales?

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Background and aims: For acute ischemic stroke caused by large-vessel occlusion (LVO), intravenous thrombolysis followed by thrombectomy is the most effective treatment. Since endovascular thrombectomy is only performed in specialized centers, successful prehospital screening would be of great importance. A number of screening tools for LVO exists, however, these have been tested retrospectively in patients with an established stroke diagnosis. Few studies have investigated the predictive values in patients presenting with acute stroke symptoms.

Methods: The Stroke Unit at Akershus University Hospital is the largest in Norway with a catchment area of about 10% of the total population in Norway. In 2012, a stroke fast track with direct access to neurologist on call, for patients with acute stroke symptoms < 4.5 hours considered as prehospital candidates for intervention was established. Initial CT scan and CT angiography are conducted at the hospital, and all patients are evaluated with the National Institutes of Health Stroke Scale by the neurologist before possibly intervention. We have conducted a retrospective review of all stroke fast tracks for the period 2012-2017 in order to validate the use of screening scales to detect LVO in a population with acute stroke symptoms of<4.5 hours.

Results: More than 2600 patients have been included in the stroke fast track. Approximately 650 have received intravenous thrombolysis, and about 6-7% of the total population had LVO detected by CT angiography at admission. As the year 2017 will be included, all data are not yet available.

Conclusion: The results will be presented at the meeting.

Disclosure: Nothing to disclose

EPO1017

Etiology of ischemic stroke in young patients: Findings from the HISTORY study

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Background and aims: Ischemic stroke (IS) in young adults is relatively less frequent, however recent data reporting an increasing incidence up to 10-15% of all IS. Moreover, the cause of IS often differs from older patients and may require a cause-specific management. Our aim was to determine the etiology of IS in young patients.

Methods: The study set consisted of young acute IS patients<50 years enrolled in the prospective HISTORY (Heart and Ischemic STrOke Relationship studY) study registered on ClinicalTrials.gov (NCT01541163). In all patients, the brain ischemia was confirmed on CT or MRI. Admission ECG, serum specific cardiac and thrombophilia markers, neurosonology, TEE, 24-hour and 3-week ECG-Holter were performed in all patients to assess IS etiology according to the TOAST classification.

Results: Out of 1348 patients enrolled in the HISTORY study, 218 (16%, 122 males, mean age 40.9 ±7.9 years) were<50 years. Large-vessel atherosclerosis was detected in 15 (6.5%) patients, cardio embolism in 26 (12%) patients and arterial dissection in 15 (6.5%) patients. Eight (3.5%) patients had hypercoagulable state, and only one patient had genetic disorder and one non-infectious vasculitis. 161 (72.5%) were identified as cryptogenic. Recurrent IS occurred in 4.5% of all IS patients.

Conclusion: The cause of IS in young adults remains often unclear, in our study were identified 72.5% patients as cryptogenic. The most common cause of IS was cardiac embolism (12%), arterial dissection (6.5%) and large-vessel atherosclerosis (6.5%).

Disclosure: Study was supported by the grant IGA LF UP_018_2018 and by the grant of Ministry of Health Czech Republic, nr. 17-30101A.

EPO1019

Clinico-radiological correlation of anterior cerebral artery stroke presenting as unilateral ataxic syndrome

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Background: Frontal lobe gait disorders, also termed frontal lobe (pseudo)ataxia, are commonly linked to insidious conditions such as frontal lobe tumors or extensive cerebrovascular disease. Its anatomical substrate is still poorly defined, though a disruption of cortico-cerebellar fibers and medial frontal wall involvement have been hypothesized.

Aims: Characterize clinical–anatomical correlation of anterior cerebral artery stroke (ACAS) with and without ataxia at presentation.

Methods: Consecutive cases of ACAS presenting with axial ataxic syndrome (atypical ACAS), out-of-proportion to motor deficits were clinically characterized. Classical (crural paresis/hemiparesis) ACAS were used as controls. All patients underwent MRI. Vascular lesion topography was compared between groups by two Neuroradiologists blinded to the diagnosis

Results: We obtained four atypical and five classical ACAS cases. All four atypical ACAS cases had right ACAS. Four patients presented with acute instability while standing and three patients also while sitting. All had left lateropulsion but no limb paresis or dysmetria. All atypical ACAS had caudal cingulate zone (CCZ) infarction on MRI (part of Brodmann's area 24, posterior to the vertical anterior commissure line), with variable involvement of other medial frontal wall areas. Among controls, only one patient had CCZ involvement.

Conclusion: We report the first case series of ACAS presenting with lateralized axial ataxic syndrome, interestingly all right-side ACA, with particular involvement of CCZ, when compared to classical ACAS. This is in agreement with previous case reports and the available evidence of a fronto-thalamic-cerebellar connection that may involve the cingulate cortex. The evidence that ACAS may present with cerebellar-like symptoms has relevant clinical implications.

Disclosure: Nothing to disclose

EPO1020

Ischemic stroke in patients with malignant solid tumors: a descriptive analysis

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Background and aims: The relationship between stroke and cancer is complex and not yet well characterized. The aim of this study is to describe ischemic stroke in cancer patients.

Methods: Retrospective review of the clinical files of adult patients of our centre with malignant solid tumors who suffered ischemic stroke between 2012 and 2017. Demographic, cancer-related and stroke-related data was collected. A descriptive statistical analysis was then performed.

Results: 55 patients were identified (39 male and 16 female), mean age 65.1±12.3 years. Digestive system tumors were the most frequent (29.1%). The median time between cancer diagnosis and stroke was 9.0 (interquatile range=[2.0;36.0]) months. By the time of stroke, 34.5% of patients had metastization and 36.4% were under chemotherapy (platinum-based regimens in 80.0% of cases). 10.9% of patients had no traditional vascular risk factors, and 20.0% had only one, mostly hypertension (67.3%). 41.8% of the strokes resulted from an apparently embolic mechanism. The cancer treatment was interrupted or suspended in 60.7% of the patients who were under chemo and/or radiotherapy.

Conclusion: Embolic mechanisms seem to play an important role in the pathophysiology of stroke in cancer patients. Our data suggest that platinum-based regimens may have a role in the occurence of stroke in patients under chemotherapy, and inferential studies shall be performed in order to verify this association. Ischemic stroke represented per se an unfavourable prognostic factor in the oncologic disease, because it interfered with the performance of the previously proposed oncologic treatment.

Disclosure: Nothing to disclose

EPO1021

Cerebrovascular disease In antiphospholipid syndrome: 20-year experience in a University hospital

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Background and aims: Antiphospholipid syndrome (APS) is an autoimmune disorder for which optimal clinical management remains controversial. Specific immunologic profiles may have prognostic relevance.

Methods: We conducted a retrospective analysis of the electronic database of our stroke centre university hospital Neurology Department and included patients admitted due to APS related cerebrovascular disease from 1997 to 2017. Clinical, immunological and therapeutic variables were registered.

Results: Seventeen patients (82% female, mean age of 48±17 years) were included. Seven patients (41%) were receiving antithrombotic therapy because of previous thrombosis; 3 antiplatelets (AP), 2 oral anticoagulants (OAC), 1 AP+OAC and 1 subcutaneous heparin (SH). Twelve patients presented with ischemic stroke, 4 patients with transient ischemic attack (TIA) and 1 patient with cerebral venous thrombosis (CVT). Triple antiphospholipid antibodies (aPL) positivity was detected in 5(29%) and lupic anticoagulant (LA) in 12(71%). On discharge most patients (9, 53%) were prescribed vitamin K antagonists (VKA), 1 dabigatran 110mg bid plus AP, 2 VKA+AP and 4 AP. After 4.9±4.5 year's follow-up, 3 recurrences (1 stroke and 1 retinal artery occlusion in 1 patient and 2 TIA) and 5 deaths (4 related to APS or antithrombotic therapy complications) were registered. Nine patients were functionally independent (mRS 0-2) and 3 were functionally dependent (mRS 3-4) at the end of follow-up. Neither triple aPL nor LA positivity were significantly associated with stroke/TIA recurrence or death.

Conclusion: In our experience, APS related cerebrovascular disease had significant morbidity and mortality. Clinical management was heterogeneous. No predictors of poor prognosis were detected, although small sample size may be responsible.

Disclosure: Nothing to disclose

EPO1022

Intracerebral haemorrhage and venous thromboembolism: ten years experience of a therapeutic challenge

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Background and aims: Venous thromboembolism (VTE) constitutes a major complication in patients with an intracerebral haemorrhage (ICH). In addition, patients on anticoagulation due to VTE may be at increased risk of ICH. Limited evidence is available to guide clinical decisions when VTE and ICH concur.

Methods: We conducted a retrospective analysis of the electronic database of our stroke centre university hospital, and included all patients admitted due to ICH from 2007 to 2017 with either previously diagnosed VTE (pVTE) or with acute VTE (aVTE) diagnosed during admission. Treatment with inferior vena cava filter (IVCF) insertion or anticoagulant drugs was individualised depending on ICH, VTE severity and overall prognosis. Clinical and therapeutic variables were registered.

Results: Thirteen patients (7, 54% male, with a mean age of 78±12 years) were included, 8 in pVTE and 5 in aVTE group (4 symptomatic and 1 incidental VTE). Eight patients (62%) were on anticoagulation prior to ICH. ICH was deep in 7 cases (54%), lobar in 4(31%) and mixed in 2(15%). During admission IVCF was placed in 6(46%). Anticoagulant therapy was prescribed in 5(38%) after a median of 30(range 7-180) days: upon discharge in 3 and later reintroduced in 2. No recurrences of ICH were registered. One patient treated with IVCF insertion developed deep vein thrombosis (DVT). After a follow-up of 25±25 months, 7 patients died (54%), 2 because of VTE related complications and 1 secondary to ICH.

Conclusion: IVCF insertion was associated with DVT recurrence but no other major complications occurred. Concomitant VTE and ICH had significant morbidity and mortality.

Disclosure: Nothing to disclose

Cognitive neurology/neuropsychology

EPO1023

Resistance to eye opening in patients with disorders of consciousness

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Background and aims: Resistance to eye opening (REO) is a commonly encountered phenomenon in clinical practice. We aim to investigate whether REO is a sign of consciousness or a reflex in severely brain-injured patients.
Methods: We recorded REO in chronic patients with disorders of consciousness during a multimodal diagnostic assessment. REO evaluations were performed daily in each patient and clinical diagnosis of unresponsive wakefulness syndrome (UWS), minimally conscious state with (MCS+) or without (MCS-) preserved language processing was made using the Coma Recovery Scale-Revised (CRS-R).
Results: Out of 150 consecutive patients, 79 patients fit inclusion criteria. REO was seen in 19 patients (24.1%). At the group level, there was a significant relationship between the presence of REO and the level of consciousness. We also observed a difference in the repeatability of REO in patients in MCS+ compared to UWS and MCS-. Out of 23 patients in UWS, six showed REO, in whom five showed atypical brain patterns activation.
Conclusion: Our findings suggest a voluntary basis for REO and stress the need for multiple serial assessments of REO in these patients, especially since most patients show fluctuating levels of consciousness.
Disclosure: Nothing to disclose

EPO1024

Neuropsychological and brain gray matter volume (GMV) changes after a computer-assisted cognitive treatment (CACT) in patients with multiple sclerosis (MS)

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Background and aims: MS negatively affects cognitive functions, causing an important impact on quality of life. The aim of this work is to study the effectiveness of a CACT in MS patients and to determine the changes in structural and functional magnetic resonance imaging (MRI) studies.
Methods: Twelve relapsing-remitting MS patients with mild-moderate cognitive impairment (9 women; average age 38.83) and clinically stable disease received 24 sessions (3/week) of CACT focused on information processing, attention, memory and executive function through the neurorehabilitation web platform Neuronup®.
Alternative forms of the Repeatable Battery of Neuropsychological Test, Multiple Sclerosis Neuropsyhcological Questionnaire and the Multiple Sclerosis Impact Scale were used to evaluate patients before and after the intervention. Additionally, a structural and functional (resting-state) MRI studies were performed pre-post treatment.
Results: After intervention, cognitive evaluation showed improvements in verbal memory (p=.04) delayed visual memory (p=.03), working memory (p=.004) and semantic fluency (p=.04). No changes were found in subjective cognitive impairment or in the impact of the disease. Structural MRI analysis (Voxel Based Morphometry) showed an increase of the global GMV (average increase of 0.7%; p=.03) in the majority of patients. Furthermore, resting-state fMRI studies showed a decrease of fALFF (fractional amplitude of low-frequency fluctuations) in the cingulate cortex after the treatment.
Conclusion: The CACT improves cognitive performance and may induce structural and functional changes in the brain of MS patients. These findings suggest that CACT may favor neuroplasticity inducing changes in the cortical reorganization and helping to improve either cognitive or brain reserve.
Disclosure: Nothing to disclose

EPO1025

Nonverbal impairment in the posterior forms of aphasia

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Background and aims: The posterior parts of the brain hemispheres are responsible for receiving, perception processing, and storage of the exteroceptive information. A local lesion leads to impairment of human verbal thinking–aphasia. The difficulty of their rehabilitation because these patients have disrupted cortical control of auditory perception and processing of speech information.

Methods: From 2006-2017 we observed 348 patients, 183 men, 165 women, aged 18-92 years, with 37% of acoustic-gnostic aphasia, 27% acoustic-mnestic aphasia, 29% semantic aphasia. In the process of rehabilitation treatment, the patients received speech therapy. At the same time, we studied impairment of non-verbal thinking and performed the cognitive rehabilitation.

Results: In the examination of patients with severe aphasia, in contrast to the moderate and mild forms, there was domination of non-verbal cognitive functions, namely: 1) neurodynamic disorders in patients with acoustic-gnostic aphasia; 2) considerable changes in the visual gnosis in patients with acoustic-mnestic aphasia; 3) disorders of visual and visual-spatial perception in patients with semantic aphasia. Based on the results of clinical studies were adjusted to a rehabilitation program: in addition to the standard voice rehabilitation of the proposed directional reconstruction of non-verbal cognitive functions.

Conclusion: As a result of complex rehabilitation, it has been a significant regression of speech disorders in more than 2/3 of patients. Thus, the use of simultaneous training of verbal and nonverbal functions, has allowed to increase almost twice the efficiency of the neurorehabilitation.

Disclosure: Nothing to disclose

EPO1026

Attention and working memory throughout the lifespan

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Introduction: Aging determines changes in cognitive performance, with an emphasis on working memory, episodic memory and processing speed. Regarding working memory, age seems to have a particularly negative effect when task requirements increase, demanding higher concentration levels, division of attention and more elaborated strategies of stimulus control.

Aims: To assess the effect of age (from adolescence to late-adulthood) on measures of attention, psychomotor control, and processing speed, namely the Toulouse-Pièron (TP), Trail Making Test A/B (TMT) and Stroop Color Test C/CW.

Methods: Cross-sectional study with 279 community-dwelling subjects without neurological or psychiatric pathology, aged between 15 and 83 years. The sample was divided according to ten years' intervals (age) and into three education groups: 1-4, 5-10 and 11 years or more.

Results: There was a significant interaction between TP, TMT and Stroop Color Test results in all groups. Multiple linear regression analysis showed that age was the most significant predictor of test performance in all measures; particularly in TP, together with education, this model explained 52% of the variance of results. The negative effect of age was only significant above the group of 45-54 years.

Conclusion: Our results demonstrated that both attention and working memory suffer a negative impact across ageing, with a most significant effect in time-dependent tasks, particularly after the age of 45.

Disclosure: Nothing to disclose

EPO1027

Worse task switching in middle-aged patients with uncomplicated grade 1-2 essential arterial hypertension: impact of vascular age

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Background and aims: Executive dysfunction is common in patients with essential arterial hypertension (EAH). Vascular age (VA) is an important factor of target organ brain damage in EAH. Our objectives were to compare vascular age using SCORE and Framingham scales and to find possible correlations with executive functions in untreated grade 1-2 middle-aged patients with EAH compared to controls.

Methods: 50 healthy volunteers (mean age 47.3±5.5 years) and 103 hypertensive patients (mean age 51.2±5.2 years) were recruited. Neuropsychological assessment included Montreal Cognitive Assessment (MoCA), Trail Making test (part A and part B), Stroop Color and Word Test, verbal fluency test, 10-item word list learning task. VA was calculated using SCORE project scales and Framingham Heart Study risk tables.

Results: Hypertensive patients had lower MoCA score (28.4±1.4 points vs 28.9±1,3 points, p=0.02), worse performance in TMT B (119.4±42.5 vs 105.5±31.4; p=0.03) and higher TMT difference score (80.7±42.5 vs 62.9±27.9; p=0.002) compared to controls. In hypertensive patients SCORE and Framingham VA (57.7±7.4 and 64.6±11.0 years) was higher than chronological one (p<0.001) and higher than the same corresponding values in the control group (p<0.001). Significant negative correlations were found between VA and mean MoCA score (SCORE: r=-0.207; Framingham: r=-0.276, p<0.05), and TMT difference score (SCORE: r=-0.128; Framingham: r=-0.254, p<0.05).

Conclusion: Patients with EAH compared to controls have worse task switching which correlates with VA, especially with VA calculated by Framingham Heart Study risk tables. Early vascular ageing is an important factor in brain damage in EAH even in middle-aged patients with early stages of the disease.

Disclosure: Nothing to disclose

EPO1028

Linguistic and Functional Mechanisms of Post-Stroke Dynamic Aphasia: Benefits of Combined Therapy with Donepezil and Memantine.

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Background and aims: Dynamic Aphasia (DA) is a rare form of language disorder characterized by considerably reduced but relatively normal spontaneous speech, with preservation of other verbal language functions. Two types of DA have been described: (I) language-specific type and (II) domain-general type. Research in physiopathology provides evidence to treat specific DA patients with cholinergic modulators. However, strategies combining two drugs have never been reported so far.

Methods: We report an open-label single case study (n=1) in a patient with a chronic type I/II DA secondary to an ischemic infarction in the left fronto-insular and supplementary motor areas (high resolution 3-T MRI). After baseline evaluation, the patient received donepezil 5 mg (2 months), donepezil 10 mg (2 months), donepezil 10 mg/memantine 20 mg (4 1⁄2 months) and washout (1 1⁄2 months). No speech-language therapy was used. A comprehensive cognitive and language evaluation was carried out at baseline and at different endpoints, performing four 18FDG-PET along pharmacotherapy.

Results: Donepezil 5 mg significantly improved type I DA features (normalization of verbs generation, p=0.01), whereas donepezil 10 mg did the same with type II traits (normalizing spontaneous speech, verbal fluency and improving generation of novel thoughts, p=0.004), along with improvement of executive-attentional functioning. Combined therapy further enhanced cognitive function, but did not additionally improved DA. No adverse effects were registered and the patient reported a considerable improvement in quality of life after treatment.

Conclusion: In our experience, pharmacological treatment improved language deficits in a chronic type I/II DA and was well-tolerated.

Disclosure: Nothing to disclose

EPO1029

Cognitive impairment in patients with progressive supranuclear palsy and multiple system atrophy

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Background and aims: In most recent neuropsychological studies, only the screening methods were applied to assess global cognition and executive functions in PSP and MSA, e.g. the Frontal Assessment Battery and the Dementia Rating Scale. Our aims were assessment, description and mutual comparison of cognitive impairment in patients with progressive supranuclear palsy (PSP) and multiple system atrophy (MSA).

Methods: In our detailed neuropsychological battery, executive functions, attention, verbal fluency and visual perception were examined; tests such as TMT, Stroop test, ROCF, Verbal fluency, Block design, FAB, MMSE and Clock drawing test were used to explore cognitive domains.

Results: Pilot results show that patients clinically diagnosed with probable MSA (17) had no cognitive impairment in 11 cases, 5 patients had mild cognitive impairment and 1 patient had dementia. Out of patients clinically diagnosed with probable PSP (35), 17 patients meet the criteria for dementia, 15 patients for mild cognitive impairment; in these 32 PSP patients dysexecutive syndrome was present. In other 3 PSP patients only attention deficit was seen.

Conclusion: In both groups of patients cognitive impairment was present. Patients with probable PSP had cognitive impairment more often and was evident already in screening methods in comparison with patients with probable MSA. If patient with probable MSA or probable PSP had at least mild cognitive impairment, deficits in executive functions were present. Nevertheless, the research in larger cohorts is planned to involve more PSP and MSA patients with different phenotypes.

Disclosure: Study supported by: Grant IGA_LF_2017_040, Institutional support MZ CZ–RVO FNOL 2017

EPO1030

Dressing apraxia – not only while dressing

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Background and aims: Apraxia usually occurs after dominant hemisphere lesions. Dressing apraxia, involving a visuospatial dysfunction, is the exception, being associated with right hemisphere lesions. We present a case of dressing apraxia with associated apraxia for other bimanual tasks after ischemic stroke.

Results: A 48-year-old right-handed female, previously healthy, presented with acute left upper limb paresis. She also complained of inability to perform some daily tasks, such as tying a garbage bag. On examination, we observed distal left upper limb paresis and hypoesthesia, with errors in position testing, optic ataxia with the left hand, and topographical disorientation. On praxis evaluation, dressing apraxia was noted. Additionally, she could fold a shirt and tie a garbage bag without mistakes using the right hand. However, with either the left or while using both hands, she was unable to perform the same tasks. There was no neglect. Brain MRI showed a right parieto-occipital ischemic stroke, involving the superior parietal lobule. Brain images were normalized to the MNI152 and the probability of interruption of each neuronal tract was calculated using the Brain Connectivity and Behaviour Toolkit software package. Tracts with >95% lesion probability were the corpus callosum, superior longitudinal fasciculus, cortico-spinal tract, and anterior segment of the arcuate fasciculus. No aetiology for the stroke was found.

Conclusion: Dressing apraxia, topographical disorientation and optic ataxia, while infrequent, occur after right superior parietal lesions. Inter-hemispheric disconnection with lesion of corpus callosum fibers could explain apraxia of the non-dominant limb, by isolating the right motor cortex from left hemisphere motor representations.

Disclosure: Nothing to disclose

EPO1031

Translation, cultural adaptation and assessment of psychometric properties of the Greek version of Parkinson's disease Cognitive Rating scale

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Background and aims: The Parkinson's Disease Cognitive Rating Scale (PD-CRS) was designed for the assessement of cognitive functions especially affected in Parkinson's disease (PD). The purpose of the present study was to translate and culturally adapt PD-CRS in the Greek language as well as to evaluate its ability to distinguish the cognitive performance of PD-patients and healthy controls.

Methods: The PD-CRS scale was translated into Greek and was initially administered to a group of 15 healthy and relatively highly educated individuals in order to identify and adequately replace culturally specific items. Four such items (included in the confrontation naming task) were found. The items were replaced with new ones, preserving the semantic heterogeneity and difficulty level of the original scale. The revised scale was then administred to a group of 118 healthy adults (selected to represent different ages and levels of education) and 59 PD-patients. Next, discriminant function analysis was performed on each scale subcore and total PD-CRS score.

Results: Healthy adults performed better than PD-patients in all PD-CRS tasks. The total cortical score and the total subcortical score contributed to optimal discrimination accuracy of the two groups (total separation accuracy 97%). The final model categorized successfully 98% of the patients and 96% of healthy participants (Wilks' λ=0.244; x2(2)=249.68, p <0.01).

Conclusion: The Greek version of PD-CRS scale exhibited an excellent discrimination accuracy of PD-patients and healthy subjects. The study is still in process.

Disclosure: Nothing to disclose

EPO1032

Acute ischemic strokes presenting as transient global amnesia

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Background and aims: Transient global amnesia (TGA) is a clinical syndrome characterized by a sudden onset of anterograde amnesia accompanied by various degrees of retrograde amnesia, lasting within 24 hours, without compromise of other neurologic functions. We want to describe 3 cases with acute ischemic stroke of extra-hippocampal location, which presented as TGA.

Methods: We retrospectively reviewed and analyzed the medical records and brain MRIs of all TGA patients, who visited our Neurology department and checked diffusion-weighted MRI from October, 2010 to June, 2017.

Results: Among 67 TGA patients, acute ischemic infarction of extra-hippocampal location was observed in 3 patients. The locations of infracted lesions were left orbitofrontal, left prefrontal, and right frontal plus left parietal cortex in each of 3 patients. Except for the presence of acute infarction, other diagnostic characteristics of TGA were well applied in all patients.

Conclusion: Transient amnesia as the main manifestation of acute ischemic stroke is rare. Our cases showed acute ischemic infarction of extra-hippocampal location (orbitofrontal, prefrontal, and parietal cortices of dominant hemisphere) can present as transient amnesia mimicking TGA.

Disclosure: Nothing to disclose

EPO1033

Executive dysfunction and mood disorders: how Chronic Obstructive Pulmonary Disease may complicate Alzheimer's Disease

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Background and aims: Chronic Obstructive Pulmonary Disease (COPD) is a common lung illness associated with cognitive and psychological impairment, which entails a clear deterioration in the quality of life. By means of a retrospective study on patients with Alzheimer's Disease (AD) with and without COPD, we analyzed clinical and neuropsychological variables to verify if COPD plays a pejorative role on neuropsychological profile in patients with dementia.

Methods: We collected data of 23 adult patients with probable AD and COPD (AD-COPD) and 23 with AD only (AD), matched for sex, age, educational level and Mini Mental State Examination (MMSE) at the disease onset. We compared cognitive and behavioral aspects assessed within two years of the disease onset: memory, executive function and constructional apraxia, language, the presence of anxiety and depression were the variables analyzed. Disease progression was evaluated comparing MMSE two years after the first evaluation.

Results: AD-COPD had worse performances in executive functions tests than AD, and also showed a higher presence of depression. No significant difference there was between the two groups considering the decrease in MMSE score.

Conclusion: COPD is known to be associated with the development of cognitive deficits and mood disorders. Our study shows a higher frequency of executive dysfunction and depression in patients with AD and COPD in comparison with patients with AD only, even in the early stages of the disease. Comorbidity with COPD may complicate the management of AD patients, that could benefit from a closer and multidisciplinary monitoring.

Disclosure: Nothing to disclose

Epilepsy 1

EPO1035

Trazodone: a new antiepileptic drug for Dravet syndrome?

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Background and aims: Dravet syndrome is an epileptic encephalopathy associated with SCN1A mutationstypically refractory to antiepileptic drugs (AED).

Methods: Woman, 25 years old, with refractory epilepsy and developmental delay since 5 months of age, had a genetic test in 2016 that confirmed a SCN1A gene mutation. Her usual pattern of seizures under triple AED was an average of 1-2 tonic-clonic seizures per night.

Results: Electroencephalographic and polysomnographic studies documented bilateral frontal spikes and polyspikes during sleep (averaging 170/h of sleep), frequently associated with subtle eye and eyelid involuntary movements (averaging 90/h of sleep). In June 2017, the patient's mother mentioned worsening of sleep pattern with significant insomnia, which led to the introduction of trazodone (225 mg/day). Since then, a remarkable improvement of both sleep pattern and seizure frequency was registered, with four nocturnal seizures in 4 months. A new polysomnographic study was conducted, that showed a substantial improvement of intercritical activity (averaging 30/h), no documentation of tonic-clonic seizures, and only rare subtle eyelid myoclonic seizures (averaging 0.7/h of sleep). Sleep structure, despite slight increase in N3, was similar.

Conclusion: Recent data from animal studies suggest that serotonergic pathway modulation may function as a therapeutic target for Dravet Syndrome. The beneficial effect of lorcaserin (serotonin receptor agonist) and fenfluramine (serotonin release agent) has been documented in a few human cases. Our case suggests a direct antiepileptic role (as opposed indirect improvement in sleep structure) of trazodone in Dravet syndrome, reinforcing the possible advantageous effect of serotonergic modulation in these patients.

Disclosure: Nothing to disclose

EPO1038

Prediction of motor function for surgical indication of hemispherectomy in epilepsy patients

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Background and aims: Prediction of motor function before hemispherectomy in patients with epilepsy is important to determine surgical approach, information about the most effective test is still restricted.

In this study we evaluated feasibility of tests for prediction of postoperative motor function (MF) in order to determine the indication of hemispherectomy for adults.

Methods: Examinations to determine surgical indication for hemispherectomy were performed in 5 patients since 2004. We examined retrospectively the following evaluations and MF after surgery.

Preoperative motor weakness

- TMS-MEP (Transcranial Magnetic Stimulation-Motor Evoked Potential)
- Wada test (WT)
- DTI–tractography (DTT) (Diffusion tensor imaging)

Results:

- 5/5 patients presented hand weakness after the injection on the affected side in WT
- DTT was detected preoperatively in all patients, not consistent for prediction. Only one patient deteriorated
- Preoperative motor weakness TMS-MEP might be useful to determine the indication for hemispherectomy.
- 2/5 patients had finger movement preoperatively, and 2/5 patients in whom MEP was provoked by TMS. One partially deteriorated the other did not undergo surgery.
- 3/5 patients who were not provoked MEP not suffered deterioration.

Conclusion:

- TMS-MEP has limitation for prediction of MF.
- Selective WT is good
- Quantitative evaluation of piramydal tract (FA value)
- WT and DTT could not be reliable for determining surgical indication
- It is so difficult to predict postoperative MF that we need to perform presurgical multi-modality examinations as TMS-MEP, DTI, WT, according to individual clinical conditon.
- Preoperative MF and TMS-MEP might be useful to predict motor deterioration after hemispherectomy.

Disclosure: Nothing to disclose

EPO1039

Emergency department management of epileptic seizures in known epileptic patients: a descriptive study.

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Background and aims: Seizure is a frequent reason of admission in emergency department (ED). Our aim is to analyse the characteristics of known epileptic patients (KEPs) admitted to ED for seizures. We focus on the seizure precipitating factors (SPFs).

Methods: We retrospectively review of patients older than 14 years admitted for seizure to a tertiary hospital ED during a 23-month period. For KEPs, we collected clinical epilepsy features and characteristics of their management in ED.

Results: 152 (42.69%) out of 356 patients admitted for seizure were KEPs (96 males; median age: 51). Focal seizures were the most frequent clinical presentation (49.3%); 120 (78.9%) of the KEPs admissions concerned single seizure and 6 (3.9%) status epilepticus. There were secondary complications in 14 (9.2%) patients. Epilepsy was structural in 75 (49.3%) patients; 88 (57.9%) KEPs were under a single antiepileptic drug and 28 (18.4%) patients were pharmacoresistant. In the 53.3% of the admissions, SPFs were found. Missing medication was the most frequent SPF (30.9%). In 85 (55.9%) patients the treatment was adjusted and levetiracetam was the antiepileptic drug most employed (35.3%); Of the 152 KEPs admissions, 130 (85.5%) were discharged without hospitalization.

Conclusion: KEPs mean almost the half of ED admissions for seizure. A SPF is found in a high percentage of KEPs seizures, being missing medication the most common factor. We consider important to improve KEPs education about seizure triggers in order to reduce ED admission and secondary complications in this group of patients.

Disclosure: Nothing to disclose

EPO1040

Prevalence and Risk Factors for Posttraumatic Epilepsy

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Background and aims: Posttraumatic epilepsy (PTE) is defined by the presence of two unprovoked seizures at least 1 week after a traumatic brain injury (TBI). It causes 5-20% of structural epilepsies. Underlaying mechanisms are unknown. Risk factors such as age, TBI mechanism and severity, presence of early seizures, skull fracture, subdural haematoma, and age above 35 years have been described. The aim of our study was to evaluate the prevalence and risk factors associated with PTE in patients with TBI admitted to the Intensive Care Unit (ICU) of our Hospital.

Methods: We retrospectively reviewed 220 medical records from patients admitted into ICU between 2010-2017. We excluded those with incomplete medical records and previous diagnosis of epilepsy. All had a previous normal electroencephalogram. Statistical analyses of demogaphics, TBI mechanism, glasgow, focal neurological deficits, skull fracture, posterior amnesia, brain CT abnormalities, decompressive craniotomy and surgical evacuation was performed with SPSS.

Results: 93 patients were included, 24% developed PTE, 77% were men, the mean age was 37.3. The most frequent mechanism was polytrauma, no statistical significance between the different mechanisms was found. Amnesia and age had statistical significance (p:0.013; p:0.013) as risk factors for PTE. Epidural haematoma doesn't increase the risk for PTE (p: 0.05). Patients who underwent craniectomy or surgical evacuation didn't develop PTE (p:0.035- 0.005 respectively).

Conclusion: The prevalence of PTE was higher in our population compared to the described in literature. We only found association regarding the development of PTE with age, amnesia, epidural haematoma, craniectomy and surgical evacuation.

Disclosure: Nothing to disclose

EPO1041

Efficacy and safety of the AspireSR® VNS at Ghent University Hospital, Belgium

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Background and aims: The AspireSR® VNS system is the first VNS device with an automated seizure detection feature providing stimulation in response to a preprogrammed ictal heart rate change. This study evaluates the efficacy and safety of the AspireSR® VNS in a cohort of 10 refractory epilepsy patients with a minimum follow up of 6 months.

Methods: We investigated the change in mean monthly seizure frequency (MMSF), responder rate (RR) and adverse events (AE) at maximum follow up (FU).

Results: One patient with a 12-month FU had a reduction in MMSF from 30 to 5. Five patients with a 9-month FU had a MMSF reduction from 6 to 4. Four patients with a 6-month FU had an increase in MMSF from 35 to 48. One patient was seizure-free during more than 3 months, but had a significant increase in anti-epileptic drugs. There was a responder rate of 30%. Five patients reported less severe seizures. The most frequently reported AE was hoarseness, experienced by 6 patients. Other AEs were rare. In 5 patients, the stimulation parameters had to be adjusted due to AEs

Conclusion: The first clinical results of the patients implanted with the AspireSR® VNS system in Ghent University Hospital show a RR comparable with previous short-term VNS studies. There appears to be an increase in MMSF at 6 months of treatment, probably due to the small sample size, inclusion of severe childhood epilepsy and short-term follow-up. The safety profile appeared to be comparable to the non-cardiac based VNS devices.

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EPO1042

Status epilepticus: a retrospective observational study.

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Background and aims: Status epilepticus is a neurological emergency that generates a significant morbidity and mortality. We analize the characteristics in our population.

Methods: Retrospective observational study based on the review of digitalized clinical records at the Hospital Reina Sofía, Murcia, from January 2011 to December 2016.

Results: There were 35 patients, with a mean age of 64 years, of whom 34.3% were diagnosed with epilepsy. The 68% of cases presented convulsive status and 43% required intensive care (37% sedation and 31.4% intubation); 30% finally did not have diagnostic confirmation with electroencephalogram. The most frequent causes were changes in their antiepileptic treatment and cerebrovascular diseases, being also significant the cases of unknown ethiology. Approximately 70% of the patients needed three or more drugs, being the most used Phenitoine, Levetiracetam, Valproate and Diazepam; 23% of status reappeared when the medications were withdrawn. Finally, 28.6% of patients died, 40% had neurological sequelae and 74% presented complications during hospitalization, especially of an infectious cause.

Conclusion: Status epilepticus is a major neurological condition. In our sample, half of patients were controlled with the third anticonvulsant, but there were cases where even nine drugs were needed. In addition, the mortality rate was notorious, as well as the percentage of sequelae, being important to use the adecuate treatment in order to eliminate seizures as soon as possible.

Disclosure: Nothing to disclose

EPO1043

The prevalence of different types of epilepsy in childhood and adolescence in the Siberian region

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Background: The prevalence of epilepsy in developed countries ranges from 1.5 to 18 people, and in some developing countries exceeds 30 per 1000 of the population. In 70-75% cases of epilepsy occur in childhood and adolescence. Long-term observations are shown that the frequency of occurrence of a particular type of epilepsy depends on the age.

Objective: to study the prevalence of different types of epilepsy in childhood and adolescence in the Siberian region.

Methods: The study and dynamic observation involved 882 patients (463 boys and 419 girls) with epilepsy and epileptic syndromes. Children from 0 to 14 years–740 people, adolescents 15-17 years–142. Among children under 14 years of age number of children 0 to 3 years amounted to 199 people, 66 children in the first year of life. Forms of epilepsy were diagnosed by neuroimaging (magnetic resonance tomography of the brain) and functional methods of investigation (EEG with standard functional tests, video monitoring).

Results: The average prevalence of epilepsy and epileptic syndromes among children and adolescents in the Siberian region in 2012-2017 was 3.54 per 1000 population (under 14 years–3.34 ; 14-17 years–4.24). Prevalence of symptomatic focal (structural) epilepsy was a statistically significant superiority (p=0.0001)-45.58% (incidence of 2.11 per 1000 population),second place is occupied by cryptogenic (unspecified) forms -17.35% (prevalence 0.80); idiopathic focal epilepsy-14.74% (prevalence of 0.68), idiopathic generalized-13.49% (prevalence 0.62). Progressive myoclonic epilepsy were rare-0.23% (prevalence 0.01).

Conclusion: Among the forms of epilepsy in childhood and adolescence in the Siberian region dominated by symptomatic focal epilepsy.

Disclosure: Nothing to disclose

Headache and pain 1

EPO1044

Predicting treatment response to candesartan in migraine patients

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Background and aims: Randomised placebo-controlled studies have reported a positive effect of candesartan, an angiotensin II receptor antagonist, in migraine prevention. The aim of our study was to identify response predictors to candesartan in a sample of migraine patients.

Methods: We audited the clinical records of patients who attended the King's Headache Clinic from February 2015 to December 2017, examining their response to candesartan. Univariate and multivariate logistic regression models were used to assess for predictors of outcome. Odds ratios (OR) with confidence intervals (CI) 95% were also calculated.

Results: The clinical history of 236 migraine patients was reviewed. A total of 100 patients (78 females) who had candesartan were included in the final analysis. One hundred and thirty-six patients were excluded cause to missing data. Forty-four patients reported a positive response to candesartan, while 56 did not have a significant therapeutic effect. The median dose of candesartan was 8mg (range: 2–32) and the average treatment period was 7 months (range: 1.5–31). In the univariate logistic regression analysis, no one of the predictors was associated with the outcome. A diagnosis of chronic migraine was associated with higher odds of a positive response to candesartan (OR 9.98, 95% CI 1.3–79.9, p=0.03) in a model adjusting for age, sex, medication overuse, disease duration, number of headache days per month, presence of aura and the total number of preventive therapies tried by patients.

Conclusion: Candesartan is effective for migraine prevention in chronic migraine patients, irrespective of previous failed preventives.

Disclosure: Nothing to disclose

EPO1045

Aura and important prodrome symptoms of migraine: A research in Greek population

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Background and aims: In some cases of migraine, the initial phase of the attack is characterized by the presence of "prodrome" or "premonitory" symptoms. These may not be recognized by the patient as part of the attack and are probably the most neglected aspect of migraine. They include a heterogeneous range of cognitive, psychological and physical changes. Prevalence rates of migraine patients reporting one or more premonitory symptoms vary.

Methods: By using a semi-structured interview, we studied the prevalence of major premonitory symptoms and aura in a population of migraine patients in a Tertiary Neurology Department of Athens University.

Results: Of 206 migraine patients who participated in the study, 176 were women and the mean age was 48.5 y.o, with a range between 18y.o. and 80 y.o. Fifty-four patients (26%) reported aura: visual (72%); sensory (27%); monitory (9%), and; language disturbances (15%). Fifty-six (27%) patients reported various prodrome symptoms. The most frequently reported premonitory symptoms were yawning (36%); mood changes (39%), and; both of them (11%). Of the 206 patients, 19 reported both prodrome symptoms and aura: most frequently yawning and language disturbances (26%).

Conclusion: The presence of premonitory symptoms is important for the diagnosis of migraine. Accurate recording of them may predict the headache phase of migraine and provide an opportunity for early treatment in order to prevent disability of the headache phase.

Disclosure: Nothing to disclose

EPO1046

Microstructural abnormalities on migraine

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Background and aims: Until now among scientists scientific discussions are conducted: whether a migraine is the disease of cerebrum. The aim of our study is to investigate the white matter microstructural differences in the brains of patients suffering from migraine without aura.

Methods: We investigated 29 patients with DT MRI (Diffusion tensor magnetic resonance imaging) and tractography. DT MRI was calculated for each voxel resulting in getting images (map) of fractional anisotropy (FA) and mean diffusibility (MD). 23 normal volunteers were a control for conducting DT MRI.

Results: FA in the control group amounted to 0.560 (0.54÷0.58) for the front quadrants and 0.565 (of 0.56÷0.57 in) for the rear quadrants. We surveyed patients with migraine without aura had lower FA values: for anterior brain–0.52 (0.5÷0.54), for the rear–0.53 (0.52÷0.54), $p > 0.05$. In the group of healthy volunteers the values of SDS made up 0.83 (0.80÷0.86) for the front quadrants and 0.85 (0.82÷0.88) for the rear quadrants ($p > 0.05$).

The obtained results revealed significant difference of the values of SDS for the rear quadrant on the side of the headache and in the opposite hemisphere in patients with migraine is 0.91 (0.89÷0.93) and 0.87 (0.86÷0.88), respectively ($p < 0.05$). While in the occipital lobes of the brain depleted traktorista picture and not visualized posterior commissure. Along with this there has been some relationship between fractional anisotropy in the hemisphere and increased severity of seizures ($r = 0.36$, $p < 0.05$).

Conclusion: All patients have microstructural changes in the brain.DTI and tractography are integral part methods in migraine diagnostic.

Disclosure: Nothing to disclose

EPO1047

Do The Inflammatory Factors Contribute to The Pathogenesis of Vestibular Migraine?

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Background and aims: Vestibular migraine (VM) is an under-recognized entity with substantial burden for the individual and society. The underlying mechanism of VM and its distinction from other migraine mechanisms still remained unclear. A handful of studies revealed that inflammatory pathways contribute to migraine. We aimed to investigate the possible role of inflammation in the pathophysiology of VM compared to migraneurs and healthy controls.

Methods: We recruited 25 patients with episodic migraine and 32 with VM, diagnosed according to ICHD-3beta criteria and 26 sex- and age-matched healthy controls after their consent and ethical approval. Blood samples could be obtained only from 12 patients during the attack, whereas the remaining samples were taken in headache-free periods. Plasma levels of CGRP, NKA, Substance P (SP), NLPR-1, NLPR-2,CASP-1, IL-1b, IL-6, IL-8, IL-10, TNF-α, IF-γ, NFκB were measured with the commercial kits by following the manufacture's instructions.

Results: Inflammatory cytokines were found positively correlated with inflammasome pathway in both VM and migraine groups. TNF-α and IL-6 were both suppressed in VM and migraine groups while SP was reduced only in the migraine group when compared to the controls. Furthermore, inflammasome pathway factors were correlated with allodynia in patients with VM. Prophylactic treatment had no effect on cytokine levels.

Conclusion: Suppression of the inflammatory cytokines both in migraine and VM patients might be associated with a compensatory anti-inflammatory mechanism. However, VM patients had higher SP concentration while it seems to be suppressed in migraineurs. This finding may suggest that different pathophysiological inflammatory processes are in charge for these two entities.

EPO1048

Familial trigeminal neuralgia: a case report

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Background and aims: Trigeminal neuralgia is a recurrent paroxistic pain affecting one or more divisions of the trigeminal nerve. Although it is clasically considered a sporadic disease, there are several reports of familial cases.

Methods: Retrospective study of a patient diagnosed of trigeminal neuralgia with several close relatives throughout three generations also diagnosed of trigeminal neuralgia. It includes clinical description, response to treatment and MRI findings.

Results: A 52-year-old woman is diagnosed of trigeminal neuralgia affecting right V3 division of trigeminal nerve. Pain does not respond to medical treatment with carbamazepine and is treated with percutaneous trigeminal thermocoagulation, becoming assimptomatic for 19 years. Then she is diagnosed of trigeminal neuralgia affecting left V2 division of trigeminal nerve. Cranial MRI shows mild neuritis in V2 division and pain is completely relieved by carbamazepine and pregabalin. Control MRI has not specific findings. Five years later, left V2 trigeminal neuralgia reappears and does not respond to medical treatment so she is again treated with percutaneous trigeminal thermocoagulation. She has a family history of trigeminal neuralgia: granddfather, father, two aunts and two sisters.

Conclusion: This is one of the few families with familial trigeminal neuralgia described in Spain and the only one in which three generations are affected. The fact that two men and several women have the disease means that inheritance could be autosomal dominant. The finding of neuritis on one MRI suggests that the mechanism of trigeminal neuralgia in familial cases might be somehow different from microvascular compresion.

Disclosure: Nothing to disclose

EPO1049

Spontaneus pneumocephalus: an uncomommon cause of headache

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Background and aims: Spontaneous pneumocephalus, an intracranial air collection without known etiology, is a rare condition. We describe two cases.

Methods: Case report

Results: Case 1–A 61-year-old male, was admitted with headache and vomiting for five days. Headache was sudden, frontally located, severe and reached the maximum intensity within firts minute, accompanied by nausea and vomiting. An uncolored nose discharge was noticed on the upright position. There was no trauma history, recent infection or previous headache. Physical examination was unremarkable except for a clear discharge from left nostril. Brain CT scan showed a probable fistula in the left cribiform plate and extensive subarachnoid air densities within several cisterns and bilateral. Cisternography confirmed the presence of a CSF leak. Transphenoidal repair of the leak was performed and CSF rhinorrhea stopped. Headache and pneumocephalus completely resolved.

Case 2–A 39-year-old pregnant woman, with no past history of headache, suddenly developed a severe generalized throbbing headache during labour. Neurological examination showed nuchal rigidity. The brain CT scan revealed extra-axial, retroclival and retrosellar hipodensity, without mass effect. Symptomatic treatment was prescribed and headache and meningeal signs remitted in 12 hours. Brain MRI at 1 month follow-up showed air reabsorption.

Conclusion: Headache can be the sole presentation of both massive and localized non-thraumatic pneumocephalus. CT scan was not only diagnostic but also oriented management. In most reported cases treatment is not consensual. In our cases, the distinct radiological severity and the identification of a CSF fistula determined different approaches (surgical versus expectant), with complete clinical and radiological resolution.

Disclosure: Nothing to disclose

EPO1050

Socio-economic impact of severe migraine in France: study in patients with at least 8 days of headaches per month

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Background and aims: Migraine is a common and disabling pathology that notably affects active and young adults. The objective of this study was to estimate the socio-economic impact of severe migraine in French patients with at least 8 days of headaches per month.

Methods: A representative panel of French adult population (15,000 people) was surveyed using an online questionnaire in July 2017 by Kantar Health. The questionnaire's different parts were: socio-demographic data, migraine diagnosis with an extended French version of IDTM Migraine screener and socio-economic impact of the disease.

Results: On the 7,720 survey participants, migraine prevalence with at least 8 days of headaches per month in patients was 3.8% (average age: 41.1, 68% of women). 63% of workers reported an impact of the pathology on their work and especially on their efficiency. Absenteeism at work was estimated at 33 days a year on average with an annual loss of 3.8 billion euros for all actors in society. More than three-quarters of patients had sleep disorders and benefited less from their free time. For 14% of patients, a relative had to adjust his working time during migraine headaches. 58% of patients needed to purchase non-reimbursed medicines for migraine (average monthly cost of 31.9 euros) and 43% others therapies (average monthly cost of 51.7 euros).

Conclusion: Severe migraine patients are affected in their professional lives but also in their social lives and personal budgets. Migraine generates a significant burden for patients and an economic loss for society.

Disclosure: This study was supported by Novartis Pharma France.

EPO1051

Effect of OnabotulinumtoxinA Prevention on Comorbidities of Depression and Anxiety in Chronic Migraine: Analysis in Headache Day Frequency Responders vs Headache Day Frequency Non-Responders

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Background and aims: This analysis of COMPEL Study data assessed onabotulinumtoxinA on comorbid depression and anxiety in people with chronic migraine (CM) who also had a ≥50% reduction in headache day frequency at week 24.

Methods: The 108-week, multicentre, open-label COMPEL Study enrolled adults with CM receiving onabotulinumtoxinA 155U. The effect of onabotulinumtoxinA on Patient Health Questionnaire (PHQ-9) and Generalised Anxiety Disorder Assessment (GAD-7) sum scores in those with clinically significant depression (PHQ-9 ≥5) and anxiety (GAD-7 ≥10) at baseline was analysed in those who had a ≥50% reduction in headache day frequency at week 24 (headache-frequency responders) vs those who did not (non-responders). A ≥1 severity category improvement in PHQ-9 or GAD-7 was considered clinically meaningful.

Results: Patients (N=715) had a mean (range) age of 43 (18–73) years, were primarily women (84.8%, 606/715), and had depression (PHQ-9≥5: 74.5%, 529/710) or anxiety 24.6% (GAD-7≥10: 175/711). Mean (SD) headache day frequency at week 108 significantly decreased from baseline: 22 (±4.8) to 11.3 (±7.4) days (P<0.0001). Depressive and anxiety symptoms significantly (P<0.001) improved in people with depression regardless of headache day response (Figure 1A, 2A). 83.7% of headache-frequency responders and 60.3% of non-responders experienced a reduction of ≥1 Severity Category in PHQ-9. 86.0% and 71.4%, respectively, experienced a reduction of ≥1 Severity Category in GAD-7.

Conclusion: COMPEL Study results demonstrate that onabotulinumtoxinA improves symptoms of depression and anxiety among people with CM, regardless of whether onabotulinumtoxinA treatment resulted in a ≥50% reduction in headache day frequency.

Disclosure: The funding source for this study is Allergan plc (Dublin, Ireland)

EPO1052

Precipitating factors of chronic migraine: description in a series of 725 patients

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Background and aims: Among patients with Episodic Migraine (EM), 2.5% progress to Chronic Migraine (CM) over the course of one year. We herein aimed to analyze precipitating factors for CM evolution in a prospective registry of CM patients.

Methods: Patients firstly attended in an outpatient headache unit in a tertiary hospital (January 2013-January 2018). They were referred from primary care or general neurology offices. CM was diagnosed accordingly to ICHD-2R and ICHD-3 criteria. We assessed demographic and clinical data, comorbidities, and risk factors. We considered in each patient latency from onset of CM to diagnosis, and if they identified any precipitating factor for CM appearance

Results: We included 725 cases (105 males, 620 females), with mean age at inclusion of 40.1±13.7 years (12-80), age at onset of migraine of 19.3±9.7 years (3-65) and latency from onset of MC to diagnosis of 38.4±64.2 months (3-600). Among risk factors, we gathered other chronic pain conditions in 77 patients (10.6%), symptomatic medication overuse in 498 (68.7%), and mood disorders in 95 (13.1%). In 280 cases (38.6%), at least one precipitating factor was remembered. Stressful life events were described in 238 (32.8%). Other precipitants were weight gain (22, 3%), new-onset pain disorders (5, 0.6%), menopause, (4, 0.5%) labour (4, 0.5%) pregnancy (3, 0.4%), or sleep disturbances (3, 0.4%). New prescription medications were observed by 8 patients (1.1%), hormonal contraceptives in 4 cases

Conclusion: In our MC population the identification of a precipitating factor, mainly stressful life events and weight gain, is not uncommon.

Disclosure: Nothing to disclose

Miscellaneous 1

EPO1054

The effect of food intake on haemodynamic parameters during tilt-up test in patients with postural orthostatic tachycardia syndrome (POTS)

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Background and aims: To determine the effect of food intake on heart rate (HR) in POTS.

Methods: In forty-one with suspected POTS on an initial tilt-table test the following protocol was performed: 10-minute supine phase, 10-minute 70° tilted phase, ingestion of 400 ml of Nutridrink Multi Fibre®, 45-minute supine phase and 10-minute 70° tilted phase. Subjects were divided into three groups: A) difference (Δ) in HR (standing vs. supine) before the meal≥30 (N=13); B) ΔHR before the meal <30, but after the meal≥30 (N=12); C) ΔHR before and after the meal <30 (N=16). Group D consisted of 10 healthy subjects.

Results: Before the meal, ΔHR was significantly higher in group A compared to all other groups, and in group B compared to group D (p<0.00000001). After the meal, ΔHR was significantly higher in group A compared to all other groups, and in group B compared to groups C and D (p<0.0000000001) (Figure 1). Patients from group A and B were pooled into a POTS, and from group C and D into a non-POTS group. According to ROC analysis before the meal, a cut-off value of 30 bpm had the sensitivity of 52.0% and specificity of 96.2%, while a cut-off value of 25 bpm had sensitivity of 92.0% and specificity of 80.8%. After the meal, a cut-off value of 30 bpm had the sensitivity 100.0% and specificity of 92.3%.
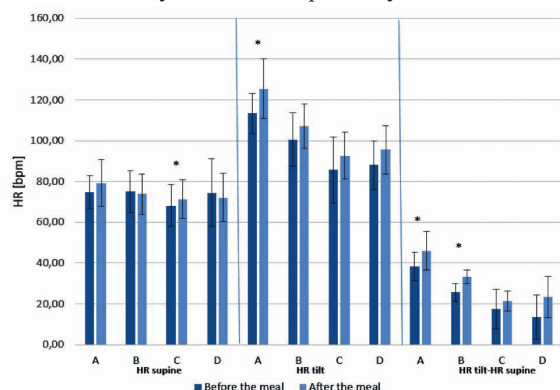
Differences in supine HR, tilted HR and the increase in HR after the tilt depending on the meal. Dark blue represents the value before the meal and light blue after the meal. Note that only in group A and B the increase in HR was significantly higher after the meal (p<0.001 and p<0.0001, respectively).

Conclusion: Food intake can significantly alter results of the tilt-table test and should be taken into account during the diagnosis of POTS.

Disclosure: Nothing to disclose

EPO1055

Evolution and predictors of symptomatic dysautonomia in people with clinically isolated syndrome

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Background and aims: One of the characteristics of structural disorders of the autonomic nervous system (ANS) is that in many patients it can be asymptomatic. Similar observations were seen in people with clinically isolated syndrome (pwCIS), where a significant discrepancy between ANS symptoms and objective assessments of ANS dysfunction was found. Therefore, we aimed to investigate the evolution and predictors of symptomatic dysautonomia in pwCIS.

Methods: In 59 pwCIS (45 females, mean age 31.88±9.12), Composite Autonomic Symptom Score (COMPASS 31) and Composite Autonomic Scoring Scale (CASS) were performed during the CIS diagnosis and 24 months later. Age, baseline Expanded Disability Status Scale (EDSS), total number of supratentorial T2 lesions and presence of brainstem lesions MRI were considered as possible predictors.

Results: Based on distribution of COMPASS 31 and CASS among the pwCIS, cut-off value of >9 and >1 were considered as significant, respectively. On M24, 8 pwCIS had both COMPASS 31 and CASS with values fulfilling pre-specified criteria. According to binary logistic regression model, total number of baseline T2 lesions and age were statistically significant predictors for symptomatic dysautonomia (Exp(B)=1.086, p=0.028 and Exp(B)=1.116, p=0.035, respectively).

Conclusion: Substantial proportion of pwCIS develops symptomatic dysautonomia over 24 months of follow-up. Total number of baseline T2 lesions and age of the patient seems to predict development of symptomatic dysautonomia over the long term.

Disclosure: Funded by the Installation Research project HRZZ UIP-11-2013-2622 of the Croatian Science Foundation.

EPO1056

Cardiovascular autonomic reflexes in syncopal migraine patients

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Background and aims: Migraine and syncope can occur in the same patient. Both conditions are known to present an impairment of autonomic regulation.

Aim: to evaluate cardiovascular reflexes in syncopal migraine patients and compare with healthy controls.

Methods: The study sample consists of 92 persons divided in four groups: Gr I (n=51)-syncopal migraine, Gr. II (n=14)-migraine without syncope, Gr III (n=15)-syncope without migraine and Gr. IV (n=12)-healthy controls. Was performed autonomic cardiovascular tests (Valsalva maneuver, orthostatic testing, deep breathing and isometric exercise). The result was classified as: normal, slight, prominent and severe modification.

Results: Abnormal cardiovascular autonomic reflexes presented 88.23% in Gr.I, 92.8% in Gr.II, 100% in Gr.III and 16.7% in Gr.IV (I vs III<0.05, t=2.6; I vs IV< 0.001, t=5.9; II vs IV< 0.001, t=12.9). Slight modification-13.7% in Gr.I, 7.1% in Gr.II, 13.3% in Gr.III and 16.7% in Gr.IV. Prominent modification: 43.1%–Gr.I, 50%–Gr.II, 60%–Gr.III and 0% in Gr.IV (I vs IV<0.001, t=6.2; II vs IV<0.01, t=3.9; III vs IV< 0.001, t=4.5). Severe modification: 31.4%–Gr. I, 35.7%–Gr. II, 26.7%–Gr.III and 0% in Gr.IV (I vs IV< 0.001, t=4.83).

Conclusion: All groups present modification of the cardiovascular autonomic reflexes more expressed than in the healthy controls, but syncopal migraine group was severely affected, which could reflect the impairment of the autonomic regulation.

Disclosure: Nothing to disclose

EPO1057

Clinical characteristics of intracranial hemorrhages in patients treated with direct oral anticoagulants in secondary stroke prevention

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Background and aims: Risk of hemorrhagic complications in patients anticoagulated after a cardioembolic stroke is double than in primary prevention. Direct oral anticoagulants (DOACs) reduce the risk of intracranial hemorrhage (ICH) by 50% compared to warfarin. We present our clinical experience of ICH secondary to DOACs in secondary prevention.

Methods: We performed an observational, retrospective study of anticoagulated patients with DOACs in secondary prevention of stroke from October 2010 to June 2015 at our tertiary university hospital. Clinical, radiological and ICH variables were collected.

Results: We included 425 patients (57.7% dabigatran, 24.7% rivaroxaban and 17.6% apixaban). 53.4% were women, mean age 77.1±10.2 years. The mean follow-up was 20±18.1 months. Median CHA2DS2-VASc was 5 (2-8) and HAS-BLED was 2 (1-4). During follow-up there were 10 (2.3%) ICH, median of 36 months (7-78) from the beginning of treatment, incidence rate: 0.015 cases / person-year. Patients were receiving treatment with Dabigatran (8), Apixaban (1) and Rivaroxaban (1). There were 5 spontaneous intraparenchymal hematomas, 3 post-traumatic subarachnoid hemorrhage, an intraventricular hemorrhage and a subdural hematoma. Anticoagulation was reversed in 3 cases. There were 2 deaths related to ICH. At 3 months 70% presented mRS≤2. Anticoagulation was discontinued in 4 patients (intraparenchymal hemorrhages). Same DOAC was reinitiated in 3 patients, in one DOAC was changed, and one percutaneous left atrial appendage closure was performed.

Conclusion: The rate of ICH in patients with DOACs in secondary stroke prevention was similar to that of the pivotal studies and patients presented low disability.

Disclosure: Nothing to disclose

EPO1058

Prognostic value of EEG in post-cardiac arrest patients

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Background and aims: In patients of post-cardiac arrest, EEG is a very useful tool to evaluate the severity of the brain damage and to determine the long-term prognosis. So we wanted to evaluate the prognostic values of various early EEG patterns of cardiac arrest patients.

Methods: We reviewed medical records and early EEG findings (within 48hours after cardiac arrest) of all postcardiac arrest patients, who were admitted to our hospital between 2013-2016. Forty-two patients were identified.

Results: Diffuse background suppression (nearly flat or flat EEG) was observed in 31 of 42 patients and was strongly associated with grave outcomes. Burst-suppressive patterns (3 patients), bilateral periodic lateralized epileptiform discharges (BiPLEDs, 3 patients), and alpha coma (2 patients) were also associated with poor outcomes. EEG findings of 4 patients who had recovered without significant cognitive sequelae were theta slowings (3 patients) and generalized beta waves (1 patient).

Conclusion: Early EEG findings have excellent prognostic values in patients of post-cardiac arrest. So called 'malignant' EEG patterns including diffuse background suppression (nearly flat or flat EEG), burst-suppression, BiPLEDs, and alpha coma were strongly associated with poor clinical outcomes.

Disclosure: Nothing to disclose

EPO1059

2-year experience of a "Store-And-Forward" e-Consultations program in a rural area in Central Spain

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Background and aims: Population aging and depopulation of the rural world are major problems in Western Europe what condition an imbalance between the volume of neurological pathologies and the endowment of neurologists. Teleneurology (TN) is an effective tool with proven efficacy in acute stroke, but there are opportunities beyond it such as chronic neurological diseases. TN can easily increase access of eldery patients to specialized care avoiding unnecessary transfers or referrals specially in rural areas.

Methods: In January 2015 a "Store-And-Forward" e-Consultation program (SAFC) was launched in the Tomelloso Hospital area. Five Health-care centers were selected and a non-face-to-face management of patients with reduced mobility was offered, as well as the management of administrative procedures and the doubts of the management of general practitioners through the SAFC program. We conducted a retrospective analysis after 2 years of experience.

Results: There were 302 e-Consultations between January 2015 and December 2017 (12.6 per month, increase of 27% in 2017). The average-resolution time was 2.66 days (50% reduction in 2017) and 51% of e-Consultations were resolved on the same day. Dementia was the main diagnostic group with administrative procedures and behavioral problems as the most frequent topics. In a conservative estimate, at least 150 face-to-face visits were avoided.

Conclusion: A SAFC program is a viable method to cope with the increased burden of neurological diseases in our aging population and can save money by avoiding unnecessary visits.

Disclosure: Nothing to disclose

EPO1062

Clinical Features in Familial Multiple Sclerosis Cases in Kütahya, Turkey

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Background and aims: Multiple Sclerosis (MS) is a chronic autoimmune disease characterized by demyelination and axonal degeneration of the central nervous system, particularly affecting young adults. MS etiology is complex and results from the interaction of multiple environmental and genetic factors.

Methods: We reviewed retrospectively 614 MS patients' records between September 2011 and January 2017.

Results: Familial MS was detected in 42 of 614 MS patients followed in our clinic(6.8%). Of these patients 34 were woman(80.95%) and 8 were male(19.04%). The disease was defined as 71.42% relapsing remitting, 11.9% primer progressive, 11.9% secondary progressive and 4.7% radiologically isolated syndrome. The mean age at onset was 29.65(except RIS). The initial symptoms of the patients were defined as 35% motor, 30% sensory, 15% diğer(sphincter disorder, hearing loss, dizziness vs.), 12.5% brainstem, 5% optic neuritis, 2.5% cerebellar findings). Distribution of MS patients according to EDSS scores at the last visit were found in 27 patients(67.5%) in EDSS 0-3, EDSS 4-5 in 2 patient(5%), EDSS 6-9 in 10 patients(25%) and EDSS 10 in 1 patient(2.5%). Of the patients 61.9% had MS in first degree relatives.

Conclusion: Familial MS frequency was investigated in various series and values ranging from 3-22% were reported. The familial MS frequency was 6.8% in our patient series in Kütahya, Turkey. We present demographic features, clinical course of our patients with MS in our familial cases.

Disclosure: Nothing to disclose

EPO1063

Spinal cord infarction: Clinical and imaging patterns, pathogenesis, and outcomes in 27 patients.

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Background and aims: Spinal cord infarction is a rare condition compared to cerebral infarction, and its clinical presentation has been poorly understood.

Methods: We prospectively investigated patients diagnosed clinically as having spinal cord infarction in our hospital.

Results: A total of 27 cases of spinal cord infarction (17 men; 10 women; aged 38–90 years; average, 64.8 years) were included in the study. Sixteen cases had risk factors of arteriosclerosis, such as hypertension and a smoking history. Many cases suddenly developed paraplegia, sensory disturbance of the lower limb, and bladder and rectal disturbances. Fifteen cases involved complains of lower back pain at onset. In 9 cases, minor exercise or trauma preceded the onset of spinal cord infarction, which tended to be more frequent in younger patients. Magnetic resonance imaging revealed that the infarction was in the anterior and posterior spinal arterial territories in 5 and 4 cases, respectively. Five cases had transverse spinal cord injuries. Seventeen and 15 cases were treated with antiplatelet drugs and corticosteroids, respectively. The average of mRS at discharge was not significantly different with or without corticosteroid treatment.

Conclusion: Relatively many cases have a history of minor exercise or trauma before onset of spinal cord infarction, and this might be associated with juvenile onset spinal cord infarction. Classification of the lesion site suggested that the prognosis of the posterior spinal artery syndrome was more favorable than that of the anterior spinal artery syndrome and transverse spinal cord injury. Corticosteroid treatment for spinal cord infarction was thought not to improve the prognosis.

Disclosure: Nothing to disclose

EPO1064

Neurolymphomatosis mimicking acute polyradiculoneuritis in a case of small B cell non Hodgkin lymphoma with monoclonal secretion of Ig G kappa, despite haematological remission

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Background and aims: Non-Hodgkin's lymphoma (NHL) can associate several neurological complications related to direct invasion of the central or peripheral nervous system, paraneoplastic involvement or iatrogenic adverse events. Neurolymphomatosis associated polyneuropathy is usually thought to follow a subacute or chronic course. We present a case of rapidly progressing demyelinating polyneuropathy due to neurolymphomatosis in the context of small B cell NHL with stable haematological markers.

Methods: A 72-year-old women diagnosed with MALT NHL with monoclonal secretion of IgG kappa 8 months before, for which she was treated with several chemotherapy drugs, was admitted for severe back pain, ascending paresthesias of the lower limbs and rapidly progressive flaccid paraparesis.

Results: Neurological examination at admission showed tetraparesis (with mild paresis of the upper limbs and severe paraparesis) and loss of deep patellar reflexes. Paraproteinemic polyneuropathy was suspected but the acute onset raised the question of acute demyelinating polyradiculopathy due to chemotherapy-associated immunosuppression. Nerve conduction studies revealed sensorymotor axonal polyneuropathy, with signs of proximal demyelination. Repeated CSF analysis showed no albuminocytological dissociation and CSF flow cytometry revealed high numbers of T-lymphocytes and no atypical cells. MRI scan of the spine displayed meningeal enhancement at cervical and lumbar levels which extended to the corresponding nerve roots. Haematological work-up confirmed the stationary phase of the MALT NHL, with no signs of disease relapse.

Conclusion: Neurolymphomatosis should be considered in patients with symptoms suggestive of acute onset demyelinating polyradiculopathy and haematological diseases. Complete haematological work-up is essential for the correct diagnosis of this disease and further guidance of treatment.

Disclosure: Nothing to disclose

Movement disorders 1

EPO1065

Aging effects of Dynein on autophagic degradation of α-synuclein in mice

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Background and aims: As we all know, aging plays an important role in the pathogenesis of Parkinson's disease, while the effect of aging of dynein is still not completely known.

Methods: The behavioral assessment was performed respectively (the rod endurance test, the climbing rod time test). We used Western blot to test the changes of expression of dynein, α-synuclein, TcTex-1, LC3 in substantia nigra of the mice, and the quantitative real time reverse transcription PCR to detect the mRNA levels of dynein, α-synuclein, LC3-IIand tctex1. The changes of expression strength of dynein and α-synuclein were detected by Immunofluorescence.

Results: Compared with the normal mice in the age of 12 months and 20 months, the motor functions of PD mice decreased more significantly($p<0.05$). Western blot showed the expression of dynein, LC3-IIand tctex1 protein in the substantia nigra of the two groups were decreased with age, while the expression of α-synuclein protein increased gradually, and the expression of α-synuclein protein in PD group was significantly higher than normal mice group at the same age($p<0.05$). These trends were found the same in immunofluorescence, which revealed that the fluorescence intensity of dynein, LC3-IIand tctex1 gradually decreased with age, whereas α-synuclein increased gradually especially in PD group.
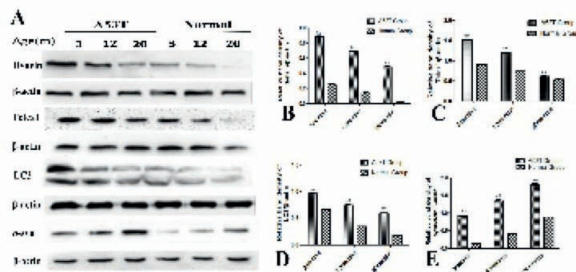
Fig. 1 The changes of protein expression in different month groups
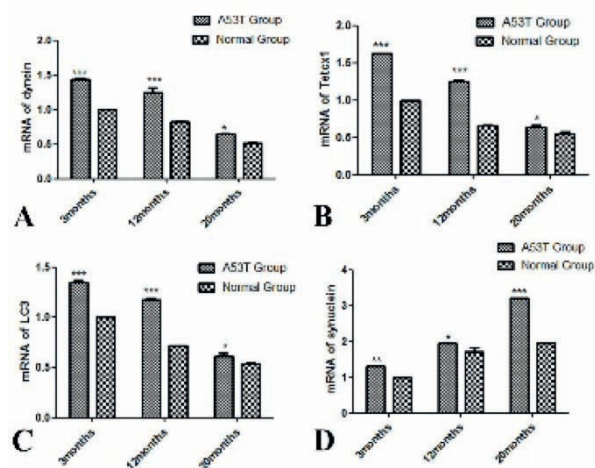
Fig. 2 The changes of mRNA expression levels of mice in different month groups
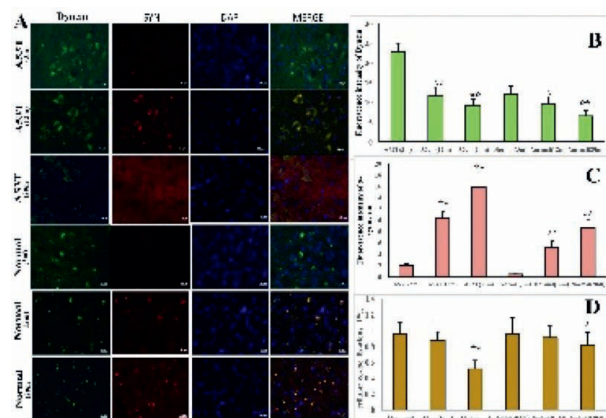
Fig.3 Colocalization of dynein and α-synuclein in cells of substantia nigra

Conclusion: Aging had important effects on the dynein functions changes of both normal group mice and PD mice, especially PD group. Therefore, the development of related drugs to reduce the aging of dynein function may provide a new treatment for Parkinson's disease.

Disclosure: Nothing to disclose

EPO1066

Cognitive Decline in Essential Tremor

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Background: Essential tremor (ET) is no longer considered as a tremorgenic monosymptomatic movement disorder but it has several non-motor manifestations including cognitive dysfunctions.

Objectives: to study the pattern of cognitive decline in ET patients and its relation to the tremor severity.

Methods: This study was performed on 30 ET patients and 15 healthy controls subjected to history taking, neurological examinations with tremor severity assessment using The Essential Tremor Rating Assessment Scale (TETRAS). They were also submitted to the Montreal Cognitive Assessment Scale (MoCA), Stroop Color Word Test, subtest of Wechsler Adult Intelligence Scale IV (WAIS-IV), Wisconsin Card Sorting Test (WCST), brain MRI volumetry and event related potential mismatch negativity (MMN).

Results: the neuropsychological tests revealed significant impairment in the global cognitive functions, attention, working memory and executive functions in ET patients. Brain MRI volumetry showed significant reduction in cerebellar cortical and white matter volumes, thalamic volume and total white matter volume. Patients also had either absent or diminished amplitude and delayed MMN.

Conclusion: Cognitive decline is a common ET manifestation despite its underdiagnoses bad impact on patients' socio–occupational activities. So, it is recommended to consider this cognitive impairment in ET management plan.

Disclosure: Nothing to disclose

EPO1067

Levodopa-induced motor complications on quality of life in Parkinson's Disease patients in Singapore

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Background and aims: The aim of this study was to evaluate the impact of levodopa-induced complications on the quality of life (QoL) of Parkinson's disease (PD) patients in Singapore.

Methods: PD patients were prospectively recruited from a tertiary care centre in Singapore. The motor disabilities were assessed with the Part III (motor) Unified Parkinson's Disease Rating Scale and the modified Hoehn and Yahr staging scale. Levodopa-induced complications were assessed with the UPDRS Part IV questionnaires and quality of life were assessed by the Parkinson's disease Questionnaire-39 items.

Results: The main levodopa-induced complications experienced by patients were wearing OFF (where 40.83% had OFF periods no more than 25% of their waking day, while 14.17% and 2.92% reported experiencing them for 26-50% and 51-75% of their waking day, respectively). The OFF periods were predominantly predictable (98.33%). A small percentage of patients (12.92%) reported having dyskinesia (a majority had either non-disabling or mildly disabling symptoms). Only a small percentage of the patients (5.42%) had presence of early morning dystonia. In the multivariable analysis motor scores (UPDRSm) were found to be significantly associated with poorer QoL (estimate 0.06, p<0.001). However, the total score of levodopa-induced complications had much greater impact on QoL (estimate 0.58, p<0.001). Early morning dystonia was the most impact complication on QoL (estimate 2.45, p<0.001).

Conclusion: Levodopa-induced complications may significantly worsen the QoL of patients with PD and physicians should take this into account throughout PD patient care.

Disclosure: Nothing to disclose

EPO1068

Experience with Incobotulinumtoxin A in the treatment of shialorrea

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Background and aims: Sialorrhea is an important comorbidity in patients with neurological disorders. Incobotulinumtoxin A (IncoA) may be useful on its treatment, although evidence is limited so far.

Methods: We performed a retrospective analysis of demographic and clinical variables of patients treated with IncoA for sialorrhea in the Movement Disorders Unit of our tertiary hospital during 2017. The severity of the sialorrhea was measured by the Drooling Frequency and Severity Scale (DSFS) scales and the clinical benefit perceived by the patient using the Patient Global Impression of Improvement scale (PGI).

Results: 36 patients with sialorrhea treated with IncoA were included (64% male; age 71.1±17 years). The most frequent diagnoses were Parkinson Disease (58.3%) and Atypical Parkinsonism (16.7%). Patients received 2.6±1.7 infiltrations with IncoA in both parotid glands (42.9±8.2 IU). Basal severity in DSS scale was 4.0±0.5 and 3.4±0.6 in DFS. After infiltrations DSS was reduced to 2.2±1.2 and DFS to 2.1±1. Clinical benefit was perceived by 90% with a mean PGI of 2.1±1.0 (moderate improvement). The average duration of the effect of the toxin was 4.8±3 months. There were no significant adverse effects related to the treatment.

Conclusion: In our experience, Incobotulinotoxin A was safe and effective in the treatment of sialorrhea.

Disclosure: Nothing to disclose

EPO1069

Safinamide improves activities of daily living in Parkinson's Disease patients with motor and non-motor fluctuations.

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Background and aims: Parkinson's Disease (PD) is characterized by a wide range of motor and non-motor symptoms with a significant impact on patients' quality of life (QoL). Safinamide (Xadago®, Zambon SpA Italy) combines dopaminergic and non-dopaminergic mode of action and has shown, in pivotal trials, to improve motor functions and control motor complications without deteriorating dyskinesia.

Methods: The effects of safinamide on the activities of daily living were investigated using the EuroQol-5D (EQ-5D) data from the Phase III, double-blind, placebo-controlled study SETTLE.

Results: Safinamide, compared to placebo, significantly improved the EQ-5D Index score in all PD patients and the EQ-5D change from baseline in patients' subgroups stratified for depression and pain.

Conclusion: When used as add-on to optimized PD therapy, safinamide 100 mg/day significantly improved QoL and activities of daily living, especially in patients with chronic pain and depression. These results were also associated with significant improvements in motor fucntions suggesting that safinamide may have a positive effect on motor and non-motor fluctuations.

Disclosure: Carlo Cattaneo, Viviana Tubazio and Paola Castellani are Zambon's employees. Erminio Bonizzoni was the statiscal consultant for this analyses.

EPO1070

Clinical effect of Safinamide in patients with Parkinson's Disease with motor fluctuations and freezing of gait

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Background and aims: Parkinson´s Disease (PD) is classically defined as dopaminergic disease although it´s clear that other neurotransmitters are also affected. Dopaminergic treatment has been useful, but a ceiling effect has been reached as there are symptoms poorly responsive, including axial problems such as freezing of gait (FOG). It seems necessary to count on new non-dopaminergic drugs. Safinamide has multiple mechanisms of action, representing a valuable therapeutic drug with disease-modifying potential.

Methods: We prospectively analyzed PD patients with motor fluctuations (MF) and FOG treated with safinamide. All of them have been studied on baseline conditions (before safinamide) and after 1 month of treatment.

Results: We studied 52 patients (35men/17women, mean aged 69 years old, mean evolution of PD was 11 years). All patients could be defined as advanced PD with MF (47/52), FOG (41/52) or both and 18 had been already treated with advanced techniques including DBS. Clinical response to safinamide was clear and sustained in 12/52 patients and mild or moderate in 13/52. FOG improved in 18 patients. Eighteen patients had dubious or no response. Nine patients had secondary side effects and safinamide treatment was interrupted.

Conclusion: Besides the already known clinical indications, safinamide can exhibit peculiar effect on axial symptoms even in advanced patients. This unexpected benefit seems to occur in a percentage of patients with PD (1/3) and recalls already described cases treated with amantadine and rasagiline. It seems that a genetic component might explain this benefit.

Disclosure: Nothing to disclose

EPO1071

Evaluating the burden of advanced Parkinson's Disease on caregivers: Real-world evidence from an international survey

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Background and aims: Objective: To evaluate the impact of advanced Parkinson's Disease (PD) on caregivers' perceived burden and health.

Background: Advancing stages of PD are debilitating and may increase the dependence on a caregiver. The impact of higher disease severity on caregivers is often not well understood and under-reported.

Methods: Retrospective analyses from a six country real-world observational study were conducted. Data on clinical, humanistic, and economic outcomes were collected based on clinician assessment and patient/caregiver self-reporting. Analytical sample included data from patient-caregiver dyads. Caregiver burden was assessed using Zarit Burden Instrument (ZBI). Caregiver's health was assessed by self-reported medication use due to PD caregiving. Generalized Linear Models (higher ZBI score indicates higher burden) and Logistic Regression Models (medication use indicates health problems) were run adjusting for patient, caregiver and geographic characteristics.

Results: The analytical sample (n=539) included caregivers of PD patients who were classified by clinicians as early, intermediate or advanced PD (21.3%, 55.3% and 23.4% respectively). Mean ZBI score for the sample was 27.1(SD:16.5). Adjusted models estimated that compared to caregivers of early PD patients, the caregivers of intermediate and advanced PD patients: (i) had a higher perceived burden [3.82(p<0.05) and 12.34 higher(p<0.001) ZBI scores respectively]; and (ii) were more likely to use additional medication due to PD caregiving [aOR:1.26.95% CI:0.56-2.81 and aOR:2.92,95% CI:1.10-7.70 respectively].

Conclusion: This is the first large-scale international study to quantify the increased burden of intermediate and advanced PD over early PD. Increased likelihood of taking medications due to PD caregiving may result in additional economic burden.

Disclosure: YJJ, PLK, JAP, MS and JZ are employees of AbbVie and may own stocks/shares in the company. DS was an employee of AbbVie at the time of the study. PMM Disclosures: Honorarium: from Editorial Viguera; International Parkinson and Movement Disorder Society; and HM Hospitales de Madrid. License fee payments for the King's Parkinson's Disease Pain scale. Grant: from the International Parkinson and Movement Disorder Society. This study was supported and funded by AbbVie Inc. AbbVie participated in study design, research, data collection, analysis and interpretation of data, writing, reviewing, and approving the publication.

EPO1072

Parkinson's disease as a multisystem disorder: whole transcriptome study in Parkinson's disease patients' skin and blood–finding the pathomechanistic link.

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Background and aims: Next to characteristic motor triad of Parkinson's Disease (PD) due to loss of nigrostriatal neurons, more symptoms associated with non-neuronal tissues are emerging. Little is known about the molecular alterations underlying dermatologic issues or epidemiologic associations like increased incidence of melanoma in PD. The aim is to give an overview of the altered gene expression profiles of PD skin and blood using the novel method of RNA Sequencing. Networks of different genes are analyzed to map affected pathways that contribute to pathomolecular mechanism of PD in the periphery.

Methods: Whole transcriptomic profiling of 12+12 idiopathic PD patients' and matched controls' skin biopsies and venous whole blood was performed with high-throughput RNA-sequencing analysis. Followingly, pathway analysis of differentially changed gene expressions was performed. The results were validated using RT-qPCR.

Results: PD skin RNA-Seq resulted in a large collection of over 1000 differentially expressed genes, among which a clear pattern of global downregulation appeared. In blood, the differential changes were more subtle, blood being a heterogenous tissue. Pathways associated with mitochondrial metabolism and protein degradation by the ubiquitin-proteasome system were dysregulated in both.

Conclusion: The concordance of these results with previous gene expression profiling studies demonstrate that the molecular alterations in PD leading to neurodegeneration in the CNS are systemic and manifest also in peripheral tissues. Major affected pathways include dysfunction in protein metabolism, mitochondrial dysfunction and impaired immune system. Homeostatic imbalance in the skin can lead to increased susceptibility to mutagenic hazards and provide a possible molecular link between melanoma and PD.

Disclosure: Nothing to disclose

EPO1073

Can we use the term Shy-Drager syndrome?

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Background and aims: Shy-Drager syndrome (SDS) was first described in 1960 as a condition characterized by autonomic dysfunction combined with motor symptoms. Later, an umbrella term, multiple system atrophy (MSA), was proposed, MSA is classified as MSA with predominant cerebellar ataxia (MSA-C) or with predominant parkinsonism (MSA-P), and SDS is not included in the disease-type classification. However, we have encountered not a few MSA patients presenting with autonomic dysfunction as the initial symptom. Here we reviewed MSA cases with autonomic dysfunction before the onset of motor symptoms, and discussed the clinical significance of the diagnostic term, SDS.

Methods: The study subjects were 38 patients (17 men, 21 women) diagnosed with probable MSA. Disease types and initial symptoms were retrospectively investigated. Patients presenting with autonomic dysfunction as the initial symptom were selected, and the incidence, symptoms, and between autonomic dysfunction and motor symptoms were examined.

Results: The final diagnosis was MSA-C in 27 patients and MSA-P in 11. There were 9 patients with autonomic dysfunction as the initial symptom. The autonomic symptom was dysuria in all 9 patients. Most of the patients developed motor symptoms within 3 years after autonomic dysfunction while 1 patient developed later than 5 years.

Conclusion: Our study showed one-quarter of the MSA patients presented with autonomic dysfunction as the initial symptom. Motor symptoms are important to diagnose MSA. However, considering the disease modifying therapy, attention should be given to the autonomic symptoms, because early diagnosis and treatment may be possible. Thus, SDS should be considered as a disease concept in clinical practice.

Disclosure: Nothing to disclose

EPO1074

Phenotypic spectrum of movement disorders in 18p deletion syndrome

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Background and aims: Deletion of the short arm of chromosome 18 is a chromosomal abnormality and occurs in approximately 1/50,000 live births. The clinical features of the 18p deletion syndrome (18p-syndrome) include short stature, facial dysmorphism, genito-urinary abnormalities, holoprosencephaly, developmental delay, mental retardation and several types of movement disorders.

Methods: The 18p-syndrome was diagnosed in the presented patient using karyotype analysis in peripheral blood cells. We have conducted a literature review and have included all previously reported patients with 18p-syndrome and movement disorders in publicly available databases.

Results: We report a 41-year-old patient with craniocervical and upper limb dystonia accompanied by a dystonic gait. The cervical dystonia started insidiously in the last 6 years. We noticed a short stature, mild mental retardation and a history of orthognathic surgery. The cervical dystonia responded well to treatment with periodic botulinum toxin injections. Dystonia is the most common movement disorder in patients with 18p-syndrome and can present as focal, segmental, multifocal or generalized dystonia. Chorea, myoclonus, tremor and ataxia have also been reported in 18p-patients. The onset age of the movement disorder in 18p-syndrome is variable and ranges from infancy to adulthood.

Conclusion: We have presented a patient with 18p-syndrome and adult-onset multifocal dystonia. Among other movement disorders, dystonia can commonly be observed in 18p-syndrome. The variable size and location of the deletion on 18p and the different involved genes are probably responsible for the broad phenotypic variability of movement disorders in this syndrome.

Disclosure: Nothing to disclose

EPO1075

Weight loss in Parkinson's disease patients under levodopa/carbidopa intestinal gel infusion treatment

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Background and aims: Weight loss (WL) has been suggested to be a biomarker of disease progression for Parkinson's disease (PD) and other neurodegenerative disorders. WL is reported as a frequent adverse event among PD patients under levodopa/carbidopa intestinal gel (LCIG) treatment. However nor its prevalence neither its causes have been systematically analyzed.

Methods: A retrospective and cross-sectional studies were performed, among all the PD patients who were under LCIG treatment at our Center, for at least six months. Weight/ body max index, MDS-UPDRS/UPDRS, Mini Mental State Examination, Beck Depression Inventory Scale, Hoehn Yahr (HY) Stage, and levodopa equivalent daily dose (LEDD) were evaluated before LCIG inset (T0), by means of a retrospective analysis, and during the last visit (T1). At T1 the Mini Nutritional assessment (MNA) and Schwab and England ADL Scale (SE) were also assessed.

Results: We recruited 44 patients out of the 55 PD patients treated with LCIG. Baseline and follow-up patients' clinical and nutritional characteristics are detailed in Table 1. WL showed positive correlations with UPDRS IV score, dyskinesia duration/disability (UPDRS item 32-33), a history of device complications/granuloma and MNA score, while no correlations were found with disease duration, LEDD/Kg, dysphagia and disease severity (MDS-UPDRS III, HY and SE). At a multiple linear regression analysis, corrected for LCIG therapy duration, the only variable that kept significance was "dyskinesia duration" (p=0.023).

	Baseline (n=44)	Follow-up (n=44)	P - value
Age (yrs)	67 ± 4	71 ± 6	/
Disease duration (yrs)	/	18 ± 6	/
Duodopa therapy duration (months)	/	50 ± 27	/
LEDD/Kg/day	20.6 ± 6.1	24.6 ± 8.6	0.002
Clinical Phenotype n (%)	AK= 34 (77%)	/	
	TD= 10 (23%)	/	
HY	3 ± 0.9	3.3 ±1.2	0.003
SE	NA	57 ± 20	/
MDS.UPDRS II	17.1 ±7.2	28.6 ± 10	<0.001
MDS.UPDRS III	31±12.4	49.1 ±15.2	<0.001
UPDRS IV, Total score (items 32–42)	9.5 ± 3.2	6.1 ± 2.4	<0.001
Dyskinesia duration (Item 32)	1.7 ± 1	1.6 ± 0.7	0.7
Dyskinesia disability (Item 33)	1.2 ± 1.2	1.2 ± 0.8	0.9
Off state duration (Item 39)	2 ± 0.6	0.9 ± 0.5	<0.001
MMSE	27.2 ± 2.5	24.1 ±4*	<0.001
BDI	14.5 ± 7.8	18.5 ±9.5	0.01
Mean Weight loss (kg) – n (%)	/	7 ± 6 – 33 (75%)	/
Weight loss > 10kg, n (%)		9 (35%)	
BMI (Kg/m²)	26.2 ± 4.7	23.1 ± 4.1	<0.001
MNA classification	NA	Normal nutrition status: 17 (39%)	/
		Undernutrition risk: 18 (41%)	
		Undernutrition state: 9 (20%)	
Enteral feeding, n (%)	0	6 (14%)	/

Table 1. Patients' clinical and nutritional characteristics. Values are presented as mean (SD) if no otherwise specified. *: two patients were not able to complete the MMSE at follow-up evaluation due to severe cognitive impairment. NA: not available.

Conclusion: WL is a common event among PD patients treated with LCIG with implications on patients' nutritional status. Dyskinesia duration seems to be the most related factor for WL occurrence.
Disclosure: Nothing to disclose

MS and related disorders 1

EPO1076

Cryptococcal meningoencephalitis in sarcoidosis patient associated with positive CSF anti-NMDA receptor antibodies–a therapeutic challenge

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Background and aims: Sarcoidosis patients are at risk for opportunistic infections, namely cryptococcal disease. Post-infectious anti-NMDA receptor (anti-NMDA-r) encephalitis has been described in cases of herpetic encephalitis (herpes simplex and herpes zoster). A 39 years-old male with pulmonary sarcoidosis treated with low-dose steroids presented with headache and vomiting for one month. Suspecting neurosarcoidosis, corticosteroid dosage was increased. However, he developed progressive behavioral changes, visual hallucinations, pronounced insomnia and gait difficulty. Neurologic examination revealed an inattentive patient, with mild language impairment and gait ataxia. Lumbar puncture revealed inflammatory CSF (polymorphonuclear predominance) with hypoglycorrhachia and India ink stain showed Cryptococcus. The patient was HIV-negative but had marked CD4 lymphopenia(66/mm3). Anti-NMDA-r antibodies (included in initial work-up) in CSF were positive. Brain MRI revealed basal ganglia enhancing lesions and subcortical white matter and splenium restricted diffusion areas. Treatment with amphotericin B, flucytosine and repeated lumbar punctures was started. Corticosteroids were reduced. Despite initial improvement, the patient deteriorated further. CSF anti-NMDA-r antibodies remained positive and EEG showed delta brush pattern. Considering a possible immune-mediated process, intravenous immunoglobulin and small increase in steroids were attempted. Thereafter, he improved, although with a fluctuating course. After 6-weeks of anti-fungal treatment, neurological deficits resolved except for mild cognitive slowing.
Conclusion: We report a cryptococcal encephalitis in a non-HIV patient with clinical and EEG features resembling auto-immune encephalitis and positive CSF anti-NMDA-r antibodies. Recent experimental studies have shown significant inflammatory response in cryptococcal CNS disease, driving tissue damage. We suggest a post-infectious immune-mediated mechanism triggering anti-NMDA-r antibodies production contributing to clinical and EEG manifestations.
Disclosure: Nothing to disclose

EPO1077

Link between health-related quality of life, occupational disability and sick leaves in patients with Multiple Sclerosis in Germany

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Background and aims: There is strong evidence that patients with Multiple Sclerosis have lower health-related quality of life (HRQOL) and that this steadily worsening neurologic disease causes enormous indirect costs mainly due to lower workforce participation. Many studies conducted research on the link between HRQOL and workforce participation of patients. However, little is known about the magnitude of the effect of specific HRQOL impairments on workforce participation. The objective of this investigation is to quantify the impact of specific HRQOL impairments on the occupational disability and sick leaves in patients with Multiple Sclerosis.
Methods: PANGAEA is a non-interventional study that assessed in a sub-study (n=559), HRQOL by the UK Neurological Disability Scale (UK-NDS). Logistic regression and negative binomial regression were used to estimate the effect of UK-NDS-dimensions and sociodemographic data on the occupational disability and number of sick leaves.
Results: Cognitive impairment (OR:1.4), mobility impairment (OR:1.6), fatigue (OR:1.2), "others" (OR:1.1), female gender (OR:2.2) and patients living in a single household (OR:1.7) have a significant impact on the occupational disability (p<5%). Mobility impairment, (IRR:1.8), pain (IRR:1.4), "other" (IRR:1.7) as well as number of reluctance (IRR:3.2) have a significant impact on the number of sick leaves (p<5%).
Conclusion: The results highlight the association between HRQOL and workforce participation. Mobility impairment has the greatest impact on occupational disability as well as on the number of sick leaves. Interventions targeting mobility, cognition, fatigue may help obtaining the workforce participation of the patients. Once again, the significance of the dimension "other" shows the great diversity of symptoms in patients with Multiple Sclerosis.
Disclosure: This study was supported by the Novratis Pharma GmbH, Nuremberg, Germany

EPO1079

Alemtuzumab Safety, Efficacy, and Tolerability in Paediatric Patients with Active Relapsing-Remitting Multiple Sclerosis Despite Prior Treatment with Disease-Modifying Therapy: LemKids Study Design

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Background and aims: LemKids (EudraCT 2016-003100-30) is evaluating efficacy, safety and tolerability of alemtuzumab in paediatric patients with relapsing-remitting multiple sclerosis (RRMS).

Methods: LemKids is a 5-year, multicentre, multinational, open-label, single-arm, before-and-after switch study. Inclusion criteria: patients aged 10 to <18 years with ≥2 relapses (≥1 on-treatment relapse in the last year after ≥6 months of disease-modifying therapy [DMT; interferon beta or glatiramer acetate]); and ≥1 new/enlarging T2 hyperintense or gadolinium-enhancing lesion while on DMT, ≥2 relapses in prior year, and/or ≥2 DMTs tried. After enrolment (target N=60), patients will continue prior DMT for 4 months (Period 1) before discontinuing that therapy and switching to alemtuzumab treatment. Alemtuzumab will be administered in 2 annual courses (Course 1: 5 consecutive days; Course 2: 12 months later on 3 consecutive days), at a dosage according to patient weight (≥50 kg, 12 mg/day; <50 kg, 0.24 mg/kg/day). MRI scans will be conducted at screening, at end of Period 1, and Months 4, 8, 12, 24, 36, 48 and 60 after alemtuzumab initiation. Primary endpoint: Number of new/enlarging T2 lesions during Period 1 versus Period 2 (Months 4-8 after alemtuzumab initiation). Secondary endpoints: Number of patients with new/enlarging T2 lesions during Period 1 versus Period 2; annualised relapse rate at Year 2; cognition scores (Brief Visuospatial Memory Test-Revised, Symbol Digit Modality Test); and quality of life (PedsQL and Pediatric NeuroQoL). Safety endpoint: AEs over 5 years.
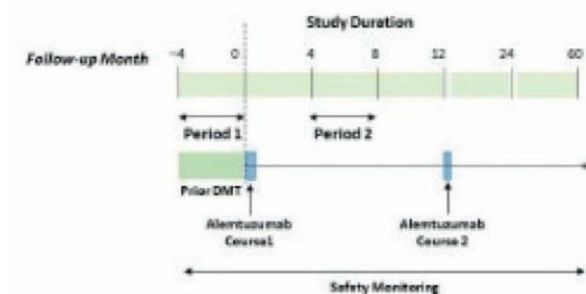
Figure 1: Schematic representation of LemKids study design

Results: Enrolment began in June 2017.

Conclusion: LemKids will provide data to help guide treatment of children with RRMS.
Disclosure: Study supported by Sanofi.

EPO1080

Atrophy of the mid-anterior and central segments of the corpus callosum is associated with impaired performance in selected cognitive tests in patients with relapsing-remitting MS

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Background and aims: Multiple sclerosis (MS) is an inflammatory and neurodegenerative disease leading to physical disability, chronic fatigue, depression and cognitive impairment. Pathomechanisms of cognitive impairment in MS are only partially understood. We hypothesized that atrophy of the corpus callosum (CC), and especially of some of its segments, occurring in the course of the disease, play an important role in cognitive decline in MS patients.

Methods: We performed neuropsychological examination (including cognitive tests assessing attention, verbal and visual memory, verbal fluency, working memory, executive functions and information processing speed (IPS) and collected MR Imaging data (1.5T scanner with a 20-channel head/neck coil) in 65 Polish-speaking patients with relapsing-remitting MS (RRMS), all receiving IFN-beta. On 3D T1-weighted sequence we calculated volumes of posterior (CC-P), mid-posterior (CC-MP), central (CC-C), mid-anterior (CC-MA) and anterior (CC-A) segments of the CC(Fig_1) using Freesurfer Software, and compared these numbers with the results of the cognitive tests (Spearman analysis).
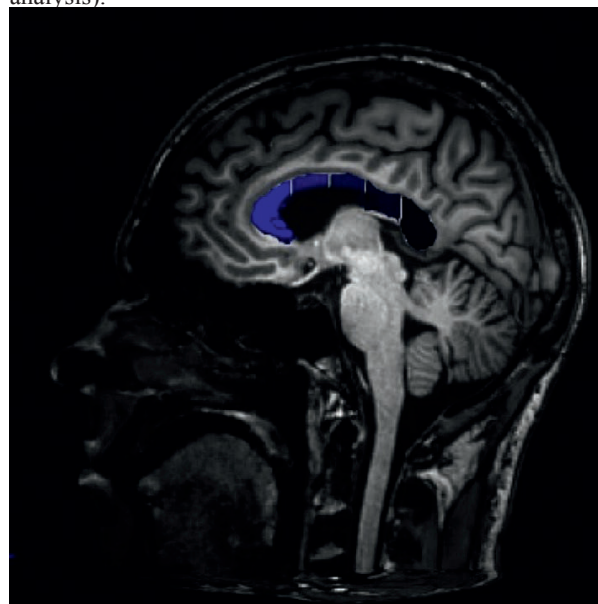
Segmentation of the corpus callosum-a schematic view

Results: Decline of volume of CC-MA was associated with phonemic and semantic verbal fluency (rho=0.31), CC-C atrophy was related to decreased IPS (rho=0.34) and second part of the Color Trail Test (rho=-0.31), whereas decreased volumes of both (CC-C and CC-MA) were associated with more frequent rotation mistakes in the right side of the visual field in the Benton Visual Retention Test (rho=-0.34).

Conclusion: Atrophy of the mid-anterior and central segments of the CC are associated with impaired phonemic and semantic verbal fluency, IPS, visual memory performance and sequential information processing and divided attention respectively, in patients with RRMS.

Disclosure: Nothing to disclose

EPO1081

Fatal outcome in aspergillosis in the natalizumab-treated multiple sclerosis patient

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Background and aims: Natalizumab is a humanized monoclonal anti-alpha-4 integrin antibody, that prevents immune system cells to cross endothelium in blood-brain barrier. It is approved for treatment of relapsing-remitting multiple sclerosis (MS).

We present a case of central nervous system (CNS) Aspergillus opportunistic infection in natalizumab-treated MS patient.

Methods: Single case retrospective observational study

Results: A 39-year-old male was diagnosed with MS in 2005. In December 2014 he started natalizumab treatment that was uneventful until May 2017. Then the first MS relapse on treatment was diagnosed. He was unable to sit or walk due to severe spasticity. Brain MRI revealed multiple new contrast-enhancing lesions interpreted as active MS plaques (Fig. 1). Intravenous methylprednisolone was started and followed by next dose of natalizumab. One month later he experienced substantial improvement in daily-life activities and was able to walk with one crutch. In July 2017 the patient was readmitted in severe condition: he was somnolent, malnutritioned, afebrile and developed pressure ulcers. MR scans revealed multiple brain abscesses (Fig. 2). Empirical intravenous antibiotic therapy, acyclovir and amphotericin B with adequate premedication were started.

Cerebrospinal fluid qualitative DNA tests were positive for Aspergillus and negative for Candida, bacteria and viruses. Both anti-HIV and anti-JCV antibodies tests were negative. Neurological status gradually deteriorated and severe brain edema developed. He was declared dead due to irreversible brainstem injury.
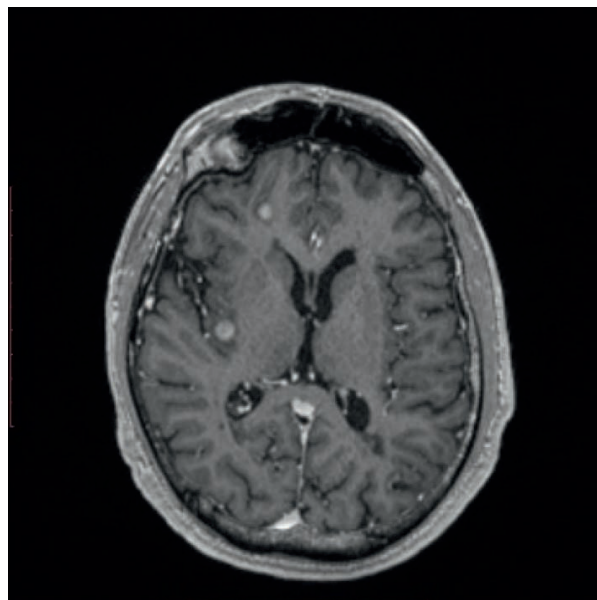
Fig. 1. Multiple contrast-enhancing lesions-ontrast ehnhanced T1 MRI, May 2017
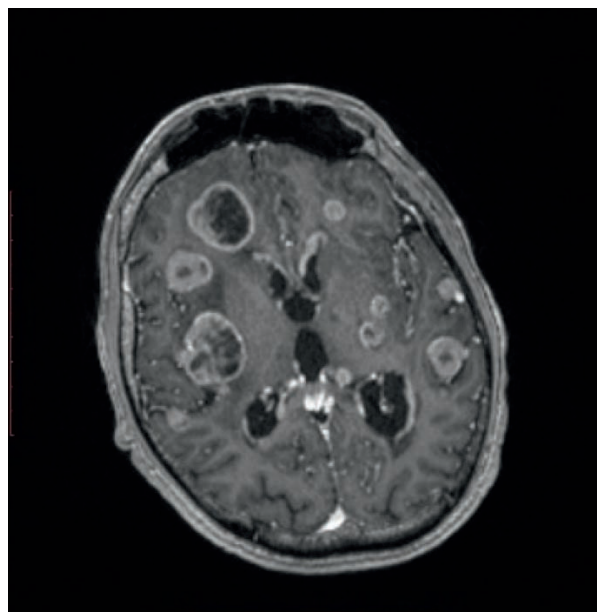
Fig. 2. Multiple brain abscesses with marginal contrast enhancement-contrast enhanced T1 MRI, July 2017

Conclusion: Probable fungal CNS infection should be considered in case of unexpected deterioration of MS patient treated with natalizumab. Our case report might help other practitioners in precise monitoring of natalizumab therapy.

Disclosure: Nothing to disclose

EPO1082

Infections during periods of Grade 3 or 4 lymphopenia in patients taking cladribine tablets 3.5 mg/kg: data from an integrated safety analysis

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Background and aims: In CLARITY, cladribine tablets 3.5 mg/kg (CT3.5) demonstrated efficacy in relapsing MS patients. The most common AE was lymphopenia, reflecting cladribine's mode of action. Integrated safety analysis showed infection incidence was not higher in patients receiving CT3.5 vs. placebo, bar a small increase of herpes zoster (HZV). Post hoc analysis examined the infectious AEs occurring concurrently with Grade 3/4 lymphopenia (with G3/4) in patients treated with CT3.5.

Methods: A CT3.5 monotherapy oral cohort was derived from CLARITY, CLARITY-Extension, ORACLE-MS and PREMIERE, encompassing 923 patients. The AE profile for CT3.5 during periods with G3/4 (defined as the onset of the Grade 3/4 lymphopenia to first Grade 2 or lower plus 2 weeks) was analysed. Adjusted-AE incidences per 100-patient-years (Adj-AE/100PY) were calculated.

Results: Adj-AE/100PY for any infections and infestations during periods with G3/4 was 57.53 vs. 24.50 outside these periods (without G3/4). Types of infectious AEs were similar during periods with and without G3/4 and did not show any specific pattern. >50% of cases occurring with G3/4 were easily-treatable infections of the upper respiratory tract (nasopharyngitis, upper respiratory tract infection, pharyngitis; Table 1). HZV was reported in 4 patients with G3/4, cases were dermatomal and mild-to-moderate in severity. Single occurrences occurred for most infectious AEs. Opportunistic infections were single occurrences, not severe, serious or difficult to treat.

Preferred Term	Cladribine tablets (n=923) with G3/4 lymphopenia			Cladribine tablets (n=923) without G3/4 lymphopenia*		
	n	T	Adj-AE per 100PY	n	T	Adj-AE per 100PY
Any infections and infestations	40	69.5	57.53	468	1910.5	24.50
Nasopharyngitis	11	81.6	13.48	152	2899.7	5.24
Upper respiratory tract infection	8	82.7	9.67	104	3045.8	3.41
Pharyngitis	4	88.6	4.51	24	3269.1	0.73
Herpes zoster	4	88.9	4.50	24	3280.4	0.73
Influenza	3	89.6	3.35	85	3096.4	2.75
Urinary tract infection	3	89.2	3.36	54	3170.9	1.70
Bronchitis	2	89.7	2.23	54	3148.4	1.72
Viral upper respiratory tract infection	2	89.6	2.23	21	3259.7	0.64

*Not necessarily the most common infectious AEs occurring during periods without Grade 3 or 4
n is the number of patients with events. T is the total patients time at risk in years (cumulative periods).
Periods of Grade 3 or 4 lymphopenia were defined as the onset of the Grade 3 or 4 lymphopenia to first Grade 2 or lower plus 2 weeks.
Adj-AE per 100PY, adjusted AE incidences per 100 patient-years; AE, adverse event; CT3.5, cladribine tablets 3.5 mg/kg; SOC, system organ class.

Table 1: Adverse events of the SOC infections and Infestations by preferred term occurring during the exact periods of Grade 3 or 4 lymphopenia occurring in >2 patients receiving CT3.5 and the corresponding incidences during periods without Grade 3 or 4 lymphopenia

Conclusion: G3/4 lymphopenia increased the frequency of infections but did not affect the type of infectious AEs in CT3.5 treated patients. HZV profile was uncomplicated; consistent with the findings of previous analyses.

Disclosure: This study was sponsored by EMD Serono Inc, a business of Merck KGaA, Darmstadt, Germany (in the USA), and Merck Serono SA, Geneva, an affiliate of Merck KGaA Darmstadt, Germany (ROW).

EPO1083

An analysis of malignancy risk in the clinical development programme of cladribine tablets in patients with relapsing multiple sclerosis

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Background and aims: An independent meta-analysis (Pakpoor et al. Neurol Neuroimmunol Neuroinflamm 2015;2:e158) in Phase III trials (with a 2-year duration) of disease-modifying-drugs (DMDs) in relapsing MS patients found no increased rate of malignancy with cladribine tablets (CT) vs. other DMDs . Here, we assess malignancy risk with CT 3.5mg/kg (CT3.5) monotherapy and placebo using data from 3 Phase III trials and the PREMIERE safety registry (up to 8 years' follow-up), and compare incidence rate with a global database.

Methods: The CT3.5 population comprised 923 patients (3433 patient-years' [PY] total exposure time) and the placebo group comprised 641 patients (2026 PY). Individual case reports of malignancies were reviewed by an independent, blinded adjudication committee. Standardised incidence ratios (SIR) were calculated using the GLOBOCAN reference population (excluding non-melanoma skin cancers [NMSCs]) and a Danish reference population for NMSC rates.

Results: The incidence per 100 PY and risk difference (95%CI) of confirmed malignancy for CT3.5 and placebo are shown in Table 1. CT3.5 malignancy SIR was almost identical (0.97, 95%CI 0.44–1.85) to the GLOBOCAN matched reference population. For placebo, SIR was numerically lower (0.48, 95%CI 0.14–1.53). There were no cases of haematological or lymphoproliferative cancers (Table 2); no clustering of specific tumour types; and incidence of skin cancer was not increased after treatment with CT3.5 vs. placebo. Incidence of malignancies with CT3.5 was constant and did not increase over time.

	Monotherapy oral cohort	
	Placebo (n=641)	CT3.5 (n=923)
Patients with events/Patients years at risk	3/2022.11	10/3414.20
Incidence per 100 PY	0.14836	0.29289
95% CI of incidence*	0.0478–0.4600	0.1576–0.5444
Risk difference per 100 PY		0.1445
95% CI of risk difference per 100 PY†		0.1656–0.4141
Risk Ratio		1.9742
95% CI of Risk Ratio‡		0.5433–7.1733

CI, confidence interval; PY, patient year.
* CI computed with the exact Clopper-Pearson formula.
† CI computed using the Miettinen and Nurminen method.
‡ CI computed with the Wald method for the number of subjects with events using a Poisson regression model with fixed effect for treatment group and log of time at risk as an offset.

Table 1: Incidence rates, risk differences and risk ratio for malignancies in patients treated with CT3.5 or placebo in the monotherapy cohort

SOC: malignancy or unspecified tumours*	Placebo (n=3)	CT3.5 (n=10)
Basal cell carcinoma	1	1
Bile duct adenocarcinoma	0	1
Breast cancer	0	1
Cervix carcinoma stage 0	2	0
Malignant melanoma	0	2
Ovarian cancer	0	1
Pancreatic carcinoma	0	1
Papillary thyroid cancer	0	1
Rectal cancer	0	1
Squamous cell carcinoma of skin	0	1

* Malignant or unspecified tumours determined by external adjudication.
SOC, System organ class.

Table 2: Type of malignancies or unspecified tumours reported in the monotherapy oral cohort

Conclusion: Analysis of malignancy rates in a cohort that includes patients with up to 8 years of follow up confirms the conclusions of the earlier meta-analysis.

Disclosure: This study was sponsored by EMD Serono Inc, a business of Merck KGaA, Darmstadt, Germany (in the USA), and Merck Serono SA, Geneva, an affiliate of Merck KGaA Darmstadt, Germany (ROW).

EPO1084

Benefit-risk assessment of cladribine tablets using Multi-Criteria Decision Analysis (MCDA) for patients with relapsing multiple sclerosis demonstrating high disease activity

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Background and aims: Relapsing multiple sclerosis (RMS) with frequent relapses is described as high disease activity (HDA). Benefit-risk assessment of disease modifying drugs (DMDs) for HDA patients is important. Increasingly, treatment decisions with multiple criteria employ Multi-Criteria Decision Analysis (MCDA). We apply MCDA to a structured benefit-risk assessment of cladribine tablets (CT) and newer DMDs for HDA patients.
Methods: Decision conferencing with physicians created an MCDA model incorporating available evidence and clinical decisions. Workshops followed the PrOACT-URL (Problem formulation, Objectives, Alternatives, Consequences, Trade-offs, Uncertainties, Risk attitude, and Linked decisions) framework. Benefit-risk assessments were conducted for DMDs in RMS and HDA patients. Experts identified 7 favourable and 11 unfavourable effects and a preference value for DMDs using hypothetical treatment effect data. Preference values were 'swing-weighted' by experts to represent trade-offs between favourable and unfavourable effects. Overall weighted preference values were calculated for each DMD. Benefit-risk profiles of CT and other DMDs were compared.
Results: CT had the highest overall weighted preference value followed by alemtuzumab and natalizumab. Comparisons of risk-benefit profiles favoured CT for severe lymphopenia, autoimmune disease, infections, gastrointestinal effects and ease of use, and favoured alemtuzumab for T1 Gd+ and T2 lesions. Differences favoured CT for progressive multifocal leukoencephalopathy, effect durability and 3-month and 6-month confirmed disability progression. Natalizumab was favoured for relapse rate, T1 Gd+ and T2 lesions.
Conclusion: Using MCDA with decisions from blinded expert physicians, the benefit-risk profile of CT in HDA patients was favourable compared to other DMDs.
Disclosure: This study was sponsored by EMD Serono Inc, a business of Merck KGaA, Darmstadt, Germany (in the USA), and Merck Serono SA, Geneva, an affiliate of Merck KGaA Darmstadt, Germany (ROW).

EPO1085

Effects of cladribine tablets on CD4+ T-cell subsets in the ORACLE-MS study: Results from an analysis of lymphocyte surface markers

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Background and aims: Lymphocyte subtype evaluation in patients from the cladribine tablets 3.5mg/kg (CT3.5) cohort of ONWARD-MS showed a transient ~82% median reduction in CD19+ B cells by week-13 with reconstitution from weeks-24 to 48. CD4+ and CD8+ T-cells were also reduced between ~40% and ~55%. Because of the durable clinical effects of CT3.5 in MS patients, the effect on regulatory-immune function cells is of interest.
Methods: Peripheral blood T-lymphocytes were immunophenotyped at baseline, and weeks-5, 13, 24, 48 in patients treated with CT3.5 at week-1 and week-5 in ORACLE-MS (n=41). Absolute numbers and proportions of CM (CD4+RO+CCR7+), EM (CD4+RO+CCR7-), Th1-type (CD4+CXCR3+), nTregs (CD4+CD25+CD127-), naïve-like nTregs (CD4+CD25+CD127-RA[HI]+) and memory-like nTregs (CD4+CD25+CD127-RA-) were measured.
Results: Greatest median reductions from baseline in absolute numbers occurred at week-13 for EM (-54%); week-24 for CM (-63%) and Th1-type cells (-51%); with similar/slightly increased levels at week-48. There was ~5% reduction in the proportion of CM, but no change in proportions of EM and Th1-type cells. Absolute numbers of nTregs (-48%), naïve-like (-67%) and memory-like nTregs (-42%) decreased by week-48. The proportions of nTregs and naïve-like nTregs were unchanged; memory-like nTregs proportions slightly increased up to 48-weeks (median 11% increase from baseline at week-48).
Conclusion: The first administration of CT3.5 has a comparable effect on CD4+ T-cell subpopulations, with no dramatic shifts in proportions.
Disclosure: This study was sponsored by EMD Serono Inc., a business of Merck KGaA, Darmstadt, Germany (in the USA), and Merck Serono SA, Geneva, an affiliate of Merck KGaA, Darmstadt, Germany (ROW)

EPO1087

Prevalence of NMOSD in Central Serbia

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Background and aims: Population-based prevalence studies on neuromyelitis optica spectrum disorders (NMOSD) are limited. The aim of our study was to estimate the prevalence of NMOSD in Central Serbia, using the 2015 criteria.

Methods: In this population-based retrospective study, we included all patients from Central Serbia diagnosed with NMOSD according to the 2015 criteria. All those patients are included in the National NMOSD Registry of Central Serbia, established at the Clinic of Neurology, Clinical Center of Serbia in 2014. All tests for antibodies to aquaporin-4 (AQP-4) were performed in a single reference laboratory at the above-mentioned Clinic. Prevalence was calculated after re-evaluation of each patient according to the 2015 criteria on the day December 31, 2017. The projective number of inhabitants in Central Serbia (2016 projections) was 7,058,322 people, 3,437,630 males and 3,620,692 females.

Results: We identified 69 patients. All patients were Caucasian, and female (81%) with a median age at disease onset of 38 years (range, 7-68 years). In total, 60 (87%) patients were positive for AQP4 antibodies. Median Expanded Disability Status Scale score at the last visit was 2.5 (range 0-8.5). The prevalence was 0.98/100,000, for males 0.38/100,000, and for females 1.55/100,000. Lowest values were seen in children and elder people and highest in women and middle-aged people (40-59 years).

Conclusion: Based on the prevalence data, NMOSD remains to be in the group of rare disorders. The differences in age- and gender-specific prevalence highlight the necessity of further investigation of these variables on the disease susceptibility.

Disclosure: Nothing to disclose

EPO1088

Clinical frontal release signs correlate with cognitive impairment in patients with multiple sclerosis

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Background and aims: Cognitive impairment (CI) is frequent in all disease stages and subtypes of multiple sclerosis (MS). Presence of CI is underestimated and the neurologist's accuracy in predicting CI is rarely better than chance. We investigated the presence of frontal release signs with a validated clinical antisaccade test (CAT) and palmomental reflex (PMR) and its correlation to a neuropsychological test for detection of CI in MS patients.

Methods: CI and fatigue were assessed with the Multiple Sclerosis Inventory Cognition (MUSIC). CAT and PMR were performed by neurologists blinded to cognitive test results. The number of errors in 20 antisaccadic tasks was counted for evaluation of CAT. PMR was rated unilateral (1 point) or bilateral (2 points) positive if a reproducible (2 of 3 attempts) contraction of mentalis muscles was observed.

Results: 47 MS patients (29 females, 18 males, 39 RRMS, 5 PPMS, 3 SPMS, mean age 43 years, mean disease duration 8 years, mean EDSS 2.6) were investigated. 16 patients (34%) had CI (9 mild, 4 moderate, 3 severe). Age (Pearson r=-0.35, p=0.015) and EDSS (Spearman r=-0.27, p=0.04) correlated inversely with the MUSIC score. CAT Error rate showed an inverse correlation trend (Spearman r=-0.23; p=0.06). PMR (Spearman r=-0.29, p=0.024) and a sum score of PMR and CAT error rate (SSPC) (Spearman r=-0.3, p=0.02) correlated inversely with the MUSIC score (figure 1). Patients with CI had a significantly higher SSPC compared to those without CI (p=0.01, figure 2).
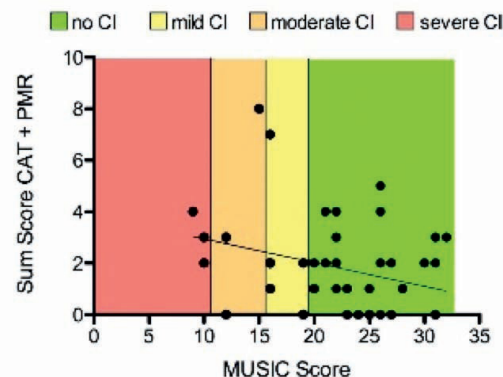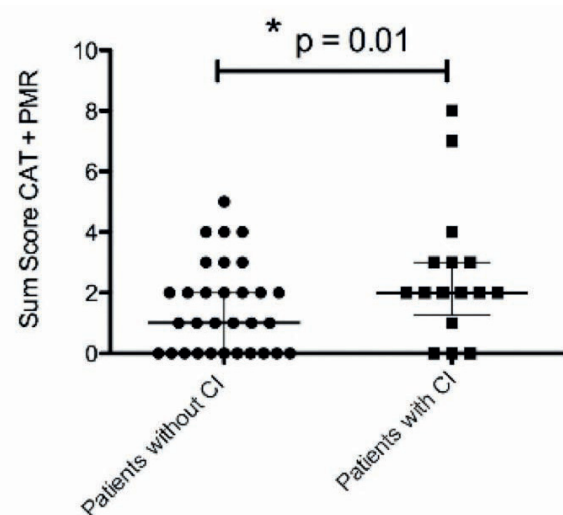
Figure 1

Figure 2

Conclusion: CAT and PMR might be useful clinical screening tests for the detection of CI in MS patients.
Disclosure: Nothing to disclose

EPO1089

Interim analysis of the non-interventional study COPTIVITY assessing the alteration of activity in ambulatory patients with relapsing MS treated with COPAXONE® 40 mg tiw.

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Background and aims: Real-world (RW) data on effectiveness, tolerability and patient-reported outcomes (PRO) of newly approved disease-modifying therapies (DMTs) are missing and gaining increasing importance in the rapidly changing treatment landscape in Multiple Sclerosis (MS). Such data are not available for newer DMTs including Copaxone® 40mg tiw (glatiramer acetate (GA) 40mg tiw) and RW evidence on effectiveness after switching from other DMTs are needed. Here, we describe the efficacy and safety profile of ambulatory MS patients treated with GA 40 mg tiw.
Methods: The ongoing two-year non-interventional study was performed to evaluate traditional clinical endpoints such as annual relapse rate (ARR), Expanded Disability Severity Score (EDSS) and emerging endpoints like Fatigue, Cognition, patient reported neurological disability, work productivity, and treatment satisfaction of patients treated with both formulations of GA. Only patients with documentation of GA dosage were included.
Results: 687 MS (86.9% RRMS and 8.0% CIS) patients (80.6% female), mean age 38.0± 10.8 years with a disease duration 4.6 ±6.6 year. 48.3% of patients were pre-treated with GA 20 mg/ml, 35.4% were de-novo and 15.3% switched from other DMTs. The ARR decreased significantly from 0.76 ±0.0.71 to 0.33 ±1.0, the EDSS score was stable (Baseline 2.00 ±1.4 vs 1.9 ±1.4) and significant improvement of the information processing scores (SDMT) and patient reported disability (UKNDS) was observed. All other parameters were stabilized at data cut-off.
Conclusion: The results provide real-world confirmation on effectiveness, tolerability and safety of Copaxone® 40mg tiw including aspects of cognitive performance and positive outcome on PRO.
Disclosure: Tjalf Ziemssen has received reimbursements for participation in scientific advisory boards from Bayer Healthcare, Biogen Idec, Novartis Pharma AG, Merck Serono, Teva, Genzyme, and Synthon. He has also received speaker honorarium from Bayer Healthcare, Biogen Idec, Genzyme, Merck Sharp & Dohme, GlaxoSmithKline, Novartis Pharma AG, Teva, Sanofi Aventis, and Almirall. U. Schulze-Topphoff and D. Fendji are employees of TEVA GmbH, Germany.

MS and related disorders 2

EPO1078

Measuring burden in informal caregivers of patients with multiple sclerosis: the psychometric properties of the CSI questionnaire

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Background and aims: The Caregiver Strain Index (CSI) is a brief self-assessment tool for measuring the caregivers' perceived level of burden. Limited information is available on the psychometric performance of the CSI in multiple sclerosis (MS). The aim of the study was to assess the factor structure and construct validity of the CSI.
Methods: A multicentre, cross-sectional study in patients with relapsing-remitting and primary progressive MS (McDonald 2010 criteria) was conducted.
Results: A total of 72 caregivers of a sample of 201 patients (86% with relapsing-remitting MS and a median EDSS score: 2.0 [IRQ: 1.0-3.5]) were studied. The prevalence of a high level of strain was 23.6% (n=17). CSI presented good reliability (Cronbach's alpha=0.84, 95% CI=0.79 to 0.89). According to Mokken analysis, CSI represented a unidimensional construct of caregiver burden although 2 of the total 13 items (#1 and #13) could not be assigned to any factor by an automatic item selection procedure. Without these items, the scalability of the CSI moved from a weak (Hi=0.37) to a medium scale (Hi=0.44). However, the item characteristic curve (ICC) of the Rasch model (including both odd items) showed a range of appropriate difficulty and the item and person parameters presented good fit (Andersen LRT=18.40, df=11; p-value=0.07; all item values for the infit).
Conclusion: Understanding strain among informal caregivers of patients with MS may be useful to identify people who would benefit from a more comprehensive support. CSI may constitute a valuable addition to measure caregiver burden in a clinical setting.
Disclosure: This study was funded by the Medical Department of Roche Farma Spain. Daniel Prefasi and Jorge Maurino are employees of Roche Farma Spain.

EPO1090

Impaired glucose tolerance in patients with multiple sclerosis: a pilot study

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Objectives: There are limited data regarding glucose metabolism dysregulation in multiple sclerosis (MS). The aim of this pilot study was to investigate the frequency of impaired glucose tolerance (IGT) using a two-hour oral glucose tolerance test (OGTT) in a cohort of MS patients.
Methods: Methods: Included in the study were 31 MS patients (24 relapsing-remitting and 7 chronic progressive, median Expanded Disability Status Scale-EDSS score 2.5) from Clinical Center of Serbia, Belgrade, diagnosed according to the McDonald criteria and age 18 years and above, and 24 healthy controls (HC) matched for age, gender, and body mass index (BMI). An OGTT (1 g glucose/kg body weight), including determination of blood glucose and serum insulin levels, was performed to investigate glucose tolerance. Glucose and insulin responses were expressed as the total areas under the curve (tAUC).
Results: Plasma glucose concentrations of MS patients were significantly higher at multiple time points during OGTT (p<0.05). Two MS patients demonstrated elevated fasting plasma glucose concentrations compared to none of the HC (p=0.299). In addition, 16.1% of MS patients and none of HC showed IGT (p=0.039). Accordingly, both glucose tAUC and insulin tAUC were significantly higher in MS patients compared to HC (p<0.05). The areas under the glucose and insulin curves were similar in patients with different MS phenotypes and levels of disability, measured by EDSS.
Conclusion: The results of our pilot study showed an elevated frequency of IGT in MS patients. Further investigations in the larger cohorts of MS patients are warranted.
Disclosure: Nothing to disclose

EPO1091

INSPIRATION: An approach to brain volume and quantitative lesion load assessments from standardized MRI acquisition in daily clinical routine of MS patients.

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Background and aims: In Multiple Sclerosis, common standards and quantitative analysis of MRI scans has mainly been realized in clinical trials. In addition, common standards in MRI acquisition are largely not applied in routine practice. Tools for quantitative data analysis do exist, but are not widely available. INSPIRATION is a non-interventional study, conducted in Germany, to validate the feasibility and explore the potential benefit of standardized MRI acquisition and quantitative MRI reading in clinical practice.

Methods: INSPIRATION included 253 patients. MRI and clinical data were documented over 3 years. Sites underwent expert training and standardized sequence implementation. A centralized quantitative MRI data analysis was performed. The results were visualized and reported to the neurologist and radiologist.

Results: 99.6% of the data sets obtained from 510 data transfers passed the quality analysis. <0.03% of cases led to site inquiries or data exclusion. The mean number ($\pm$SD)/ml volume ($\pm$SD) of T2 lesions at baseline was 30.1 ($\pm$2.8)/11,033.1 ($\pm$1,578.9) and black holes 4.0 ($\pm$0.9)/490.3 ($\pm$136.6). After 12 months follow-up the mean number and volume of T2 lesions was 32.3($\pm$3.6)/11,479.9($\pm$1927.5) and of black holes 4.1($\pm$1.1)/488.9($\pm$165.2). Whole brain volume at baseline was 1,142,397($\pm$15,988) mm^3. Brain volume reduction after 12 months was 3,231$\pm$1,944 mm^3 (0.28$\pm$0.1%). Here we present follow up data 36 months after baseline.

Conclusion: A centralized quantitative MRI-analysis is provided in a real-world situation and might improve the comparability of MRI scans in daily clinical routine. The quantification of lesion volumes and visualization of MRI abnormalities may facilitate MRI data integration by the responsible neurologist to support patient management.

Disclosure: This study was supported by the Novartis Pharma GmbH, Nuremberg, Germany

EPO1092

Dimethyl Fumarate demonstrates Cost-effectiveness vs Teriflunomide in Treatment-naïve Patients with Relapsing-remitting Multiple Sclerosis in Sweden

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Background and aims: Dimethyl fumarate (DMF), oral 240mg twice daily, and teriflunomide (TER), oral 14mg once daily, are first-line standard of care oral disease-modifying therapies for relapsing-remitting multiple sclerosis (RRMS) in Sweden. A cost-utility analysis was conducted to assess the health economic impact of DMF versus TER for RRMS from the Swedish societal perspective.

Methods: A cohort-based Markov model simulated treatment-naïve patients' disease progression over 50 years through a series of health states based on the Expanded Disability Status Scale (EDSS). Over time, patients could also experience relapses or progress to secondary-progressive MS (SPMS). Natural history for EDSS progression was obtained from the placebo arms of the CONFIRM and DEFINE studies and extrapolated with data from the British Columbia database. Relapse rates were based on a population-based MS survey. A network meta-analysis provided treatment efficacy inputs for disease progression and relapses. Public databases and literature provided cost data for: direct and indirect disease management, relapses, direct treatment-related attributes, and adverse events. All utility-related inputs were acquired from the literature including: patient and caregiver utilities, for patient EDSS; and relapse and adverse event disutilities. Costs and health outcomes were discounted at 3.0% per year.

Results: DMF yielded greater clinical benefits (0.86 additional quality-adjusted life years [QALYs]) and cost savings (642,573kr; approximately €65,044) over 50 years compared with TER (ie. DMF dominated). Results were robust across a wide range of one-way and probabilistic sensitivity analyses.

Conclusion: DMF is a cost-effective treatment for treatment-naïve patients with RRMS in Sweden, delivering cost savings and improved health outcomes compared with TER.

Disclosure: Study Funding: Biogen

EPO1093

The Rao's Brief Repeatable Battery (BRB): Normative values corrected for age, education and gender in an Italian pediatric population.

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Background and aims: The Brief Repeatable Battery (BRB) is the most used tool to estimate cognitive dysfunction in patients with multiple sclerosis (MS). However, the availability of normative data in pediatric population currently limits its applicability.

Methods: We administered the BRB version A to healthy subjects aged 14 to 17. All the subjects underwent the complete BRB. When a significant relationship between test scores and age, gender and education was found, the regression coefficients were used to adjust raw data. 5°percentile of corrected score for each test was used as cut-off for pathological performances.

Results: We included 76 subjects (45 females) with a mean age at baseline of 15.8±1.6 years, and a mean education of 10.6±1.5 years. Raw scores of neuropsychological tests for the BRB are shown in Table 1. Table 3 shows the mean scores and cut-off values for the BRB tests after correcting for relevant demographic factors.

Table 1.

Test	Meand Score (SD)
SRT-LTS	52,95 (±9,87)
SRT-CLTR	44,84 (±12,41)
SRT-D	9,868 (±1,87)
SPART	24,29 (±4,56)
SPART-D	8,763 (±1,82)
SDMT	59,8 (±11,21)
PASAT 3	43,42 (±10,33)
PASAT 2	35,83 (±10,85)
WLG	21,33 (±4,74)

Table 1

Table 3.

Test	Mean Score (SD)	Percentile 5%
SRT-LTS	50,65(9,54)	35,38
SRT-CLTR	41,13(12,21)	19,93
SRT-D	9,37(1,77)	6,76
SPART	20,90(4,35)	14,36
SPART-D	7,36(1,75)	3,99
SDMT	55,59(10,99)	38,13
PASAT 3	40,35(9,73)	24,27
PASAT 2	30,76(9,68)	15,80
WLG	19,69(4,11)	13,57

Table 3

Conclusion: Compared to adults, in younger subject, education can only predict verbal memory, whereas other functions are mainly predicted by age and gender. This could reflect the lower educational level of juvenile subjects (max 13 years) or the low inter-sample variability due to mandatory school attendance. Moreover, we found that the calculated cut-offs for each BRB test were generally higher than those calculated for adults, as in previous reports, apart from verbal fluency, that we could speculate to be linked to higher education and social stimulation in adults life.

Disclosure: Nothing to disclose

EPO1094

A SCA7 premutation suggested to influence the course of MS. A case report.

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Background and aims: While MS has a polygenic background, mutations pathogenic for monogenic disorders may augment symptoms from specific systems in MS patients, as reported for hereditary spastic paraparesis (HSP), and Leber's mutations. To discuss the notion that mutations which should be unable, in themselves, to produce symptoms may nevertheless influence the manifestations of MS, we here present the case history of an MS patient carrying a premutation for SCA7.

Methods: The diagnosis of primary progressive MS was based on polyfocality, characteristic MRI findings including periventricular right angle lesions, and an intrathecal olicoclonal IgG reaction, in accordance with the 2017 revisions of the McDonald criteria. The CAG trinucleotide expansion was examined using a PCR based diagnostic analysis for SCA7, showing an expansion in his ATXN7 gene with 29 CAG repeats, in the range of mutable normal alleles not expected to influence the phenotype.

Results: The patient's father died from MS dominated by a central paraparesis. With insidious onset at age 15 the patient developed a cerebellar tetraataxia which soon became debilitating, and a severe visual deficit. From age 20 a progressive paraparesis dominated the deficit. At age 45 he has an expanded disability status scale (EDSS) of 9.5. Features indicating MS (rather than SCA) lesions were oscillopia (not slow sackades), optic atrophy (not retinopathy), and the partial remission of ataxia coincident with paraparesis.

Conclusion: We suggest that the SCA7 premutation explains the extremely atypical onset of devastating cerebellar ataxia at age 15, a feature never observed in an MS incidence cohort of 308 patients.

Disclosure: Nothing to disclose

EPO1095

Machine-learning approach identifies a pattern of alterations that can discriminate Relapsing-Remitting Multiple Sclerosis Patients and Healthy Controls using pupillary response characteristics measured by pupillometry

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Background and aims: One of the most common symptoms of MS is optic neuritis, which can cause relative afferent pupillary defect. The objective of this study was to identify major features of pupillary light response by using machine learning technique which enables us to discriminate healthy cases from patients and, thereby, to realize the value of manual quantitative pupillometry for assessing relative afferent pupillary defects (RAPD) in Relapsing-Remitting Multiple Sclerosis (RRMS) patients

Methods: In the cohort of 182 RRMS patients, pupillometry parameters of 100 randomly selected subjects equal to the size of healthy control were included in this study.We have used six base learners including Linear SVM, Poly SVM, Radial SVM, random forest, decision tree and Cart tree. Majority voting on the base learners' decisions has been used to make the final decision about each sample. This ensemble learning method, achieved the sensitivity, specificity, and accuracy of 0.85, 0.78, and 0.77, respectively in a 10*10-fold cross-validation procedure.

Results: Among all pupillary response features Constriction Velocity (CV), Maximum of Constriction Velocity (MCV), Dilation Velocity (DV), Latency and discrepancy between two eyes in neurological pupil index (Npi), DV, and MCV were more discriminative than other features according to the calculated feature importance.

Conclusion: We observed that applying machine learning technique to pupillometry data has potential to yield better discrimination of group differences. In conclusion, with this innovative approach pupillary response features of pupil reflex velocity and initial latency are altered significantly under the course of MS.

Disclosure: Nothing to disclose

Muscle and neuromuscular junction disease 1

EPO1096

Collagen VI-Related Myopathy: A mutation of COL6A3 gene

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Background and aims: Mutations in collagen VI-related genes cause collagen VI-related myopathies, which cover a broad clinical spectrum. We are exposing a case report of a patient who presents Collagen VI-related myopathy.

Methods: When our patient was nine years old, presented elevation of creatine-kinase levels. When he was thirteen, he was diagnosed facioscapulohumeral dystrophy because he presented muscular atrophy in scapular and peroneal girdles, mild dorsal scoliosis and pes cavus. When he was twenty he experimented muscle fatigue and some difficulty climbing stairs (now incapability for climbing three floors).

Results: In the neurologic examination, we detected bilateral pes cavus, weakness in psoas-iliac(4+/5), knee flexors(4+/5), tibialis anterior(4-/5) and peroneus(3/5); tibialis anterior atrophy; upper limbs and patellar hyporeflexia; walking tiptoes was very difficult and walking on heels was impossible.

The creatine-kinase levels were 1973 IU/L. Lysosomal acid alpha-glucosidase and Emery-Dreifuss and Miyoshi genetic tests were normal.

Electroneurogram was normal. In electromyography, we detected myopathic pattern in quadriceps and neurogenic pattern in tibialis anterior and gastrocnemius.

In genetic tests, we detected c.7447A>G variant in homozygosis in COL6A3 gene. This was present in homozygosis in a diseased brother. In his healthy parents and one brother, we found it in heterozygosis.

Legs photographs of our patient.

Conclusion: The mutations in the COL6A3 gene cause collagen VI-related myopathy with the same neuromuscular clinic that our patient presents.

C.7447A>G variant detected in homozygosis in our patient has been reported in the literature in compound heterozygosity in a patient with attenuated collagen VI-related myopathy. The residue is very conserved and the bioinformatic study suggests it is pathogenic.

Disclosure: Nothing to disclose

EPO1097

Baseline Characteristics and Disease Burden in the Myasthenia Gravis Foundation of America (MGFA) Registry

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Background and aims: The MGFA Registry is a large, US-based, voluntary, patient-driven, online database of persons diagnosed with myasthenia gravis (MG) initiated in 2013. The goal of the Registry is to improve understanding of patient care and disease impact on daily living. Disease burden assessment in this large cohort of patients has not previously been reported.

Methods: Cross-sectional analyses included all available records (n=1140) with data on MG-ADL or MG-QOL15 as of 7/2017, two validated scales assessing health-related quality of life in MG, at baseline entry into the Registry.

Results: Mean age was 54.6 years, 66.2% were female, and 80.4% Caucasian. The majority of patients reported moderate to severe impairment in their activities of daily living and health-related quality of life as indicated by a median MG-ADL score of 6 (range 0-21) [Figure 1] and a median MG-QOL15 score of 21 (range 0-60) [Figure 2]. There was good correlation between these measures (r=0.778, p<0.001).

71% of patients reported currently receiving pyridostigmine; 42% corticosteroids; 24% mycophenolate mofetil; 19% azathioprine; 19% intravenous immunoglobulin (IvIg); and 4% plasma exchange. Prior therapies included corticosteroids (36%); IvIg (28%); and plasma exchange (26%). Few patients (<5-10%) reported ever receiving other treatments, although around 40% were unsure whether they had received any of these rarely used therapies [Figure 3]. 40% had undergone thymectomy.

Conclusion: While a disease registry may attract somewhat sicker patients, these data nevertheless highlight that, contrary to common belief, MG remains a disease that negatively impacts the health-related quality of life of many patients despite symptomatic and immunosuppressive therapies.

Figure 1
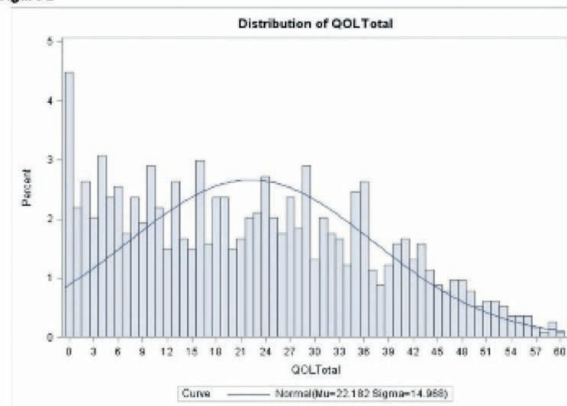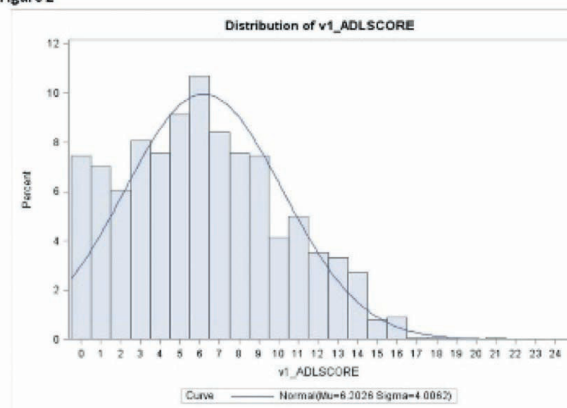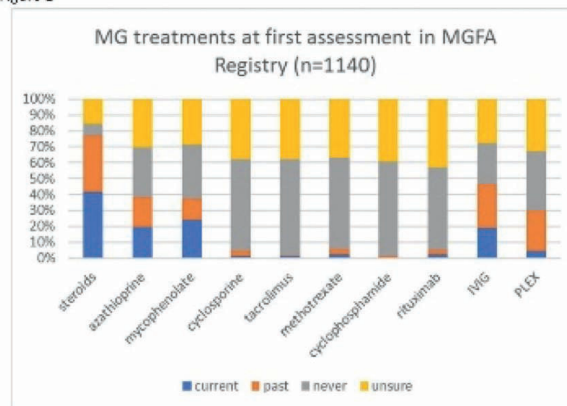
Distribution of QOLTotal

Figure 2

Distribution of v1_ADLSCORE

Figure 1

MG treatments at first assessment in MGFA Registry (n=1140)

EPO1098

Effectiveness of treatment based on the simultaneous administration of pyridostigmine, prednisolone, calcineurin inhibitor, and intravenous immunoglobulin (PPCI therapy) in patients with myasthenia gravis

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Background and aims: Intravenous immunoglobulin therapy (IVIG) is recommended in patients with myasthenia gravis (MG) during acute exacerbations. However, according to existing reports, it takes about one week before the full effects of IVIG are achieved. Recently, we preferentially and simultaneously administered pyridostigmine (cholinesterase inhibitor: ChEI), prednisolone (PSL), a calcineurin inhibitor (CNI), and IVIG to patients with MG receiving the initial treatment (PPCI therapy). We evaluated the daily therapeutic effects of PPCI therapy using the quantitative myasthenia gravis (QMG) score.

Methods: Twenty patients in our hospital who were receiving PPCI therapy were evaluated. MG symptoms were reviewed using the daily consecutive QMG scores, starting just before the onset of PPCI therapy and continuing through the 15th day of therapy. We performed a retrospective analysis, assessing MG symptoms via daily QMG scores and the MG-ADL (ADL=activities of daily living) scale.

Results: The mean QMG score in this group of patients was 12.55 ± 4.64 before IVIG, decreased significantly to 10.3 ± 5.14 on the third day of the IVIG therapy ($p=0.001$), and then decreased further to 8.2 ± 4.35 on the 15th day of therapy.

Conclusion: Patients with MG receiving PPCI therapy may experience therapeutic effects more quickly and more vigorously when compared to currently existing treatments. The addition of IVIG may improve the quality of life in patients with MG.

Disclosure: Nothing to disclose

EPO1099

ANO5 mutations in a Portuguese limb girdle muscular dystrophy population – A case series

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Background and aims: The limb-girdle muscular dystrophies (LGMDs) are a group of disorders with wide genetic and clinical heterogeneity. The LGMD-2L is an autosomal recessive subtype LGMD due to mutations in ANO5 gene. We aim to describe the clinical, pathological and molecular features of patients, diagnosed between 2004 and 2017, at our center with ANO5 mutations.

Methods: We obtained retrospective data from clinical history, neurological examination, blood workup, biopsy and genetic study.

Results: A total of 9 patients were included, all male and Caucasian. Parental consanguinity was documented in just one patient and family history of similar neuromuscular affection was described in 6 patients. Mean age of symptom onset was 59.44(SD=18.86) years. 4 patients (44.4%) presented initially with isolated hyperCKemia, 3(33.3%) with a Miyoshi distal myopathy(MDM), and 2 with LGMD (22.2%) phenotype.

During follow-up, all the patients that initially presented an MDM phenotype progressed to a mixed phenotype. All remaining patients did not change phenotype during follow-up. Gait autonomy loss was described in just one case. Dystrophic changes on muscular biopsy were described in 5 patients. Mean highest CK value was 3198.44(SD=2013.62) mg/dL. The mutation c.191.dupA was the most frequent, present in 7 patients.

Conclusion: These findings are in line with the previously described in the literature, despite the discrepancy regarding the main presenting phenotype. This case series helps to further characterize a rare disorder in our country and reinforces the clinical value of novel molecular diagnostic tools in the face of an overlapping and heterogeneous disorder.

Disclosure: Nothing to disclose

EPO1100

A novel c.2717G>C benign polymorphism of SCN4A gene responsible of severe myotonia in a family with myotonic dystrophy type 2: a precision medicine approach

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Background and aims: Myotonia is mild and inconsistent in myotonic dystrophy type 2 (DM2) and it is related with CLCN1 alternative splicing deregulation. Mutations in CLCN1 and SCN4A can act as modifier genes in these patients leading to an intensification of myotonia. Recently, a 32 years old DM2 patient with an early severe myotonia since he was 12 came to our Neuromuscular Center. Mexiletine treatment resulted ineffective. No mutation was found on CLCN1, but SCN4A gene showed a c.2717G>C base exchange, a variant considered a benign polymorphism. In his mother, affected by DM2 but without the polymorphism, no clinical myotonia was observed.

Methods: The biophysical alterations of the polymorphism was studied in combination with DM2 mutation in muscle cells from the proband and his mother. Patch clamp in voltage and in current clamp mode was used for electrophysiological recordings.

Results: Myoblasts showed no change in the steady state activation properties, but a significant shift in the availability curve (V1/2 -73.9±1.3 mV n=8 and V1/2 -78.8±1,0 mV n=9 proband and mother respectively). No differences were found in the recovery from the fast inactivation. In myotubes, the minimum current necessary to elicit an action potential was lower in the proband than in his mother (352.4±80.7 pA n=59 and 578.6±134.1 pA n=57 respectively).

Conclusion: SCN4A polymorphism induces a more excitable substrate potentially aggravating the effect of the DM2 mutations in our proband. When phenotype is uncommon, additional genes and/or modifying factors need to be explored to account for the phenotype and for the identification of appropriate drug treatment.

Disclosure: Nothing to disclose

EPO1101

Myasthenia Gravis in octogenarians and beyond: What is the difference? A tertiary hospital experience

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Background and aims: Myasthenia gravis (MG) is a treatable autoimmune disorder affecting patients of all ages. It is uncertain whether age affects clinical profile of the disease and/or its management.

Methods: Retrospective analysis of Neurology admissions (2011-2017) with diagnosis of MG. Patients were assigned to MG-elderly (MG-E) group if ≥80 years and to MG-non elderly (MG-NE) if <80.

Results: 87 admissions were included (61% female, 64 ±20 years), 71% of patients in MG-NE and 29% in MG-E group. 48% of MG-NE and 38% of MG-E had a previous MG diagnosis. There were no significant differences between groups on symptoms duration, clinical involvement (15% ocular in both, bulbar in 61% MG-NE vs. 73% in MG-E, respiratory in 28% vs. 31%, generalized in 85% vs. 88%). Myasthenia Crisis occurred in similar proportion (51% vs. 58%) and acute treatment was similar (steroids >96% in both, gammaglobulin in 44% vs. 54%, intensive care in 13% vs. 11%), without fatal cases. Upon discharge, Acetylcholine esterase inhibitors and steroids were scheduled in 96% in both groups, but immunosuppressants were prescribed more in MG-NE (36% vs. 19%, p: 0.03). Thymoma was less frequent in MG-E group (0% vs. 36%, p<0.0003) and anti-striatal muscle (SM) antibodies positivity higher (77% vs 44%, p:0.0051), without differences in other serological markers.

Conclusion: We ascertained differences on thymoma frequency and anti-SM antibodies positivity in elderly patients with MG, which might relate to a different underlying mechanism of disease. MG-E patients benefited from the same acute therapies and shared the same good prognosis as younger ones.

Disclosure: Nothing to disclose

EPO1102

Myopathies acutely admitted to the adult intensive care unit – a single centre case series.

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Background and aims: We present a series of patients acutely admitted to the adult ICU in whom a previously undiagnosed primary muscle disease was found to be the underlying diagnosis, and investigated whether the outcomes justified a decision to provide invasive intensive care.

Outcomes of intensive care myopathy-single centre.

Methods: We studied patients admitted directly to intensive care at our institution in whom a primary myopathy was newly diagnosed and considered to be the underlying cause for admission. The diagnosis was established either through muscle biopsy or genetic analysis. Clinical course and outcomes were analysed retrospectively from case notes or follow up examination.

Results: 14 patients were identified between 2012 through 2017 in whom a specific diagnosis of myopathy was established during their ICU stay. The reason for admission was respiratory (n=9), cardiac (n=4), or renal failure (n=1). The diagnosis was established histologically in 11 patients and genetically in 3. 4 patients stayed in ICU for <7 days, and 4 >50 days. 12 patients required ventilatory support. 2 patients had heart transplants. 11 were discharged home or transferred to a rehabilitation unit. All survivors regained their previous functional status except 1 patient with a tracheostoma for dysphagia.

Conclusion: Chronic, unrecognised myopathies can present with an acute admission to the ICU. Intensive care in these patients is complex, but most return to their baseline function even after a prolonged stay. This study underlines the feasibility of advanced intensive care in patients with severe degenerative muscle disease.

Disclosure: Nothing to disclose

EPO1103

Treatment and follow-up of late onset myasthenia gravis

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Background and aims: An increasing incidence of myasthenia gravis (MG) has been reported in the elderly. Treatment decisions may be especially complicated at this age, because of comorbidities and higher risk of iatrogenicity. We aim to describe our cohort of patients with late onset MG (LOMG) with an emphasis on treatment regimen, its efficacy and complications.

Methods: Retrospective analysis of medical records of a cohort of patients followed in a Portuguese tertiary centre. LOMG is defined herein as disease onset after the age of 50 and no clinical evidence of thymoma.

Results: Of 192 myasthenic patients, we identified 39 cases with LOMG (20.3%). Age at onset ranged from 50 to 81 years (median=70) and 61.5% were man. Nineteen patients (48.7%) had generalized disease and anti-AChR antibodies were positive in 64.1%. Almost all received pyridostigmine (35/39;89.7%). At some time, 28 patients (71.8%) required prednisolone (average maximum daily dose=21mg) and 17 (43.6%) immunosuppressive therapy (AZA, MMF or MTX). Intravenous immunoglobulins were used in 8 patients and only one needed ventilatory support. Treatment complications included diabetes (1), cataract (2), elevated liver enzymes (2), infections (2), tumours (4), cytopenia (3), vertebral fracture (1) and hypertension (2). Nineteen patients had mild (4) or significant (15) improvement, 3 are in complete remission, 13 in pharmacological remission and 4 had no change.

Conclusion: In our series, the prognosis of MG in older people seems to be favorable, with a good rate of improvement and remission, although most patients required corticosteroids/immunosuppressants. Treatment was overall well tolerated, but side effects are still a concern.

Disclosure: Nothing to disclose

EPO1104

Atypical desminopathy with new mutation and autosomal recessive transmission

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Background and aims: Desminapathies may manifest different clinical profiles, ages of presentation and even different types of inheritance. We aim to report a family with desmin myopathy with an atypical phenotype and recevise transmission.

Methods: A 14-year-old male patient was attendeded in our clinic presenting myalgia, exercise intolerance and serum creatinine kinase (CK) levels m around 1000 IU/L; his middle sister has the same symptomatology and an older brother was healthy. Their parents were consaguineous.

Results: A non-invasive hyperCKemias protocol was applied, including Pompe DBS and MLPA DYS that were normal. MRI presentented a pattern of local muscle involvement (soleus, gastronemius and semitendinosus (grade 1) and paravertebral (grade 2)). Cardiac investigation were normal. Muscle biopsy presents a dystrophic profile with vacuoles. In successive years he developed mild palpebral ptosis and minimal facial, scapular and axial weakness (4-). A NGS genetic study with 40 genes detected a not described homozygous DES gene variant (c.1372-1G> A). The mutation segregated with a recessive pattern in the family study. Myofibrillar protein markers were abnormal, highlighting Desmin accumulations. Currently both siblings have similar manifestations at 22 and 28 years of age.

Conclusion: We describe a new pathological variant in the DES gene (c.1372-1G> A) with AR transmission causing a desminopathy that presents as paucisintomatic HCK and evolved with an atypical phenotype of palpebral ptosis and facial scapular weaknesss.

Disclosure: Nothing to disclose

EPO1105

Clinical, pathological and molecular characterization of a Limb-girdle muscular dystrophy type 2I (LGMD-2I) cohort

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Background and aims: LGMDs are rare hereditary muscular diseases with a wide clinical and genetic variability. The autosomal recessive account for 90% of cases and the subtype LGMD-2I (FKRP gene) is the third most common. Studies regarding clinical and molecular characterization of this subpopulation are sparse.

Methods: Retrospective analysis of the clinical, pathological and molecular findings of patients with LGMD-2I diagnosed at our center in CHUC between 2004-2017.

Results: We report 8 patients (mean age 45.9yo, 37% female) with a mean follow-up time of 18.9y. Parental consanguinity was identified in 75% of cases. The mean age at onset of symptoms was 15.1yo. Seven patients underwent muscle biopsy, with a mean interval between it and the first symptoms of 8.3y. The biopsy revealed a dystrophic pattern in 57% of the cases and immunohistochemistry was normal in all. The mean time between molecular diagnosis and symptom onset was 16y. The most frequent mutation identified was g.826C> A (87.5% of cases). At the first assessment, 75% of patients presented with LGMD phenotype and the remaining with an isolated hyperckemia. During follow-up, 62.5% of the patients presented a restrictive respiratory pattern and 37.5% developed dilated cardiomyopathy. The mean time till autonomy gait loss was 36y and the mean CK concentration was 4382 mg/dL.

Conclusion: The clinical characterization of LGMD subtypes is of major importance to increase the information on the progression and clinical characteristics of each of these conditions. It is of utmost importance in optimizing the multidisciplinary care that these patients require.

Disclosure: Nothing to disclose

Neurological manifestations of systemic diseases

EPO1106

Peculiarities of associations between the neurological status, EEG parameters, and hepatic morphofunctional changes in Wilson's disease

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Background and aims: Unlike other hepatic encephalopathies, in Wilson's disease (WD) its neurological manifestations and impairments of brain functional conditions result both from liver damage and from accumulation of copper in brain, an acute elevation of serum copper levels, and iatrogenic effects.

Methods: During 2012-2017, 40 patients (mean age 24.23±1.90 years old) with WD (E83.01) were evaluated regularly for their neurological status (with the Unified Wilson's Disease Rating Scale (UWDRS)), EEG parameters (indices, powers, ratios), and hepatic morphofunctional changes (liver parenchyma stiffness (LPS)).

Results: Dynamically some patients had changes on EEG with unchanged LPS parameters, whereas other patients had signs of deterioration/improvement of liver morphofunctional conditions, which were not reflected in EEG parameters. Moreover, patients with a poor outcome (7 persons) had a various degrees of hepatic damages, but similar EEG changes. Correlation between LPS and delta/alpha-ratio was not found (r=-0.002), but delta/alpha-ratio correlated with UWDRS scores (r=0.40). Similarly, UWDRS scores demonstrated stronger than LPS correlation with alpha-index (r=-0.397 vs r=-0.049), power of alpha-activity (r=-0.491 vs r=-0.193), and a specific power (r=-0.453 vs r=-0.226). There was a weak correlation between UWDRS scores and LPS (r=0.32).

Conclusion: In WD, a close association between hepatic morphofunctional changes and EEG changes was characteristic only for the WD hepatic form; for other WD forms, this association was complex, as poor outcomes can be occurred not only in cirrhosis, but in initial stages of liver fibrosis. The LPS median value in WD was not a reliable classifier of EEG changes and a marker of neurological manifestations.

Disclosure: Nothing to disclose

EPO1108

Neuropsychiatric Manifestations of adult-onset Rheumatoid Arthritis

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Background and aims: Rheumatoid arthritis (RA) is an autoimmune disease that mainly affects synovial joints but also has an impact on other organ systems. Neuropsychiatric manifestations (NP) are quite common in RA, involving both the central and peripheral nervous system.

Methods: We performed complete rheumatological and neurological evaluation using ACR- EULAR 2010 Classification Criteria, DAS28, Health Assessment Questionnaire-Disability Index (HAQ-DI). Immunological blood tests include RF, Anti-CCP, Anti-MCV, we also performed lumbar puncture, vascular biopsy, neuropsychological testing, Doppler sonography, EMG and EEG, brain MRI/CT.

Results: A total of 150 patients were observed in the period of 2 years /2015-2017/-85 female, (57%), 65 men (43%). NP manifestations include: brain involvement, depression, anxiety, cognitive dysfunction, headache, seizures, cerebrovascular disease, cranial nerve involvement, movement disorders such as Parkinson's disease, atlantoaxial subluxiation, acute myelitis, compressive neuropathy, mononeuritis multiplex and polyneuropathy.

Conclusion: About 70% of patients with RA present with NP manifestations. Potential causes include systemic inflammatory process, neural compression due to bone and joint destruction, side effects of medications. There is a high correlation between the presence of neuropsychiatric symptoms and disease activity, disease duration and treament with DMARDs, corticosteroids or biologics.

Disclosure: Nothing to disclose

EPO1109

Developing a framework to optimise the ongoing assessment of ATTR-amyloidosis

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Background and aims: Transthyretin-related amyloidosis (ATTR) presents in many different forms and with considerable variation in signs and symptoms and across geographic locations. There are important differences in TTR gene mutations, which in turn are associated with different phenotypes. Even within a specific gene mutation, phenotypes are not always uniform. Many diagnostic tests and investigations are not useful for adequately assessing treatment outcomes or identifying thresholds of disease progression. For optimal patient management, we must consider the changing status of a diagnosed and treated patient, and how to understand the rate of progression of disease.

Methods: A structured follow-up that targets specific signs and symptoms was proposed as an appropriate framework, within which, minimum clinical criteria for disease progression could be defined. No formalised approach had been developed to date.

It was agreed that the different phenotypes observed in clinical practice could help define two major phenotype groups:

A. V30M early-onset

B. Non-V30M and V30M late-onset

Results: Novel techniques as well as the combination of tests (composite scores) should be incorporated within the framework, along with assessment of multiple organ systems. The need to be assessed through a multi-disciplinary approach is key, with patient-reported aspects also deemed as essential components.

Conclusion: A framework outlining the recommended specific tests and investigations is proposed to facilitate in making optimal treatment decisions for physicians managing patients with this fatal, progressive disease.

Disclosure: Support provided by Pfizer Inc, and Medical writing support provided by Synergy Medical Education, UK.

EPO1110

Developing a framework to optimise the ongoing assessment of ATTR-amyloidosis in patients with a cardiac phenotype

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Background and aims: Transthyretin amyloidosis (ATTR) is a progressive, autosomal-dominant disease characterised by deposition of transthyretin-derived amyloid fibrils. Amyloid may deposit in the peripheral and autonomic nerves, as well as heart, gastrointestinal tract, kidneys, and eyes. Accordingly, disease presentation is heterogeneous and considerable variation in signs and symptoms can be observed, based on the TTR gene mutation. ATTR is categorised as a neurologic, cardiologic, or mixed phenotype.

Many tests and investigations for initial diagnosis are not useful for adequately assessing treatment outcomes or identifying thresholds of disease progression in neurological or cardiological manifestations: often due to a 'floor' or 'ceiling' effect where no further measurable change in a given parameter is possible.

Methods: A structured follow-up targeting specific signs and symptoms was proposed as an appropriate framework within which clinical criteria for disease progression could be defined. No formalised approach had been developed to date.

When considering a patient with a cardiologic phenotype, key tests and investigations that could be routinely undertaken to capture the necessary information were considered to build a framework.

Results: New techniques and the combination of tests should be incorporated within the framework, along with assessment of multiple organ systems. The need to be assessed through a multidisciplinary approach, where specialties in cardiology and neurology work closely together, should also be considered.

Conclusion: A framework for addressing cardiac phenotypes, and specific tests and investigations that should be recommended, is proposed. This will facilitate optimal treatment decisions for physicians managing patients with this fatal, progressive disease.

Disclosure: Supported by Pfizer Inc with Medical writing support provided by Synergy Medical Education, UK

EPO1111

A case of disseminated Bartonella henselae infection (cat-scratch disease) with encephalitis in an adult patient

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Background and aims: Bartonella henselae is the primary cause of Cat Scratch Disease (CSD). Bacterial infection due to Bartonella henselae commonly develops in children and young adults following cat/dog contacts and/or scratches. The disease is usually self-limited with rare serious complication. Diagnosis is usually based on serologic tests.
Methods: Here, we present a report of a patient with cat scratch disease who presented with aphasia and altered mental status secondary to encephalitis.
Results: A seventy seven years old male patient admitted to our clinic with speech impairment and confusion. In his past medical history no underlying illness was known. He had a history of respiratory tract infection that has not healed for about two months. Physical and neurological examination revealed word substitution errors, trapped aphasia, purpuric rash on the arms and right supraclavicular lymphadenomegaly. Brain MRI showed no acute changes and no contrast enhancement. The EEG findings showed doubtful hypersynchrony on the basis of widespread organization disorder in bilateral frontosentrotemporal regions. Cerebrospinal fluid tests showed normal glucose, high protein levels and 40 leukocytes. CSF viral PCR, tuberculosis tests, CSF cultures were all negative. Right supraclavicular biopsy material showed necrotizing granulomatous lymphadenitis. After antibiotic administration, the patient's symptoms and aphasia resolved. The patient had a history of contact and stratch with kittens. Bartonella henselae serology titers were IgG positive (>1:320) and IgM negative.
Conclusion: We recommend consideration of CSD in the differential diagnosis of any adult with a history of lymphadenopathy, recent contact with a cat who presents with neurological complications.
Disclosure: Nothing to disclose

EPO1112

Low level of consciousness as a debut of Macrophage Activation Syndrome

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Background and aims: The syndrome of macrophage activation (SMA) is an unusual syndrome that can appear related to neoplasms, infectious diseases and autoinmune diseases. Mortality related to the syndrome is high, consequently, a high index of suspicion must be maintained and treatment mus be started early.
Methods: A 42-year-old man was studied for febrile symptoms with adenophaties and hepatosplenomegaly over 3 weeks with diagnostic suspicion of Still's disease of the adult, and stars with deterioration of the level of consciouness, tonic-clonic movements in both upper-limbs. The analysis taken the following mosninrg revealed an LDH and Triglycerids levels increased, as well as ferritin of 150,000. Lumbar puncture was performed with aseptic meningitis and an EEG that reports epileptic status, so the patient was finally intubated and admitted to the ICU.
Results: With these data, with suspicion of SMA, a FNAB of bone marrow was performed, and it confirmed the presence of hemophagocytosis in bone marrow. Inmediately treatment was initiated with Inmunoglobulins cycles as well as antiepileptic drug with clinical improvement in 3 days and complete recovery un 3 weeks after subsequent corticoid therapy.
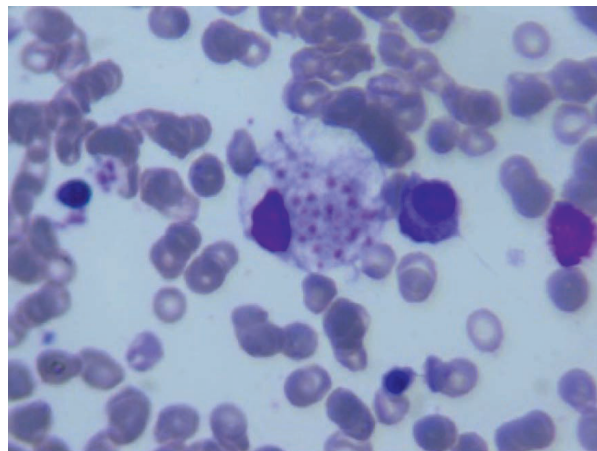
Hemophagocytosis in bone marrow

Conclusion: SMA is a syndrome that must be suspected and treated early. It is important to consider it in all patient with systemic infection, rheumatic or haematological

disease that starts with high fever, elevation of LDH and triglycerids, and ferritin levels>1000. One third of the patients occurs with neurological symptoms (seizures, meningism, cranial nerve palsies, decreased state of consciousness, ect). The treatment of choice is corticoids at high doses, Inmunoglobulins cycles or ciclosporines.

Disclosure: Nothing to disclose

EPO1113

Erdheim-Chester Disease as a rare cause of progressive ataxia

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Background and aims: Erdheim-Chester disease(ECD) is a form of non-Langerhans' cell histiocytosis, with clonal proliferation of histiocytes of monocyte-macrophage descent. Skeletal involvement is pathognomonic, and presentation varies from focal to multiorganic, life-threatening disease. CNS involvement is present in half the cases and worsens prognosis.

Methods: Case Report

Results: 66-year-old female progressively developed gait ataxia and dysarthria. At first medical contact (2014), the remaining neurological and physical examination were unremarkable. Complementary exams directed at hereditary, infectious and autoimmune causes of ataxias were innocent. During the following years general and neurological status worsened, with multiple hospital admissions due to renal disease and multiple-site infections.

Echocardiogram revealed a thickened aortic wall and chest CT showed bilateral ground-glass opacities; at that time, these were considered non-specific.

In 2017, renal function and neurologic status worsened and the patient was re-admitted. Neurological examination revealed generalized hypotonia and tetraparesis, severe truncal and limb ataxia, hyperreflexia, dysarthria, dysphagia and altered ocular movements. Tibial radiographies showed bilateral diametaphyseal osteosclerosis; abdominal MRI revealed extensive retroperitoneal fibrosis with infiltration of perirenal fat. Brain MRI showed bilateral orbitary/supratentorial tumefactive lesions, T2/FLAIR hypersintensities of the mesencephalon, pons and cerebellum, generalized atrophy and diffuse white-matter disease.

Renal fascia biopsy was compatible with ECD. The patient was started on IFN-alfa and BRAF mutation study is underway.

Sagital T2

Abdominal T2

Tibial XRay

EPO1114

A rare case of central nervous system involvement following the onset of multiplex multineuritis in an otherwise typical case of acute eosinophilic granulomatosis with polyangiitis

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Background and aims: Eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome, CSS) is a rare life-threatening immune-mediated vasculitis. In Europe, its annual incidence is less than 3.7 per million. The peripheral nervous system is affected in up to 75% of cases, while central nervous system (CNS) involvement is uncommon (8-14%). We report a rare case of acute CSS presenting with multineuritis multiplex followed by lower limb monoparesis caused by a CNS lesion.

Methods: A 31-year old man without any medical history except for the recent onset of asthma, presented with weight loss, haemorrhagic alveolitis, sinusitis, vasculitic skin lesions, intestinal ulceration, inflammatory syndrome and eosinophilia, accompanied by multiplex mononeuritis with sensory and motor symptoms. He was diagnosed with CSS and high dose methylprednisolone and cyclophosphamide were started. A few days later his neurologic condition worsened due to left lower limb paresis without other signs. Brain magnetic resonance imaging was performed, revealing a small ischemic lesion in the right precental gyrus. Ancillary investigations excluded other aetiologies. The case was compatible with small cerebral vessel vasculitis in the context of CSS, therefore no therapeutic adjustment was required.

Conclusion: ECD is a rare and widely unknown disease with a variable course. CNS involvement may precede the classical skeletal signs, making ECD a complex and demanding diagnosis. We suggest adding this clinical entity to the workup of rare causes of progressive ataxia.
Disclosure: Nothing to disclose
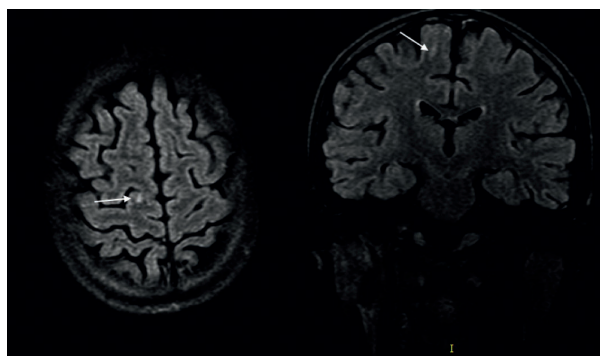
Axial fluid-attenuation inversion recovery MR image (right) revealing small ischemic lesion located in the right precentral gyrus. Coronal fluid-attenuation inversion recovery MR image (left) showing the same lesion, oval-shaped, suggestive of perivascular localization.
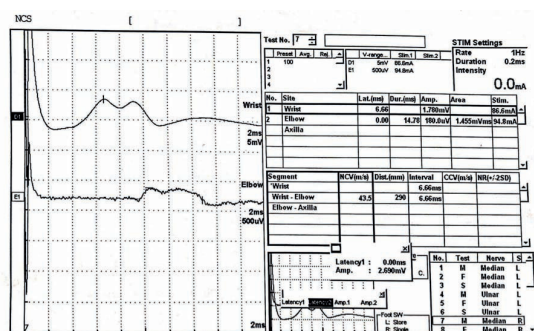
Nerve conduction study graphic, which reveals decreased amplitude of muscle compound action potentials on proximal compared with distal left median nerve stimulation (conduction block) and temporal dispersion of compound muscle action potential.

Results: Cyclophosphamide was continued for 6 applications, attaining remission. Subsequently, azathioprine was started. After 1 year, the patient had complete resolution of neurological deficits and after two years, continued to be asymptomatic.

Conclusion: Sudden onset of neurological impairment in people with CSS should prompt the consideration of CNS involvement directly related or accompanying the disease. Coexisting peripheral nevritis may hinder the clinical diagnosis, therefore a high awareness index is advised.

Disclosure: Nothing to disclose

EPO1115

Acute autonomic neuropathy and Waldenstrom disease: a case report

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Background and aims: Acute idiopathic dysautonomia is an uncommon syndrome consisting of sympathetic and parasympathetic dysfunction, which can be pure or associated with sensory or sensorimotor impairment. It can be primary or associated with various diseases such as diabetes mellitus, amyloidosis, paraneoplastic syndrome and Sjögren's syndrome. The monophasic clinical course, the presence of previous infections in many cases and an albuminocytologic dissociation suggest an immuno-mediated pathogenesis similar to Guillain-Barré syndrome.

Methods: We report a case of acute autonomic and sensory neuropathy and Waldenstrom's macroglobulinemia treated with intravenous immunoglobulin (IVIg).

Results: A 42-old-year man presented with subacute autonomic dysfunction, consisting on abnormal perspiration, erectile dysfunction, urinary retention and diarrhea with loss of 17kg. He also complained of feet paresthesia.

Nerve conduction studies showed a moderate sensitive axonal neuropathy, and abnormal Sudoscan electrochemical skin conductances. Skin biopsy confirmed the loss of unmyelinated fibers. Lumbar puncture showed an albuminocytologic dissociation (proteins 81 mg/dl and 1 cell/mm3). The diagnosis of acute autonomic and sensory neuropathy was evoked. Biological investigations revealed a Waldenstrom macroglobulinemia, with monoclonal IgM Kappa protein. The patient received 2 courses of intravenous immunoglobulin with total recovery of both autonomic and sensory dysfunction.

Conclusion: Several types of neuropathies have been described in WD, but the relationship between Acute autonomic neuropathy has not been reported. We describe the first case of acute autonomic neuropathy associated with Waldenstrom disease.

Disclosure: Nothing to disclose

Sunday, 17 June 2018

Cerebrovascular diseases 2

EPO2001

The role of admission cholesterol levels on short- and long-term survival after ischaemic stroke.

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Background and aims: Ischaemic stroke (IS) remains a leading cause of death and disability worldwide. Blood-based biomarkers have been used to identify patient-subgroups with increased risk for recurrent vascular events and death. Cholesterol has been studied in stroke and an inverse association to mortality has been reported. In our study, we aim to further investigate the role of admission cholesterol and its subfractions in short- and long-term survival after IS.

Methods: Our study is a retrospective, hospital-based, follow-up cohort of all patients with IS admitted in the stroke unit between January 2005 and February 2016. Of 3753 patients evaluated, 2364 had available cholesterol values. Time of observation was calculated from admission until death or until the end of observation period (May 1st, 2017). Logistic regression analysis, and Cox proportional hazard analysis were used for short- and long-term mortality investigation respectively.

Results: During a median follow-up period of 44 months, 842 of 2364 patients (36%) died. Of those, 113 patients (median age 84 years, IQR 10; 42% males) died within the first month. Patients with low cholesterol were older and had more vascular comorbidities. Increasing low density lipoprotein (LDL) cholesterol was independently associated with decreased 1-month mortality (OR 0.7; 95% Confidence Interval 0.51-0.96; p=0.03). Cholesterol levels were not associated with long-term mortality.

Conclusion: Our results show a possible association between low LDL levels at admission after IS and increased short-term mortality, that may be a marker of less severe stroke and more favourable outcome. No association was confirmed between cholesterol and long-term mortality.

Disclosure: Nothing to disclose

EPO2003

Posterior reversible encephalopathy syndrome associated with accidental intravascular injection of local anaesthetics

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Background and aims: Posterior reversible encephalopathy syndrome (PRES) is an increasingly recognised acute neurological disorder with various precipitating conditions. Endothelial dysfunction is the pathophysiological key factor of PRES, and a frequent overlap with reversible cerebral vasoconstriction syndrome (RCVS) has been reported. We here present a series of three recently observed cases where PRES occurred immediately after accidental intravascular injection of amino-amide type local anaesthetics.

Methods: Single centre retrospective case series from a primary and tertiary care university hospital.

Results: Case 1: PRES/RCVS with altered vigilance, bilateral blindness and right-sided hemiparesis in a 74-year-old female patient after periradicular high cervical injection of ropivacaine for chronic neck pain.

Case 2: PRES/RCVS with associated refractory status epilepticus and cerebral air embolism in a 47-year-old male patient after dental anaesthesia with lidocaine.

Case 3: PRES with altered vigilance, bilateral blindness and left-sided hemiparesis in a 74-year-old male patient after periradicular cervical injection of ropivacaine for chronic cervicalgia. All three patients had an onset with severe clinical symptoms including reduced consciousness and were therefore admitted to the neurointensive care unit. MRI served to identify the presence of vasogenic oedema in a typical pattern and its subsequent resolution. Functional outcome at the time of hospital discharge was good in all cases (modified Rankin Scale scores of 0, 1, and 2, respectively).

Conclusion: Acute neurological symptoms immediately after the application of local anaesthetics should raise the suspicion of PRES/RCVS. Accidental intravascular drug injection is the most likely cause. Particular caution is required when local anaesthetics are administered in well-vascularised regions.

Disclosure: Nothing to disclose

EPO2004

Mechanical trombectomy in acute basilar artery occlusion.

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Background and aims: Research suggest that mechanical trombectomy (MT) and intravenous trombolysis (ivT) are safe and effective treatment options in patients with acute basilar artery (BA) occlusion. However, optimal choice is still equivocal. This study gives retrospective assessment of MT efficacy in acute BA occlusion.

Methods: In the group of 107 patients treated with MT between Jan 2016 and Dec 2017 we found 7 patients with acute BA occlusion. In all patients CT angiography confirmed BA occlusion before MT.

Results: In MT-treated patients frequency of acute BA occlusion in 6.5%. Clinical characteristics is depicted in Tab. Median age was 75 years. Median NIHSS score at admission was 21 points. In 5 patients BA patency restitution was accompanied by neurological improvement. In 1 patient, despite complete BA reperfusion, neurological condition remained severe due to complete stroke in posterior circulation. In 1 patient BA patency was not restituted and patient died due to circulatory insufficiency. Median NIHSS score after MT was 5 points. Median time from stroke onset to BA reperfusion was 318 minutes. In all cases BA patency was restored with aspiration catheter. In 3 cases MT was preceded by ivT.

Conclusion: MT provides effective treatment method in patients with acute BA occlusion. The main factor that influences final clinical outcome seems to be restoration of BA patency. It must be emphasized that despite relatively long time interval between stroke onset and BA patency restoration substantial clinical improvement was observed.

Disclosure: Mechanical trombectomy treatment is performed by a team of hihgly specialized interventional neuroradiologists from Department of Interventional Radiology and Neuroradiology of Medical University of Lublin, Poland: Roman T, Sojka M, Górnik M, Pyra K, Jargiełło T. Stroke team in Department of Neurology of Medical University of Lublin is supervised by Szczepańska-Szerej H.

EPO2005

Safety and Efficacy of Cerebrolysin in Early Post-stroke Recovery: A Meta-analysis of Nine Randomized Clinical Trials

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Background and aims: This meta-analysis combines the results of nine ischemic stroke trials, assessing efficacy of Cerebrolysin on global neurological improvement during early post-stroke period. Cerebrolysin is a parenterally administered neuropeptide preparation approved for treatment of stroke.

Methods: All included studies had a prospective, randomized, double-blind, placebo-controlled design. The patients were treated with 30-50 ml Cerebrolysin once daily for 10-21 days, with treatment initiation within 72 hours after onset of ischemic stroke. Data Sources: For five studies original analysis data were available for meta-analysis (individual patient data analysis), for four studies aggregate data were used. Study Selection: The combination by meta-analytic procedures was pre-planned and the methods of synthesis were pre-defined under blinded conditions. Search deadline for the present meta-analysis was December 31st, 2016.

Results: The nonparametric Mann-Whitney (MW) effect size for NIHSS on day 30 (or 21), combining the results of nine randomized, controlled trials by means of the robust Wei-Lachin Pooling Procedure [MERT], indicated superiority of Cerebrolysin as compared with placebo (MW 0.60, P<0.0001, N=1879). The combined number-needed-to-treat (NNT) for clinically relevant changes in early NIHSS was 7.7 (95% CI 5.2 to 15.0). The additional full scale ordinal analysis of mRS at day 90 in moderate to severe patients resulted in MW 0.61 with statistical significance in favour of Cerebrolysin (95% CI 0.52 to 0.69, P=0.0118, N=314). Safety aspects were comparable to placebo.

Conclusion: Our meta-analysis confirms previous evidence that Cerebrolysin has a beneficial effect on early global neurological deficits in patients with acute ischemic stroke.

Disclosure: Nothing to disclose

EPO2006

The reliability of prehospital diagnosis of stroke or transient ischemic attack

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Background and aims: Early and correct suspicion of acute cerebrovascular accident (CVA) is necessary for shortening time to reperfusion treatment. Our aim was to evaluate the reliability of prehospital diagnosis of stroke or transient ischemic attack made by healthcare professionals referring patients directly to a neurological Emergency Department (ED).

Methods: This retrospective analysis included all consecutive patients referred between January 2014 and December 2014 by ambulance physicians, paramedics or outpatient physicians to a neurological ED providing care for the population of 300–350 thousand inhabitants of a highly urbanized area. We calculated sensitivity and positive predictive value (PPV) with 95% confidence intervals (95%CI) for each group of healthcare professionals and compared the proportions of undetected CVAs.

Results: During the study period there were 690 patients with confirmed CVAs, including 639 formally referred by healthcare professionals. The highest sensitivity for detection of any CVA was observed among ambulance physicians (96%, 95%CI: 92-98%), followed by paramedics (85%, 95%CI: 80-90%, $p<0.001$) and then outpatient physicians (74%, 95%CI: 70-79%, $p<0.001$). PPV for stroke was 83% (95%CI: 77-87%) among ambulance physicians, 73% (95%CI: 65-80%) among paramedics and 56% (95%CI: 47-64%) among outpatient physicians.

Conclusion: Ambulance physicians are highly sensitive in diagnosing any CVA. Their prehospital diagnosis of stroke was correct in 8 of 10 cases, and only in 7 of 10 cases if made by paramedics, which indicates the necessity of two-way communication between ambulance and the stroke team before arrival at the ED. Suboptimal sensitivity urges additional training for paramedics and primary care physicians.

Disclosure: Nothing to disclose

EPO2007

Body Mass Index, Waist-to-Hip Ratio and Body Surface Area in patients with acute central nervous system ischemia in north-eastern Poland – preliminary examination.

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Background and aims: Obesity is an important risk factor for stroke and probable predictor of functional outcome following ischemic stroke. The aim of our study was to measure and compare body mass index (BMI), Waist-to-Hip Ratio (WHR) and Body Surface Area (BSA) in patients with acute central nervous system ischemia in north-eastern Poland.

Methods: A total of 104 (63 male and 41 female) patients diagnosed with acute central nervous system ischemia were included. This was a retrospective pilot study of patients admitted in the last 3 months of 2017. Standard norms for BMI and gender specific norms for WHR were used as references.

Results: The patients' age ranged from 31 to 94 years (the average age of men and women was 71.1 and 69.06 years respectively). The average BMI for both sexes was 28.7, the average WHR was 0.98. BMI above 24.9kg/m² was present in 72.12% and WHR above normal in 83.65% of patients. More male than female had WHR above normal values. Among patients with BMI above the norm BSA, calculated by Du Bois formula, was about 2.04m² for men and 1.82m² for women.

Conclusion: In the majority of patients with acute central nervous system ischemia in north-eastern Poland WHR, BMI and BSA are significantly increased.

Disclosure: Nothing to disclose

EPO2009

Large vessel occlusions with low NIHSS-Frequency, clinical course and outcomes in a tertiary stroke center

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Background and aims: Most patients with acute large vessel occlusions (LVO) such as occlusion of carotid-T or proximal middle cerebral artery (MCA) present with severe stroke symptoms and according to large randomized clinical trials there is a clear indication for iv-thrombolysis in combination with mechanical recanalisation. However, there is a small number of patients with LVO with mild symptoms only. Not much is known about frequency, clinical course and outcome of these patients.

Methods: Consecutive patients with acute infarcts in the MCA-Territory and initial CTA were assessed for presence and site of vessel occlusions. Patients with initial NIHSS ≤4 and Occlusion of Carotid-T, M1-3-Segments of the MCA were assessed for treatment, clinical course and outcome at discharge.

Results: 1869 patients with acute stroke were referred to our hospital from 01/2012-09/2014. Of these, 1046 had ischemic stroke in the MCA territory and 936 obtained CTA or MRA on admission. Large vessel occlusions (LVA) were present in 432 patients and 343 subjects showed up within a therapeutic time window for IVT and/or MR. 99 patients had LVO and NIHSS≤4 (23% of all LVO) and secondary deterioration occured in13 (13%) of these patients. Due to different times from onset and contraindications patients were treated differently: secondary prevention only in 3; IVT in 1; MR in 4; IVT+MR in 5.

Conclusion: LVO with mild stroke NIHSS≤4 was not rare (23%). In 13% of these patients, without specific treatment on admission, secondary deterioration occured. These patients need special attention and monitoring in order to immediately start treatment when deterioration occurs.

Disclosure: Nothing to disclose

EPO2010

withdrawn

EPO2011

Intraplaque hemorrhage in symptomatic and asymptomatic progressive carotid artery stenosis–a pilot study

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Background and aims: Intraplaque hemorrhage (IPH) belongs to potential mechanisms of unstable plaque development. Study aims to compare the IPH occurrence in patients with asymptomatic stable (ASS), asymptomatic progressive (APS) and symptomatic (SS) carotid artery stenosis >50%.

Methods: Serial duplex ultrasound (DUS) in a 6-month period and magnetic resonance imaging (MRI) using axial 3DT1w sequence were used for IPH detection in patients with carotid stenosis. Stenoses in patients with ipsilateral stroke/transient ischemic attack within previous 4 weeks or acute ischemic lesion on diffusion-weighted MRI were evaluated as symptomatic. Stenoses with progression of >10% since last DUS examination were evaluated as progressive. Echolucent part of atherosclerotic plaque >8 mm2 on DUS and hyperintensity on 3DT1w-MRI were evaluated as IPH. Differences in IPH occurrence between ASS, APS and SS patients were statistically evaluated.

Results: Totally 32 patients (18 males, mean age 71.3±7.7 years) were enrolled during 18 months; 5 patients with ASS, 18 with APS and 9 with SS. MRI examination was not performed in 3 ASS and 1 SS patient. IPH was detected using DUS/MRI in 1 (20%)/2 (40%) of ASS patients, 9 (50%)/8 (53%) of APS patients, and 5 (56%)/4 (50%) of SS patients (p>0.05 in all cases). IPH on both DUS and MRI were detected in none of ASS patients, 5 (28%) APS patients and 3 (33%) SS patients (p>0.05 in all cases).

Conclusion: No significant difference in IPH occurrence was found between ASS, APS and SS patients. Totally 200 patients will be enrolled to the ongoing study.

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Disclosure: Supported by grants MHCR 17-31016A, 16-30965A.

Child neurology/developmental neurology

EPO2013

X-linked Adrenoleukodystrophy: a metabolic disorder in young male psychiatric patients

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Background and aims: X-linked adrenoleukodystrophy (XALD) is a rare disorder of peroxisomal fatty acid beta-oxidation which leads to the accumulation of very-long-chain fatty acids (VLCFA) in body tissues, and is caused by mutations in ABCD1 gene. Clinical picture results from the affection of central nervous system, adrenal cortex, and testicular Leydig cells, while the onset may be in childhood, adolescence, or adulthood. Unlike the childhood-onset XALD which is mainly a rapidly progressive neurologic disorder, the adult-onset forms have variable initial manifestations. We describe a case of adult-onset XALD which remained undiagnosed for almost a decade as presented with pure psychiatric features years prior to the appearance of the neurologic symptoms.

Methods: A male patient was diagnosed with schizoaffective disorder at 23 years of age. No other symptoms existed at the time and no neurologic work-up was performed. A slowly progressive limb weakness and instability appeared eight years later, thus prompting extensive neurologic, radiologic, metabolic, and genetic investigations.

Results: Neurologic assessment revealed bilateral pyramidal and cerebellar signs. No endocrine dysfunction was found. Specific white matter lesions were seen on magnetic resonance imaging of the brain, which, along with the finding of elevated serum VLCFA values and the confirmation of a known mutation in ABCD1 gene, proved the diagnosis of XALD in the patient.

Conclusion: Adult-onset XALD may persist as a psychiatric illness long before the onset of the other XALD-related symptoms. Therefore, early screening for XALD in young male psychiatric patients helps in reducing the diagnostic errors, enables proper genetic counselling and timely therapeutic decisions.

Disclosure: Nothing to disclose

EPO2015

Acute Necrotizing Encephalopathy: applying the diagnostic criteria to two cases
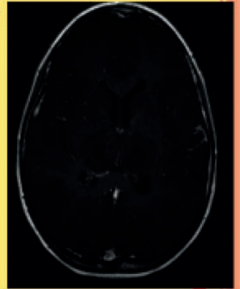
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Background and aims: Acute necrotizing encephalopathy (ANE) is a rare para-infectious inflammatory process that causes rapid coma in previousy healthy children following viral illness. The hallmark radiographic feature is bilateral restricted diffusion of the deep gray matter with punctate hemorrhage. The pathogenesis is thought to be cytokine mediated breakdown of the blood brain barrier. Early and aggressive immunotherapy is the treatment of choice; however, treatment may be delayed in cases where the diagnosis is not clear. In this paper, I apply the diagnostic criteria established by Mizuguchi et al (1995) for ANE to elucidate pitfalls in diagnosis and treatment.

ACUTE NECROTIZING ENCEPHALOPATHY

Diagnostic criteria for ANE
- 1) acute encephalopathy preceded by viral febrile disease with rapid deterioration in the level of consciousness
- 2) increased CSF protein without pleocytosis
- 3) MRI with symmetric, multifocal brain lesions involving bilateral thalami, cerebral periventricular white matter, internal capsule, putamen, upper brain stem, tegmentum and cerebellar medulla
- 4) elevation of serum aminotransferase level to a variable degree without hyperammonemia
- 5) exclusion of other resembling diseases

Mizuguchi diagnostic criteria

Methods: Two patients with influenza and radiographic findings consistent with ANE presented to Vanderbilt Children's Hospital in 12/2017. The Mizuguchi diagnostic criteria were applied and the cases shared all 4 criteria, although one patient was ultimately found to have a straight sinus thrombosis and ANE was ruled out as it is a diagnosis of exclusion.
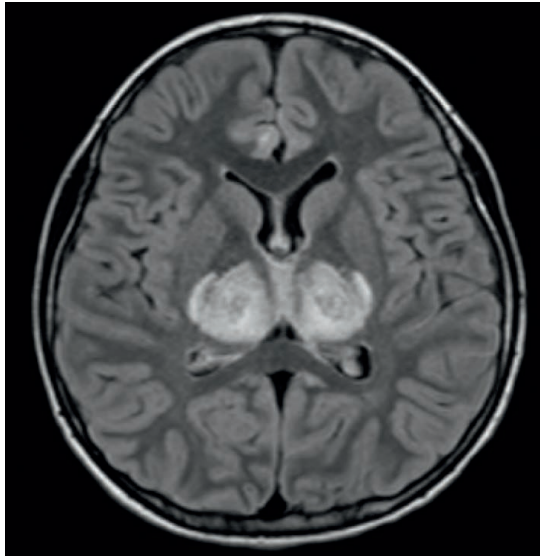
Patient one axial flair MRI
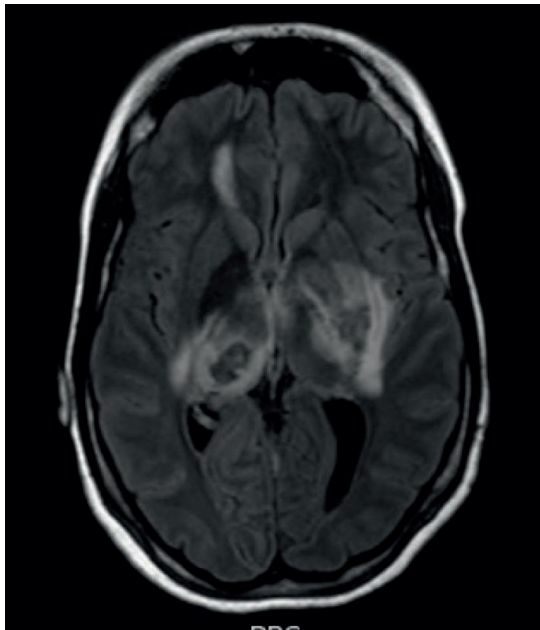
Patient two axial flair MRI

Results: Patient one was treated with high dose steroids, PLEX and IVIG, and is now walking, talking and feeding herself. Patient two was treated for her venous sinus thrombosis and continues to have significant deficits, most notably bilateral CN VI palsies.

Conclusion: The Mizuguchi criteria help clinicians move quickly to life saving immunotherapy where delay in treatment can be the difference between life and death. It is important to exclude other resembling diseases, specifically venous sinus thrombosis, as this can be a mimicker of this rare disease.

Disclosure: Nothing to disclose

EPO2016

Spinal cord lesion in a 5-year-old girl with LHON G3460A mtDNA mutation

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Background and aims: Leber's Hereditary Optic Neuropathy (LHON) is a mitochondrial disease characterized by visual loss consequent to optic nerves atrophy. In some cases, LHON is associated with heterogeneous neurological extra-ocular manifestations, referred as "Leber plus syndrome", and rarely to a multiple sclerosis (MS)-like syndrome. We described a large Italian family with the G3460A mtDNA mutation, six of them presenting with LHON. A 5-year-old girl who carried the mutation was referred to clinical examination for an acute spinal cord lesion, mimicking a spinal cord vascular injury.

Methods: PCR-RFLP and Sanger sequence.

Results: The girl presented in Emergency department after acute back pain, followed by tetraparesis and impaired bladder control. Brain and Spinal cord Magnetic Resonance Imaging (MRI) showed hyperintense signal alterations in T2- weighted sequences and restricted diffusion in Diffusion Weightened Imaging (DWI) sequences in the anterior portion of spinal cord from C6 to D2, suggesting anterior spinal artery territory involvement, but inflammation could not be excluded. Angio-Computed Tomography (CT) was normal. Autoimmunity and thrombofilia screening yielded negative findings. Anti-AQP4 and anti-MOG resulted negative. An ecocardiography assessed normal heart and aorta features. A control spinal cord MRI together with 31Phosphorus- Spectroscopy was performed 10 days later, showing the complete regression of alterations and no abnormal metabolites.
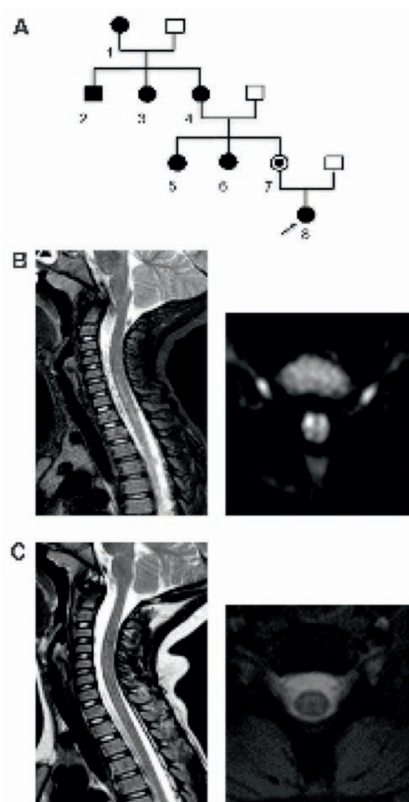
Fig.1

Conclusion: Aspirin was introduced at low doses, and high dose Methilprednisolone and Idebenone were administered. A mechanism of energetic dysfunction similar to stroke-like cannot be excluded. Our case reports a novel infantile clinical manifestation associated to G3460A mtDNA mutation, broadening the clinical spectrum of this disease.

Disclosure: Nothing to disclose

EPO2017

Symptomatic Brain Telangiectasias in Ataxia-Telangiectasia: from brain MRI to the anatomopathological findings

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Background and aims: Ataxia telangiectasia (AT) is an autosomal recessive genetic disease caused by mutations in the ATM gene. It is a multisystemic disorder characterized by progressive cerebellar ataxia, conjunctival and dermal telangiectasias, immunodeficiency with recurrent sinopulmonary infections and predisposition to malignancies. Some of the patients that survive till adulthood present MRI brain lesions, of unknown nature, but proposed to be telangiectasias. We present a case where autopsy findings were indeed consistent with brain telangiectasias. Furthermore, this is the first reported case where these lesions were symptomatic.

Results: A 31-year-old woman with classical AT phenotype was admitted for a 1-week history of headache suggestive of intracranial hypertension. Brain MRI revealed multiple nodular enhancing lesions with extensive oedema causing a 7mm midline shift. A malignancy was suspected and brain biopsy was scheduled. However, after some days of clinical stability, the patient quickly deteriorated. She became progressively stuporous with signs of brainstem compression and eventually died. The autopsy revealed that the nodular lesions were cerebral telangiectasias.

Conclusion: Recent reports that include adult patients with AT revealed the presence of nodular lesions in brain MRI. It is proposed that they are brain telangiectasias associated with microbleeds, gliosis and oedema. The anatomopathological study of our patient confirms that these are indeed brain telangiectasias. Moreover, to our knowledge, there are no reported cases where brain telangiectasias were responsible for intracranial hypertension. In adult AT patients the differential diagnosis of brain space-occupying lesions should not only include malignancies and infectious complications, but also brain telangiectasias.

Disclosure: Nothing to disclose

EPO2020

Proposed practical recommendations of stress management for headaches in children and adolescents

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Background and aims: Stress is considered to be the most common factor reported to trigger headaches in children and adolescents. Although tension-type headache and migraine are the two most common types of headache in children and adolescents, they are often untreated, ignoring their stressful background. Since stress-induced alterations of the stress system are involved in the onset and maintenance of headaches, we suggested that practical stress management could be used for prevention and therapy of stress effects of childhood and adolescence.

Methods: We conducted a systematic literature review from 1989 to December 2017 in databases: MEDLINE, EMBASE, Scopus, and Web of Science. Supplementary citations were recognized through the references of relevant articles. All English-language studies were evaluated for for health-care professionals involved in stress-related headache management and health promotion programs.

Results: 17 of 52 studies were included; 8 randomized-controlled trials, 6 non controlled and 1 prospective (total of 767 patients). An integrative plan is delivered through lifestyle improvement and biopsychosocial modifying stress response techniques. Healthy dietary choices, sleep hygiene, and regular exercise, although limited, are effective for young sufferers. Biopsychosocial therapies such as relaxation, biofeedback, hypnosis, yoga, cognitive behavioral therapy, and acupuncture focus at stress physiological and behavioral relief.

Conclusion: Stress management techniques are effective to moderate the effects of stressors and reduce distress, by normalizing stress responses the sensitive stages of childhood and adolescence. We suggest a stress-related headache management to empower children to make healthy choices in order to improve their lifelong well-being and quality of life

Disclosure: Nothing to disclose

Clinical neurophysiology

EPO2021

Evaluation of motor impulsivity in Huntington Disease with a choice reaction time task and brain metabolic (PET 18FDG) imaging

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PET 18FDG in HD : 5 hypometabolic clusters (bilateral striata, bilateral frontal medial cortex, right inferior parietal cortex and right temporal lateral cortex)

Disclosure: Nothing to disclose

Background and aims: Impulsivity is an early behavioral change in Huntington disease (HD), experimentally described as an urge to act/react and/or as the impossibility to stop and correct this impulse. Our aim was to determinate which component of impulsivity was early affected in HD.

Methods: 11 symptomatic genetically proved HD patients (5≤motor UHDRS≤ 35) and 17 controls performed a choice reaction time task (Simon Task) with electromyographic (EMG) recordings of bilateral muscle agonists. Common behavioral measures of performance and "EMG-augmented" data were analyzed, in particular those reflecting expression and suppression of subthreshold muscle impulses. Assessment of cognitive functions, impulsive behavior (UPPS scale) and a brain PET-TDM 18FDG at rest were also performed.

Results: While HD patients had a higher impulsivity score in the UPPS scale (p<005), they didn't make more errors or partial errors (subthreshold of wrong muscle impulses) than controls (p=018). Correction rate was similar in both groups (p=064). Partial errors latency was similar in both groups (p=016) but correction time was significantly longer in HD patients (p<001). This correction time was significantly correlated with the TMTB time score (p<0001) and inversely correlated with the Mattis (p<0001) and Stroop test (p<001) performances. Striatal metabolism was inversely correlated with the correction time (p<005) and with Stroop (p<005) and TMTB time (p<005) performances.

Conclusion: A dissociation between motor impulsivity and impulsive personality (UPPS scale) seems to exist because the former may more likely be linked to an executive motor control dysfunction than a complex personality disorder. Besides, psychotropic treatments may interact with the task.
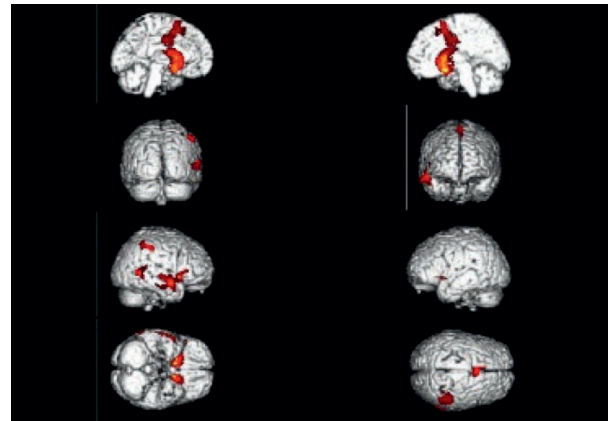
EPO2022

Fatigue is associated with impaired intracortical inhibition in patients with progressive multiple sclerosis: a transcranial magnetic stimulation study

S. Gelibter, M. Pisa, M. Fichera, A. Giordano, R. Chieffo, M. Congiu, V. Martinelli, M. Comola, G. Comi, L. Leocani

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Background and aims: Fatigue is one of the most reported symptoms in people with multiple sclerosis (MS), affecting up to 75% of patients. In relapsing patients, fatigue has been associated to imbalance between intracortical motor excitatory and inhibitory circuits, with conflicting results. We aimed at testing this hypothesis in patients with progressive MS (PMS), compared to healthy controls (HC), using double-pulse transcranial magnetic stimulation (TMS).

Methods: We enrolled 45 patients (F=22 age=49.24±7.41, median EDSS=6.0, range=4.0-6.5) with PMS. Patients were divided into 3 groups according to Fatigue Severity Scale (FSS) score: no-fatigue (MS-NF;FSS≤4.0), borderline-fatigue (MS-bF;4.0<FSS<5.0) or fatigue (MS-F;FSS≥5.0). Short-interval-intracortical-inhibition (SICI) (interstimulus interval, ISI 1, 3ms) and facilitation (ICF, ISI 10, 15ms) to TMS was tested in patients and in 9 aged-matched HC (F=6 age=51.6±4.34).

Results: Groups did not significantly differ in age, EDSS, motor evoked potentials, walking performance and symptomatic treatment. Significant difference in best inhibition at SICI was found among groups (Kruskal-Wallis, p=0.017), in particular between HC vs MS-bF and vs MS-F (Mann-Whitney p=0.01, p=0.039) and between MS-NF vs MS-bF and vs MS-F (p=0.021, p=0.049). No significance was found between HC vs MS-NF and MS-bF vs MS-F. No significant difference was found at ICF.

Conclusion: In progressive MS, fatigue might be associated with impaired GABAergic intracortical circuits in primary motor cortex, with relative preservation of excitatory activity. Even if this mechanism might not be causative, these data, consistent with findings in relapsing MS, shed more light about the pathogenesis of fatigue in progressive MS.

Disclosure: M. Pisa, S. Gelibter, M. Fichera, A. Giordano, R. Chieffo, M Congiu, M. Comola have nothing to disclose. G. Comi has recieved compensation for consulting services and / or speaking activities from Novartis, Teva, Sanofi, Genzyme, Merck, Biogen, Roche, Almirall, Celgene, Forward Pharma L. Leocani has received compensation for consulting services and/or speaking activities from Novartis, Merck, Biogen, Roche, Almirall. V. Martinelli received honoraria for consulting services or speaking activities from Biogen, Merck KGaA, Bayer, Teva, Novartis, and Genzyme. Part of this work was supported by FISM, Fondazione italiana Sclerosi Multipla-Via Operai, 40-16149 Genova

EPO2023

withdrawn

EPO2024

Posterior auricular muscle response: observations in brainstem lesions

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Background and aims: Posterior auricular muscle response (PAMR) is a myogenic potential recorded over posterior auricular muscle (PAM) after auditory stimulation. Its circuit is formed by cochlear and facial nerves with the generator in the brainstem. Here, we investigated whether addition of posterior auricular muscle response (PAMR) examination would add an additional use in determining or localizing isolated brainstem lesions since the importance of blink reflex (BR) in determining or localizing brainstem lesions is known. Our hypothesis was that examination of both reflexes would increase the clinical utility.

Methods: We included 34 patients with isolated brainstem lesions (multiple sclerosis, ischemic stroke and cerebellopontine angle schwannoma) and 41 healthy subjects. PAMRs were recorded over posterior auricular muscle (PAM) after auditory stimulation. BR was elicited by the electrical stimulation of the supraorbital nerve.

Results: PAMR was present in 82.9% of healthy subjects whereas presence was quite low in the patient group (38.2%, p=0.001). Mean latency of PAMR was delayed in patients compared to healthy subjects (p=0.001). BR was obtained in all healthy subjects whereas prolonged latencies or absence of BR was observed in the patient group. There were no differences according to the different etiologies or localization.

Table 1. Demographical and clinical features of patients and healthy subjects.

	Patients n=34	Healthy subjects n=41	p	Stroke patients n=14	MS patients n=18	Tumor patients n=2
Age, y	44.3±17.4	43.5±12.1	0.808	59.3±13.9	32.2±8.6	55.0±22.6
Gender, M/F	19/15	15/26	0.095	5/9	8/10	0/2
MR localization, n (%)						
Mesencephalon	0 (0)	-	-	0 (0)	0	0
Pons	20 (58.8)			10 (71.4)	10 (55.5)	0
Bulbus	7 (20.6)			2 (14.3)	5 (27.8)	0
Pons-bulbus	5 (14.7)			2 (14.3)	3 (16.7)	0
Cerebellopontine angle	2 (5.9)			0 (0)	0 (0)	2 (100)

MS, multiple sclerosis; M, male; F, female

Demographical and clinical features of patients and healthy subjects.

Table 2. Blink reflex and PAMR parameters in patients and healthy subjects.

	Patient group n=34	Healthy subjects n=41	p
R/R1 latency	11.6	10.1	0.000
L/R1 latency	11.4	10.1	0.010
R/R2 latency	37.5	32.7	0.001
L/R2 latency	38.5	32.5	0.000
R/R2C latency	39.3	33.1	0.000
L/R2C latency	39.7	32.9	0.000
R/PAMR latency	11.5	9.3	0.001
L/PAMR latency	11.4	9.3	0.001
R1 abnormality n (%)	14 (41.2)	0 (0)	0.000
Asymmetrical/long	9 (26.5)		
Absent bilaterally	1 (2.9)		
Absent unilaterally	2 (5.9)		
Long bilaterally	2 (5.9)		
R2 abnormality n (%)	11 (32.3)	0 (0)	0.001
Asymmetrical/long	6 (17.6)		
Absent bilaterally	0 (0)		
Absent unilaterally	1 (2.9)		
Long bilaterally	4 (11.8)		
R2C abnormality n (%)	13 (38.2)	0 (0)	0.000
Asymmetrical/long	4 (11.8)		
Absent bilaterally	0 (0)		
Absent unilaterally	3 (8.8)		
Long bilaterally	6 (17.6)		
PAMR			
Normal	13 (38.2)	34 (82.9)	0.001
Absent bilaterally	11 (32.4)	5 (12.2)	
Absent unilaterally	7 (20.6)	2 (4.9)	
Long bilaterally	3 (8.8)	0 (0)	

Blink reflex and PAMR parameters in patients and healthy subjects.

Conclusion: Although presence of PAMR is quite high, its absence does not always indicate a pathology. But prolonged latencies almost always suggest an involvement of PAMR pathway. Likewise, absent PAMR with an abnormal BR provides information for the involvement of brainstem facial nucleus or proximal part of the facial nerve.

Disclosure: Nothing to disclose

Table 3. Blink reflex and PAMR parameters in patient subgroups according to different etiologies.

	CPA Tm n=2	Stroke n=14	MS n=18	p
R1 abnormality n (%)				0.599
Normal	2 (100)	9 (64.3)	9 (50.0)	
Asymmetrical long	-	4 (28.6)	5 (27.8)	
Bilateral absent	-	1 (7.1)	-	
Unilateral absent	-	-	2 (11.1)	
Bilateral prolonged	-	-	2 (11.1)	
R2 abnormality n (%)				0.889
Normal	2 (100)	10 (71.4)	11 (61.1)	
Asymmetrical long	-	2 (14.3)	4 (22.2)	
Bilateral absent	-	-	-	
Unilateral absent	-	-	1 (5.6)	
Bilateral prolonged	-	2 (14.3)	2 (11.1)	
R2C abnormality n (%)				0.650
Normal	1 (50.0)	9 (64.3)	11 (61.1)	
Asymmetrical long	1 (50.0)	2 (14.3)	1 (5.6)	
Bilateral absent	-	-	-	
Unilateral absent	-	1 (7.1)	2 (11.1)	
Bilateral prolonged	-	2 (14.3)	4 (22.2)	
PAMR abnormality n (%)				0.948
Normal	1 (50.0)	5 (35.7)	7 (38.9)	
Asymmetrical long	-	-	-	
Bilateral absent	1 (50.0)	4 (28.6)	6 (33.3)	
Unilateral absent	-	3 (21.4)	4 (22.2)	
Bilateral prolonged	-	2 (14.3)	1 (5.6)	

CPA, cerebellopontine angle; MS, multiple sclerosis

Blink reflex and PAMR parameters in patient subgroups according to different etiologies.

EPO2025

Exploring the neurophysiological basis of balance impairment in multiple sclerosis patients

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Background and aims: Balance impairment is very common in multiple sclerosis (MS), and it has a deep impact on quality of life. However, the causes of MS-related unbalance remain unclear. Some authors hypothesized that the main mechanism is a dysfunction in the lower limbs sensorimotor control. Aim of the present study is to evaluate, by evoked potentials (EP), the contribution of motor and somatosensory pathways on balance performance in MS patients.

Methods: Patients underwent brain and spine MRI and clinical evaluation. Balance was assessed by Tinetti Scale (TS). Disease severity was measured by EDSS. The functionality of central somatosensory and motor pathways was tested by somatosensory EP (SEP) and motor EP (MEP), respectively. OLS regression with robust standard errors of TS on EP was employed, controlling for gender, age, MS type, EDSS, and spine MRI findings.

Results: 40 patients were included. 19 patients (47.5%) had balance impairment. SEP were abnormal in 18 patients (45%). MEP were abnormal in 14 patients (35%). 27 patients (67.5%) had spinal cord lesions.

Linear regression model revealed negative significant correlations between TS and EDSS ($p<0.01$) and between TS and central conduction time at SEP ($p<0.05$). No significant correlation was found between TS and spine MRI findings, and between TS and MEP.

Table 1

OLS Regression of Tinetti Scale

Model	N = 40	F(7,32) = 8.00	P > F = 0.000	R^2 = 0.669
Variable	**Coefficient**	**Standard Error**	**t stat**	**p value**
Gender (M=1)	0.9403	0.6427	1.46	0.153
Age	-0.0406	0.0319	-1.27	0.212
MS Type (RR=1)	0.9469	0.6151	1.54	0.134
EDSS	-0.8728	0.2116	-4.12	0.000
Spinal MRI (Y=1)	-1.2751	0.747	-1.71	0.097
MEP	-0.1345	0.0992	-1.36	0.185
SEP	-0.1788	0.0807	-2.22	0.034
Constant	23.175	1.5575	14.88	0.000

Conclusion: In MS, balance impairment is related to a dysfunction of lower limbs somatosensory ascending pathways conveying proprioceptive and somatosensory information. More in general, EP are useful in the study of pathophysiology of unbalance and seem to be more sensitive than MRI in assessing sensorimotor pathways functionality.
Disclosure: Nothing to disclose

EPO2027

The relationship between callosal transfer and anxiety in multiple sclerosis: A transcranial magnetic stimulation study

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Background and aims: Among the frequently encountered symptoms in multiple sclerosis (MS) stand anxiety and depression. They could occur at any time during the disease course and can severely compromise the patients' functioning. Nevertheless, no single study has addressed the neurophysiological underpinnings of these symptoms.

Methods: Fifty consecutive MS patients aged between 18 and 75 years participated in the study protocol. Patients were excluded if they were on any pharmacological intervention that could affect cortical excitability measures. Anxiety and depression were assessed by means of the Hospital Anxiety and Depression Scale (HADS). Cortical excitability measures were recorded using transcranial magnetic stimulation (TMS) and included resting motor threshold, motor evoked potentials, contralateral silent period, interhemispheric inhibition, short-interval intracortical inhibition and facilitation at different interstimuli intervals, as previously described. Correlation analysis was employed to assess the relationship between HADS scores and TMS variables.

Results: Patients had a mean age of 51.82 ± 12.72 years and a mean physical disability score of 5.52 ± 1.64. Their depression scores ranged from 0 to 14 (mean±SD: 6.08 ± 3.66) and their anxiety scores ranged from 1 to 15 (mean±SD: 5.82 ± 3.42). A significant direct correlation was found between anxiety scores and interhemispheric inhibition ($r=0.43$, $p=0.003$).

Conclusion: The results of the current work highlight the relationship between anxiety and callosal transfer and are consistent with those obtained in a previous study. Compared to MS patients with low anxiety scores, those with higher scores seem to exhibit a relatively more efficient callosal transfer, a finding that merits further assessment.

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Epilepsy 2

EPO1036

Seizure-free 6 months follow-up after surgical treatment in a Lennox-Gastaut syndrome patient: a case report.

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Background and aims: We report the case of a 7-year old that developed different type of seizures (atypical absences, epileptic "spasms", tonic and clonic seizures) together with a cognitive decline. Before age of 5, she had an unremarkable history. EEGs showed multifocal interictal abnormalities (predominant in right fronto-temporal region), as well as bilateral slow sharp-and-waves and paroxysmal fast rhythms. Electro-clinical features were consistent with a Lennox-Gastaut syndrome (LGS).
Methods: Brain-MRI, cerebrospinal fluid, metabolic and genetic analyses didn't show any abnormalities. PET-FDG showed a hypo-metabolism of left temporal and right superior-frontal regions. 3D-FLAIR brain-MRI allowed identification of a right fronto-polar dysplasia. Patient was refractory to several anti-epileptic drug treatments and ketogenic diet. Intracranial monitoring confirmed pluri-focal right frontal seizures. Therefore, a right fronto-polar disconnection surgery was realized.
Results: At 6-month follow-up, patient was seizure free and cognitive improvement was noted as well.
Conclusion: LGS is an age-related epileptic encephalopathy that may be cryptogenic or symptomatic, the latter having a worse prognosis. Resective surgery can have encouraging results, especially when seizure onset zone is confounded to one lobe or a limited area in the brain. With respect to cognitive function, the younger the patient at surgery or the shorter the interval between seizure onset and surgery, the better the cognitive outcome. We report here a case of medically refractory LGS with a complete remission after surgical treatment. This case highlights the importance of surgery for symptomatic LGS.
Disclosure: Nothing to disclose

EPO2029

Esclicarbazepin in the treatment of patients with refractory and super-refractory status epilepticus

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Background and aims: Refractory status epilepticus (SE) is a life-threatening condition with limited therapeutic options. New antiepileptic drugs should be investigated in refractory SE in order to improve treatment of this condition. Eslicarbazepine (ESL) is a new sodium channel blocker, which efficacy have not yet been investigated in refractory SE. Our aim was to analyze data on treatment of SE with ESL.
Methods: In terms of the Mainz Epilepsy Registry (MAINZ-EPIREG) we analyzed data on the efficacy and safety of ESL in treatment of refractory and super-refractory SE.
Results: Five patients with refractory or super-refractory SE have been treated with ESL. The mean age of patients was 62 ± 7 years. The median number of antiepileptic drugs administered prior to initiation of ESL was 4. The mean duration of SE prior to initiation of ESL was 2 days. Initial dose of ESL was 800mg, titrated to a daily dose of 1200 to 1600mg. SE was resolved in 2 of 5 patients (40%) within 36 hours after initiation of ESL. No serious adverse effects have been recorded.
Conclusion: According to our data, ESL may prove useful in the treatment of SE. Farther trials are encouraged to investigated ESL in larger populations of patients with SE.
Disclosure: Nothing to disclose

EPO2030

Gamma oscillation in EEG recordings in patients with epilepsy.

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Background and aims: Gamma waves in the EEG record include frequencies between 30 and 100 Hz. Due to the increasing possibilities of registration by computerized EEG apparatus, more research on the significance of gamma waves in various physiological and disease states has appeared, and one of the more promising discoveries was the statement that the seizure discharges present in patients with epilepsy may be preceded by increased oscillations of EEG activities with a gamma frequency. The aim of our study was to record gamma oscillations in EEG records in epileptic patients and to evaluate their clinical relevance for better monitoring of patients' treatment.

Methods: The research material consisted of 10 EEG records of epilepsy patients and 10 patients with no CNS findings. The research was done in our diagnostic EEG laboratory with EEG apparatus EBNeuro (32-channel). The EEG EBNeuro Neurotravel is equipped with the company's EEG Galileo .NET software. We also used our own application for EEG analysis and evoked potentials averaging, written in C ++ (fig.1).
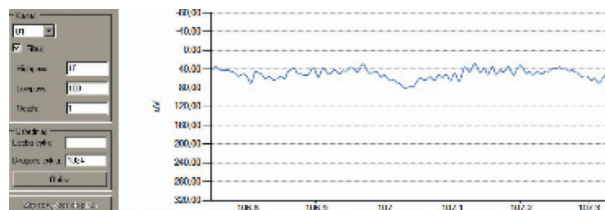
Fig.1. A fragment of the EEG curve of a 14-year-old woman suffering from epilepsy. We used our own C ++ application to analyze the curve; oscillation of gamma waves in the O1 lead (left occipital region).

Results: We found that gamma oscillations are present in EEG recordings of patients with epilepsy in contrast to healthy individuals. They are often accompanied by interictal discharges in the EEG record and may precede them.
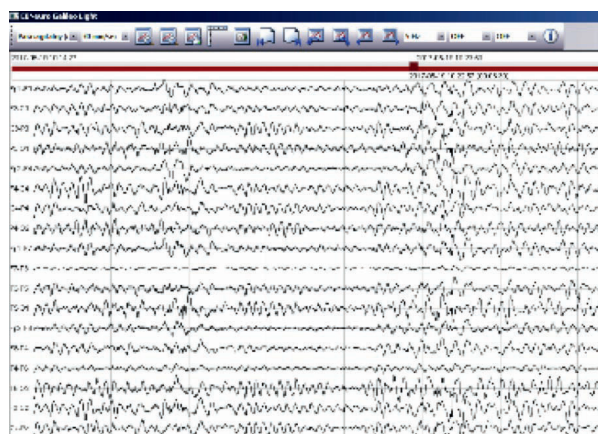
Fig.2. A fragment of the EEG record of a 23-year-old woman suffering from epilepsy. The record made during the treatment shows generalized discharges of a series of high-voltage free waves theta 3.5-6Hz and spike-and wave discharges against the background of regular alpha with a frequency of about 9-10Hz.
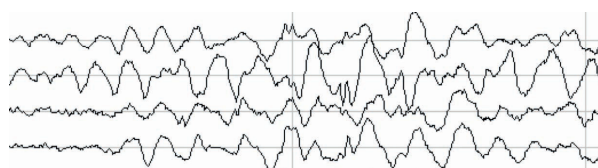
Fig.3. Fragment of the EEG curve of the patient, which is shown in Fig. 2. Gamma oscillations accompanying epileptic discharges.

Conclusion: Gamma oscillations are more frequent in EEG recordings in patients with epilepsy in comparison with the records of healthy people. They are often accompanied by interictal discharges in the EEG and can precede them. Registration of gamma oscillations requires increasing the routine frequency of EEG signal sampling and effective elimination of artefacts.

Disclosure: Nothing to disclose

EPO2031

Screening tools for depression and adverse events in epilepsy-experiences from clinical practice

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Background and aims: Depression is the most frequent comorbidity in people with epilepsy (PwE). Adverse events (AE) of antiepileptic drugs (AEDs) are frequent as well, particularly with add-on AEDs. Aim of the present study was to identify PwE suffering from depression and AE of AED and to evaluate its impact on quality of live (QoL).

Methods: All patients attending the local epilepsy outpatient clinic were asked to fill a questionnaire. This included LAEP, NDDI-E, ET5, EQ-VAS and questions regarding current seizure frequency. Questionnaires filled between October 2015 and December 2016 were included. An inclusion criterion was diagnosis of epilepsy. In case of multiple attendances, the first filled questionnaire was included only.

Results: 509 questionnaires were included. 20.4% showed significant AEs (LEAP>44), increasing with the number of AEDs. Negative correlation on LAEP was found for Lacosamide, Gabapentin and Perampanel. Screening for depression was positive for 18.3% in ET (cut-off >15) and 15.3% in NDDI-E (cut off >13). 11.2% had a clinical diagnosis of depression and a further 12.2% another psychiatric co-morbidity. 20.6% were on regular psychiatric medication. QoL correlated with seizure freedom but not with seizure frequency. Almost 30% of the variance of QoL depended on depression, AEs of AED and seizure freedom in the last year.

Conclusion: QoL in PwE depends on seizure control but also on comorbidity of depression and AEs of AEDs. Screening tools help to identify PwE with comorbidity, which might respond well to treatment, and with AEs, which might require a change in AEDs.

Disclosure: Nothing to disclose

EPO2032

The effects of periodic discharges on the prognosis of patients with status epilepticus

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Background and aims: It is important to predict prognosis of status epilepticus (SE). The aim of this study was to assess the prognostic significance of PDs on the functional outcome of patients with SE and the occurrence of refractory status epilepticus (RSE).

Methods: The author analyzed the clinical history, neuroimaging data, routine EEG and continuous video-EEG monitoring records of consecutive patients with SE. We selected patients with PDs in EEG records which included more than 50% of epochs that were composed of more than 50% seconds with PDs. We excluded patients with anoxic brain damage, SE with simple partial seizures, absence SE or incomplete medical records. Functional outcome at the time of hospital discharge was assessed by Modified Rankin Scale (MRS).

Results: Among 86 consecutive patients with SE, fourteen patients were excluded. In 72 patients with SE, 31 had PDs in EEG. Thirty eight out of 72 had good functional outcome (MRS 0-3) and 34 had bad functional outcome (MRS 4-6). The presence of PDs (p=0.033, odd ratio 3.651, 95% CI 1.107-12.040) and stuporous or comatose mentality at presentation (p=0.044, odd ratio 3.351, 95% CI 1.036-10.840) were independent risk factors for bad functional outcome in multivariate analysis. The occurrence of RSE was significantly higher in patients with PDs (p=0.001, odd ratio 11.059 95% CI 2.788-43.872).

Conclusion: PDs is an independent predictive factor of bad functional outcome and the occurrence of RSE, so patients with SE and PDs should be given early and rigorous management.

Disclosure: Nothing to disclose

EPO2033

Temporal lobe epilepsy with amigdala enlargement.

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Background and aims: Temporal epilepsy with amygdala enlargement (TE-AE) is a distinct electroclinical entity that is becoming increasingly recognized. Focal cortical dysplasia, low grade tumors, and seizure-related changes have been reported as probable causes. An autoimmune cause, even with negative antibody testing, raises the possibility of immunotherapy in these cases. We report the clinical characteristics and therapeutic response of a series of 18 patients with TE-AE.

Methods: Patients with focal epilepsy and amygdala enlargement after MR visual inspection were included. Volumetric analysis was performed in order to confirm the findings.

Results: We found 18 patients with amygdala enlargement after visual inspection and excluded one after volumetric analysis. Mean age at epilepsy onset was 40.4 years old. Seizures were classified as temporal (10 mesial, 4 lateral), extratemporal (2) and unclassified (1) according to the corresponding semiology. 3 patients had another identifiable cause (100% ipsilateral to AE) and 1 patient's amygdala enlargement proved reversible after removal of a cavernoma. Antibody testing was negative in all 5 patients tested. Neuropsychological testing was performed and found to be abnormal in 6/6 patients. Psychiatric disorders were reported in 6 patients.

Conclusion: TL-AE is an emerging epileptic syndrome with certain identifiable features (late onset, neuropsychological abnormalities, and mood disorders). Amygdala enlargement can be seizure-related and other lesions should be searched for.

Disclosure: Nothing to disclose

EPO2034

Personality Disorders in Temporal Lobe Epilepsy

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Background and aims: Personality Disorder (PD) is defined as a pattern of inflexible and maladaptive personality traits that cause functional disability or subjective suffering. They consist of 10 types, grouped into 3 clusters-A (Schizoid, Schizotypal, Paranoid), B (Borderline, Narcissistic, Histrionic, Antisocial) and C (Dependent, Avoidant and Obsessive Compulsive). People with epilepsy (PWE) are at greater risk of suffering from PP with prevalence's that may reach 75%.
Our aim is to analyze the frequency and type of PD, in a sample of PWE, accompanied at the Reference Center for Refractory Epilepsy of Hospital de Santa Maria (CHLN).

Methods: Retrospective analysis of pre-surgical evaluation of 121 people with refractory epilepsy (RE). The personality assessment was done using the Millon Multiaxial Clinical Inventory-II. A score > 85 was considered for the definition of PP. When scores > 85 were obtained on more than one type of PP it was considered "Not Otherwise Specified" (NOS). The types of PP and their frequency were analyzed according to the location of the epileptogenic zone (temporal vs. extra temporal).

Results: 70% of those with ER had at least one of the PD types. The most frequent types were PD NOS (40; 47%), followed by Obsessive PD (17; 20%) and Dependent PD (14; 16%). No statistically significant differences were found regarding the epileptogenic zone (p=0.297).

Conclusion: In our population, the prevalence of PP in PCE is much higher than that described in the general population. They may be associated to either the psychological or biological factors.

Disclosure: Nothing to disclose

EPO2036

Anti-NMDA receptor encephalitis triggered by epilepsy surgery

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Background and aims: Anti-NMDA receptor (NMDAR) encephalitis is a nosological entity associated with antibodies directed against the glutamatergic NMDAR.
Herpes simplex virus 1 (HSV1) is a common cause of viral encephalitis. It may be reactivated by brain surgery with a latency of many years after the index event. A recently described complication of HSV1-encephalitis is induction of anti-NMDAR-encephalitis.
So far, brain surgery has not been described as a trigger of anti-NMDAR-encephalitis in patients post-HSV1-encephalitis.
Methods: We report on a patient who had suffered from HSV1-encephalitis as a child. 37 years later, anti-NMDAR encephalitis was triggered by epilepsy surgery.
Results: A 40-year-old male patient presented at our hospital for epilepsy surgery. He suffered from drug-resistant frontal lobe epilepsy post-childhood HSV1-encephalitis. Postoperatively, the patient developed semiologically new seizures and focal neurological symptoms. FLAIR-MRI showed progressive bilateral hyperintensities. Cerebrospinal fluid (CSF) analysis revealed slight lymphocytic pleocytosis. HSV1-PCR in the CSF was negative and there was no improvement on virostatic therapy. Serum and CSF NMDAR-antibodies returned positive, and immunosuppressive therapy with rituximab and cyclophosphamide led to significant improvement of the clinical and imaging parameters.
Conclusion: To our knowledge, this is the first published case of anti-NMDAR encephalitis triggered by brain surgery. Two pathomechanisms are feasible:
1) HSV1 encephalitis was triggered by epilepsy surgery with subsequent induction of anti-NMDAR encephalitis.
2) Anti-NMDAR encephalitis was directly induced by brain surgery.
We favor the latter hypothesis and argue that intracellular antigens may have been released by surgical trauma, triggering an autoinflammatory cascade. We discuss the consequences for indicating brain surgery in patients post-HSV1-encephalitis.
Disclosure: Nothing to disclose

EPO2037

Epilepsy treatment gap in Cameroon

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Background and aims: The availability of AEDs differs between high-income countries and low and middle ones. In many Sub-Saharan African countries, like Cameroon, the coverage is very low and limited (carbamazepine, phenytoin, phenobarbital and valproic acid). Despite other AEDs as lamotrigine have been added to the WHO List of Essential Medicines (2017), they are not available in most of these countries yet.
The objective of our study was to increase our knowledge about the management of epilepsy by general healthcare providers (GHP) in Cameroon.
Methods: A four-day training course in neurology was organized for GHP by Spanish neurologists in Cameroon. During the course, we investigated the availability and management of AEDs in the country through a questionnaire.
Results: Of the 42 GHP, 88.1% would use medicines to treat epilepsy. 76.2% knew the existence of only one to three AEDs. Regarding the management: 21.4% reported using haloperidol, 69% carbamazepine, 73.8% valproic acid, 88.1% phenobarbital and 35.7% phenytoin. Most of them (92.9%) would maintain AEDs during pregnancy, considering carbamazepine (38%), valproic acid (33,4%), phenobarbital (38.2%), haloperidol (4,8%) and phenytoin (7.2%) good choices for pregnant women. No mention was made to any other antiepileptic drugs, including lamotrigine.
Conclusion: Most of the GHP use medicines to treat epilepsy, but only a few AEDs are available. These results raise concerns about the lack of procurement and distribution of AEDs in many countries. Further studies inquiring into the hurdles of this reduced access to new generation AEDs are needed.
Disclosure: Nothing to disclose

Infectious diseases; Sleep disorders

EPO2038

The Impact of a Specialist Joint Neurology/Infectious Diseases Outpatient Clinic in Managing HIV-infected patients with Neurological Problems

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Background and aims: A specialist, tertiary Neuroinfectious Diseases (NeuroID) clinic, where patients are seen jointly by a Neurologist and Infectious Diseases physician was set up in 2005 to address neurological problems in patients with infectious diseases. A joint discussion involving investigation, diagnosis and management of patients remains the main approach of this clinic.

Methods: We conducted a retrospective case review of all patients attending the NeuroID clinic between the 1st of January 2011 until the 31st December 2012.

Results: 61 patients were seen in the NeuroID clinic during the dates studied. 40 (66%) of these patients were known to be HIV positive. Patients with HIV infection were on average older had fewer known neurological conditions, compared to those without HIV. Epilepsy, peripheral neuropathy and memory impairment were the most common neurological comorbidities. The majority of patients had good HIV control (89% had an undetectable HIV viral load).

Patients with HIV infection were mostly referred due to undiagnosed neurological symptoms, most commonly neuropathic sounding pain, focal motor symptoms and paraesthesiae. HIV positive patients had on average more investigations (mean of 2.6 compared to 0.9). 83% of HIV positive patients had atleast one new diagnosis made in the NeuroID clinic. Common new diagnoses in HIV positive patients were movement disorders, HIV associated neurocognitive disease and myeloradiculopathy.

Conclusion: At least one new diagnosis was made in the clinic in 83% of HIV-infected patients demonstrating the benefit of a specialised integrated approach in managing HIV-infected patients with neurological disease.

Disclosure: There is no commercial or institutional support to disclose for this research.

EPO2039

Stroke in HIV Patients: 41 cases in the neurology department of Ignace Deen Hospital

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Background and aims: The literature suggests a strong association between Human Immunodeficiency Virus (HIV) and stroke. Although HIV infection is endemic in sub-Saharan Africa, few authors are interested in this association. The aims is to evaluate the frequency of HIV infection during stroke, describe the clinical and paraclinical aspects of this association

Methods: This was a prospective study of the descriptive and analytic type that included for 12 months all subjects admitted to the neurology department of the Conakry University Hospital for a stroke with HIV positive serology (Western Blot confirmed Elisa) and who agreed to participate after counseling. Sociodemographic, clinical, paraclinical and progressive data (National Institutes of Health Stroke Scale(NIHSS) and modified RANKIN scores) were collected for each patient. The statistical significance level was fixed at 0.05.

Results: Forty-one out of 423 (9.69%) had positive HIV serology. In this population, the mean age was 48.56±10 years; the female sex was predominant (Sex ratio=1.3). More than half of the patients had no cardiovascular risk factors. The clinic was superimposable to that found in the general population; however, the fever was constant. Ischemic strokes predominated and the area of the superficial sylvian artery was the most concerned. Stroke occurred at all stages of HIV infection; the prognosis at the acute phase was severe.

Conclusion: the occurrence of stroke in HIV is still underestimated in Africa. It is necessary to systematize retroviral serology (VRS) in patients with stroke.

Disclosure: Nothing to disclose

EPO2040

Interferon via Ommaya reservoir in Subacute sclerosing panencephalitis(SSPE): A success story

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Background and aims: SSPE is a chronic progressive and fatal neurological disorder usually in children due to persistent measles virus infection of CNS characterised by myoclonic jerks, cognitive decline and typical EEG findings.

Our aim was to treat SSPE and assess the efficacy of interferon-alpha injected through intraventricular route via Ommaya reservoir.

Methods: Our prospective study was conducted in Department of Neuromedicine, CNMC between 1.5.16-30.4.17. Twenty (20) children with a probable diagnosis of SSPE as per Dyken's criteria were included and evaluated for H/O measles infection, vaccination, symptoms of cognitive decline and myoclonic jerks and were investigated through CSF study (anti-measles antibody titre), EEG and neuroimaging. All were treated by body weight adjusted doses of Inj. Interferon alpha through intraventricular route for 6 weeks via Ommaya reservoir.

Results: The mean age was 9.4 yrs. M:F ratio was 3:2. 8 had past H/O measles and 4 were vaccinated. 12 were in Jabbour stage III B and 8 in stage III A. All 20 patients had positive measles antibodies in CSF and titres were more than 1:4 in CSF and 1:250 in serum. 16 children had typical periodic discharges in EEG. Following interferon therapy coupled with oral Ribavirin for 1 month after discharge, modest clinical improvement was noted as per Jabbour staging.

Conclusion: Although no curative treatment is available for this degenerative disease, interferon therapy provides ample hope and intraventricular route obviates the need for twice weekly lumbar punctures which is both painful and cumbersome.

Disclosure: Nothing to disclose

EPO2041

First case report of Herpes Simplex Virus Encephalitis During Immunosuppressive Treatment of Autoimmune Hepatitis.

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Background and aims: Herpetic encephalitis (HE) causes high morbidity and lethality. Immunosuppressive therapies have spread during the last decades, and it has been demonstrated that they worsen outcomes in patients with HE. In a review of the literature, we have not found any case of HE associated with the immunosuppressive treatment of Autoimmune Hepatitis (AH). Here, we describe a patient with AH, who developed HE during immunosuppressive treatment, and share our experience in the management of these specific patients.

Methods: We report a case of HE in a patient with AH on azathioprine (AZA) therapy. A literature review was performed with search items including "encephalitis" and "immunosuppression" in the thesaurus of Medline.

Results: We found just one series comparing immunosuppressed patients and immunocompetent ones both with HE, and one case report with HE on AZA in Crohn's disease. Our patient presented with prodromal syndrome and severe focal deficits, which is not consistent with literature. However, absence of CSF pleocytosis and atypical MRI manifestations were. AZA was suspended and acyclovir therapy was completed for 21 days. Liver profile did not worsen and patient considerably improved, remaining at discharge with mild dysarthria and persisting currently with no immunosuppressive therapy and with hepathology follow up.

Conclusion: HE in immunosuppressed patients has particular features. In patients on AZA, this should be discontinued and restarted again if indicated, preferably after completion of HSE therapy. Individualization and consensus between physicians are key features of management. Further investigation is needed to provide stronger recommendations according to subgroups of patients.

Disclosure: Nothing to disclose

EPO2042

Gliomatosis cerebri mimicking PML in an immunocompromised patient.

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Background and aims: Progressive multifocal leukoencephalopathy (PML) is a feared complication in immunosuppressed patients. Indeed PML most frequently develops in a context of HIV, malignancy or medication induced immunosuppression. The diagnosis is made based on clinical and radiological findings and often confirmed by highly specific CSF JC-virus PCR.

Results: We present the case of a 48-year-old man with a medical history of Crohn's disease and multiple preceding immunosuppressive treatments in the past few years (azathioprine, adalimumab, methylprednisolone). After starting a new treatment with infliximab (TNF-alfa blocker) there was a progressive generalized malaise. 4 months later he presented at the emergency department with complaints of headache, transient visual obscurations, urinary urgency, aphasia and mild right hemiparesis. Imaging showed multifocal white matter lesions with a mild mass effect. IV corticosteroid treatment, in suspicion of TNF-A mediated demyelination, was started immediately without significant improvement. Later JC-virus PCR on CSF was positive (560 copies/mL) and a diagnosis of PML was made. As a progressive deterioration was present further examinations showed papilledema and a spinal lesion. A second lumbar puncture could not detect JC virus anymore, a brain biopsy was performed but was inconclusive. 2 months later the patient died and autopsy revealed a diffuse infiltrative astrocytoma WHO grade III.

Conclusion: As a conclusion, we like to emphasize the differential diagnosis of PML and diffuse glioma (gliomatosis cerebri). Intracranial hypertension and spinal lesions are highly atypical of PML and JC-virus PCR specificity is not 100%.

Disclosure: Nothing to disclose

EPO2043

B-amyloid metabolism disregulation in sleep disorder

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Background and aims: Recent studies have demonstrated that sleep disorders are associated with cognitive dysfunctions and nocturnal sleep modifies B-amyloid metabolism.Obstructive Sleep Apnea Syndrome (OSAS) is characterized by repeated episodes of upper airway obstruction during sleep that result in intermittent hypoxemia and arousal. Periodic limb movements in sleep (PLMD) are repetitive, stereotypical involuntary movements of the lower extremities that appear during sleep. These sleep disorders are very frequent, in particular in elderly patient.This study aimed at evaluating CSF B- amyloid metabolism in patients with OSAS and PLMD.

Methods: We enrolled patients affected by OSAS and PLMD compared with controls. Both patients and controls underwent nocturnal polysomnographic monitoring and lumbar puncture to determine CSF levels of amyloid-β1-42, amyloid-β1-40, total (t-)Tau, and phosphorylated (p-)Tau.

Results: We recruited 20 OSAS patients, 12 PLMD and 10 controls. The OSAS group had lower levels of B-Amyloid compared to PLMS subject and controls. Furthermore PLMD patients showed lower levels of B-Amyloid compared to controls. Sleep structure was altered in both group of patient in a similar way.

Conclusion: This report showed alteration of CSF biomarkers in both OSAS and PLMD patients. However, beta-amyloid dynamics were more altered in OSAS group possibly because these patients show
 both alterated sleep structure and intermittent hypoxemia, while PLMS group presents only alteration of sleep architecture.

Disclosure: Nothing to disclose

EPO2044

Transcranial Magnetic Stimulation reveals cognitive impairment in obstructive sleep apnea syndrome

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Background and aims: Patients with obstructive sleep apnea syndrome (OSAS) show neurocognitive impairment, but the exact mechanisms that cause cognitive dysfunctions remain unknown. The cholinergic system is known to play a key role in all attentional processes and cognitive functions. A transcranial magnetic stimulation (TMS) protocol may give direct information about the function of some cholinergic circuits in the human brain; this technique relies on short latency afferent inhibition (SAI) of the motor cortex. The objective of this exploratory study was to test the hypothesis that impaired cognitive performances in OSAS patients are associated with a dysfunction of the cholinergic system, as assessed by SAI.

Methods: We applied SAI technique in a group of 13 patients with OSAS and compared the data with those from a group of 13 age-matched healthy subjects. All the patients underwent a sleep study, an extensive neuropsychological evaluation, and TMS examination.

Results: Mean SAI was significantly reduced in our OSAS patients when compared with controls. The neuropsychological evaluation showed impairments in most cognitive areas in the OSAS patients. SAI values were strongly correlated with the neuropsychological test scores.

Conclusion: These findings suggest that the cognitive deficits in OSAS may be, at least in part, secondary to alterations in cholinergic neurotransmission, presumably caused by nocturnal hypoxemia. TMS studies may shed light on the pathophysiological mechanisms of the cognitive disturbances in OSAS patients.

Disclosure: Nothing to disclose

EPO2045

Delayed diagnosis in narcolepsy

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Background and aims: Sleep disorders are very prevalent in the population. However, narcolepsy is one of the most infrequent, classified as a rare disease. We describe the reasons of the delayed diagnostic of our patients with narcolepsy, attended in the Multidisciplinary Unit of Sleep Disorders of the Infanta Sofía University Hospital in Madrid, Spain.

Methods: Retrospective observational descriptive analysis of 30 patients, diagnosed with narcolepsy, attended in the consultation of Neurology of our center from October 2012 to December 2017. We reviewed the sex, the age of the patients to the diagnosis in specialized consultation, and the beginning of the symptoms, the time of delay of diagnosis, the reasons for consultation, and the patient´s previous information search in Internet or social networks.

Results: 601 patients attended in our consult between 2012 and 2017, 30 have narcolepsy, 17 with cataplexy, 13 without it. 15 Men, 15 women. The delayed diagnostic time from the onset of symptoms was 11.8 years. The main reason for consultation was the labor repercussion. 33.33% of the patients had consulted their symptoms using Internet or social networks.

Conclusion: The main reason for consultation in our series is the labor repercussion, including driving. The diagnosis of 30 patients of the potential 70-90 that we should have (in relation to the population of our health area), despite our experience and interest in this pathology, and that only 33.33% of patients had consulted previously their symptoms using Internet or social networks, suggest the need to make this disease better known to the general population.

Disclosure: Nothing to disclose

EPO2047

Kleine-Levin-Syndrome in Pregnancy: A Case Report

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Background and aims: Kleine-Levin syndrome (KLS) is a rare sleep disorder, predominantly affecting males during adolescence. We report a female patient with recurrent episodes of hypersomnia and a long sleeping episode during pregnancy.

Methods: A 26-years-old female patient is presented with recurrent episodes of hypersomnia, starting at the age of 12, shortly before menarche.

Results: Sleep episodes occurred in a frequency of 2-3/year with varying duration, the longest being 3 weeks in 2008, when the patient presented at our clinic the first time. In addition, altered perception and cognitive dysfunction were present, but no hyperphagia or hypersexuality, fulfilling the criteria of the international classification for sleep disorders. Polysomnography, actigraphy and MSLT showed normal results during asymptomatic phases. Encephalopathy was excluded by laboratory results, normal cMRI and normal hypocretin-1 level in cerebrospinal fluid.

After 2010, the episodes became less frequent and shorter until 2017, when the patient developed hypersomnia lasting from the 8th to the 18th week of pregnancy. Polysomnography showed a sleep duration of >14 hours with normal sleep architecture, 8 sleep cycles. Genetics confirmed HLA positivity for HLA DQB1*0201 with maternal transmission. For 2 weeks the patient was treated with i.v. infusions and s.c. heparin to prevent dehydration and thrombosis. The patient slowly became more vigilant and mobile without using any medication because of pregnancy.

Conclusion: This is the first case of KLS with a dramatic hypersomnia episode during pregnancy. Sleep studies and HLA-results are presented and discussed together with pathophysiology.

Disclosure: Nothing to disclose

Movement disorders 2

EPO2049

Trust the Patient not the Doctor: Health-related Quality of Life in Cervical Dystonia

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Background and aims: Non-motor symptoms are a feature of cervical dystonia and can affect quality-of-life, despite effective therapy with botulinum toxin. It has been postulated, disordered subcortical mechanisms related to the interpretation of salient emotional stimuli might be a factor in their pathogenesis.

Methods: We prospectively collected data on health-related quality-of-life(HrQoL) and anxiety and depression measures in patients with cervical dystonia attending a University Hospital specialist clinic. Cervical Dystonia Impact Profile–58(CDIP-58) assessed HrQoL; mood disorder was assessed via Beck Anxiety Index(BAI-II) and Beck Depression Index(BDI-II); dystonia severity was assessed using the TWSTRS-2 severity-scale and pain-scale

Results: The 38 patients who completed all assessments indicated: 1): HrQoL measured by the CDIP-58 inversely correlated with depression by the BDI(r2=0.39; p< 0.0001), anxiety by BAI-II(r2=0.43; p< 0.0001). 2):HrQoL measured by the CDIP-58 significantly inversely correlated with the TWSTRS Pain scale(r2=0.30; p=0.0004) but not with dystonia severity measured by TWSTRS-2(r2=0.09; p=0.064). 3):The TWSTRS–2Severity-Scale correlated weakly with the BAI(p=0.037), and the CDIP sub scales sleep(r2=0.13; p=0.02), Head & neck (r2=0.24; p=0.002), pain(r2=0.13;p=0.026).

Conclusion: Initial findings from this patient cohort suggest that self-report measures, are a valid measure of the impact of cervical dystonia in everyday life highlighting the importance of psychological symptomatology in . These findings also question the sensitivity and relevance of the measurement of dystonia severity by physicians using the TWSTRS–2 severity-Scale.

Disclosure: Nothing to disclose

EPO2050

Complications and side effects of DBS surgery in patients with Parkinson's disease

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Background and aims: DBS is effective surgical treatments in advanced PD. DBS is a minimally invasive procedure but may be burdened by complications due to the surgical procedure, to the hardware and side effects (SE) during the chronic stimulation. The frequency of complications and SE depends on the experience of an multidisciplinary team and surgical methods of the DBS center.

To study complications and SE of DBS surgery in PD patients in Belarus.

Methods: 48 patients have undergone surgery for PD since 2011. 26 male and 22 female, mean age 55.5±7.4. There are 30 patients–II stage of H&Y, 18–with III-IV. 36 patients with DBS STN, 8–DBS Gpi, 3–DBS Vim, 1–DBS STN LE, Gpi RE.

Results: Complications due to the surgical procedure: pneumocephaly in one patient with transient decrease in strength in the right hand and motor aphasia, in another patient ischemia in the left subthalamic nucleus with hemiballism in the right limbs. Complications due to the hardware: migration of IPG in one patient, lead migration in one patient, IPG infection in two patients, chronic erosion with local infection at the scalp in two patients. SE dysphonia/dysarthria in 5 patients, gait and balance disturbances (freezing) in 8 patients, transient paresthesias in DBS STN patients, weight gain in 38 patients, personality and mood changes in 5 patients.

Conclusion: The incidence of complications and SE of DBS surgery in PD patients in Belarus is comparable with other DBS center with surgical team's experience and methods of operation.

Disclosure: Nothing to disclose

EPO2051

Screening Adults with Neurodegenerative Disorders for Niemann-Pick type C Disease: A retrospective study of a large cohort of a Greek tertiary Academic center

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Background and aims: Niemann–Pick type C (NPC) disease is a rare fatal lysosomal storage disease of autosomal inheritance, resulting from mutations in NPC1 or NPC2 genes. Disease presentation has a broad clinical spectrum, ranging from a neonatal rapidly fatal disorder to an adult onset neurodegenerative disease. Recently, patients aged over 50 years, with the late form of the disease, have been increasingly described, indicating that many patients in this spectrum may remain unrecognized. We retrospectively accessed with the NPC-Suspicion Index (NPC-SI) adults with neurodegenerative diseases for further biochemical evaluation for NPC.

Methods: We conducted a chart review of symptom presentation in 1000 patients during the period of 2012-2017. Of those 117 'suspected NP-C' cases, plasma oxysterols (OxTs) and chitotriosidase (ChT) levels were determined. Lyso-SM-509 was additionally measured in six patients, and one patient, with the highest OxT and ChT levels, was genetically tested.

Results: Out of 1000 patients, 72.6% were classified as low, 21% as moderate and 6.4% as high likelihood in the NPC–SI. Eight patients presented with elevated OxT, and 10 with increased ChT levels. Lyso-SM-509 and genetic testing were negative.

Conclusion: NP-C in adults may be extremely rare in Greece. The NPC–SI is more sensitive than specific, since other more common neurodegenerative disorders presented with gaze palsy abnormalities and/or an ataxia syndrome, scoring high in the NPC –SI, are prevalent. Plasma OxT and ChT are not NP-C specific, while methodological issues, such as cut-off levels, should be considered in order to improve screening specificity.

Disclosure: Nothing to disclose

EPO2052

Sleep disorders and other non-motor symptoms in a cohort of p.A53T alpha-synuclein (SNCA) mutation carriers.

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Background and aims: Parkinson's disease (PD) has a long prodromal phase with non-motor signs which form the pre-clinical phase of the disease. Asymptomatic carriers of the p.A53T mutation in the SNCA gene represent a population at high risk for developing PD. Non-motor symptoms, and in particular sleep disorders, have not been sufficiently assessed in such subjects. Thus, the aim of this study was to evaluate non-motor symptoms in asymptomatic p.A53T carriers and sleep disorders in both asymptomatic and symptomatic carriers.

Methods: Seven asymptomatic p.A53T carriers underwent UPDRS III, Epworth Sleepiness Scale, RBDSQ, UPDRS I, UPDRS Ia, SCOPA-AUT, QUIP, UPSIT, GDS and MOCA. Five of them underwent DAT Scan and four polysomnography (PSG). We have also assessed eight symptomatic carriers with PSG, Epworth Sleepiness Scale, RBDSQ and MOCA.

Results: DAT Scan was normal in all 5 asymptomatic carriers tested. Cognition and olfactory function were within normal limits, except for one case of relatively advanced age with a marginal MOCA and a very low UPSIT score. All seven asymptomatic subjects reported anxiety, four reported bowel and urinary dysfunction, and five mild depression. As far as sleep disorders are concerned, six out of eight symptomatic and only one asymptomatic carrier, treated with antidepressants, had polysomnographic evidence of REM Sleep Behavior Disorder (RBD) or REM Sleep without Atonia (RWA).

Conclusion: Certain non-motor symptoms may antedate nigrostriatal dopaminergic degeneration in p.A53T SNCA-related Parkinsonism. RWA or frank RBD seem not to precede motor symptoms, but to manifest in the majority of symptomatic carriers who already have motor dysfunction.

Disclosure: Nothing to disclose

EPO2053

Normal substantia nigra echogenicity in suspected Parkinson's Disease: False negative or true negative results? A follow-up study

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Background and aims: Substantia nigra hyperechogenicity (SN+) as detected by Transcranial Sonography (TCS) is useful for Parkinson's Disease diagnosis, although a proportion of 15% false negative results of unknown significance exists. However, most TCS studies are transversal, and diagnosis of PD may change during follow-up.

Methods: We analysed our prospective database of TCS (December 2012-January 2015): patients with sufficient bone window, to whom TCS was performed because of suspected PD, with a minimum follow-up of three years were selected and classified regarding basal SN echogenicity (SN+/SN-). Clinical variables were compared with appropriate statistical tests.

Results: 149 patients (104 SN+, 45 SN-), with mean age of 71 years (25-90) and 46 months (36-60) follow-up were included. Male sex was more frequent in SN+ group (69 vs. 51%, p 0.03). There were no differences in atypical sonographic features, non-motor symptoms or family history. At the end of follow-up, PD diagnosis was retained by 88% in SN+ vs. 55% subjects in SN- group (p:0.000016). Conversely, final diagnosis of Atypical Pakinsonism (AP) (7% vs. 20%, p:0.016) and essential tremor (3% vs. 11%, p:0.004) were more frequent in SN- group. Dopaminergic therapy response was associated with baseline SN+ (87% vs. 53%, p:0.000011), as were abnormal DaT-scans (91% vs 59%, p:0.009).

Conclusion: Our patients with suspected PD and baseline normal SN echogenicity responded less to PD therapy and converted to a diagnosis different from PD more frequently than SN+ subjects. In this setting, normal SN appears to be a caveat for clinicians to check for AP features during follow-up.

Disclosure: Nothing to disclose

EPO2054

Tolerability, Pharmacokinetics and Pharmacodynamic Effects of ODM-104 a Novel Catechol-O-Methyltransferase Inhibitor, after Single Escalating Doses in Healthy Subjects

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Background and aims: ODM-104 is a novel Catechol-O-methyltransferase (COMT) inhibitor aimed at the treatment of Parkinson's disease in combination with levodopa and an aromatic amino acid decarboxylase (AADC) inhibitor. The objectives of this first-in-man study were to evaluate the tolerability, pharmacokinetics and pharmacodynamic effects (COMT inhibition in erythrocytes) of ODM-104 following single oral doses in healthy male volunteers.

Methods: This was a randomised, double-blind, placebo-controlled, single-dose escalation study with an alternating 3 panel crossover design and 8 dose levels (2, 10, 25, 50, 100, 200, 400 and 800 mg). There were 6 study subjects on ODM-104 treatment and 3 subjects on placebo at each dose level. Each subject received active treatment or placebo for a total of 2 or 3 periods.

Results: ODM-104 was well tolerated at all doses tested. The absorption of ODM-104 was rapid, tmax was achieved in 0.8-2.2 h. Systemic exposure of ODM-104 and its main circulating metabolite increased in an approximately dose-proportional manner. The terminal elimination half-life of ODM-104 was 4.2-21.1 h. Maximum COMT inhibition by ODM-104 was dose dependent, ranged from 22% (2 mg) to 87% (800 mg), and reached statistical significance at all doses tested. In similar setting 200 mg of entacapone has produced maximum COMT inhibition of 38-65%. After ODM-104 the COMT inhibition lasts substantially longer than after entacapone.

Conclusion: ODM-104 was well tolerated and presented rapid absorption and close to dose-proportional kinetics. ODM-104 produced clear and long lasting COMT inhibition.

Disclosure: The study was sponsored by Orion Pharma

EPO2055

Cerebrospinal fluid flow dynamics in Huntington's disease using phase contrast MRI: a pilot cross-sectional study

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Background and aims: The objective of this study was to generate pilot data on cerebrospinal fluid (CSF) flow dynamics in Huntington's disease (HD) using phase contrast MRI (PCMRI), to inform the design of future intrathecal drug trials in HD.

Methods: We performed a prospective cross-sectional analysis of 10 age- and gender-matched healthy controls and 10 manifest HD gene expansion carriers. All participants underwent extensive clinical evaluation and cardiac-gated PCMRI at the level of the Aqueduct of Sylvius, T1 and T10. CSF velocities and flow measurements were derived using a semi-automated method. The influence of age, gender, CAG repeat-length, serum osmolality, whole-brain volume, and ventricle volume on these measurements were tested using Spearman correlations or Fisher's exact tests. Group comparisons between healthy controls and manifest carriers were achieved via two-sample Wilcoxon rank-sum tests. All tests were two-sided with a significance level of 0.05, and corrected for multiple comparisons.

Results: Twenty participants were recruited, and no significant age- and gender-imbalances were found. None of the studied covariables was found to have an effect on the CSF velocities and flow measurements after corrected for multiple comparisons. No apparent differences were found between study groups in regards to CSF velocities and flow measurements.

Conclusion: Although under-powered, our pilot results add to the view that CSF dynamics are not altered in HD. These results need external validation but offer reassurance that clinically-relevant disease-related alterations in CSF flow, that might justify dose-adjustments of intrathecal drugs, are very unlikely to exist.

Disclosure: Nothing to disclose

EPO2056

Movement disorder specialists' determination of eligibility for device aided treatment in advanced Parkinson's disease: Results from the OBSERVE-PD study

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Background and aims: To characterize the clinical and non-clinical features of PD patients considered to be eligible or ineligible for device-aided treatment by movement disorder specialists.

OBSERVE-PD was a cross-sectional, observational, multicenter study. A previous analysis reported that physicians judged 51% of the PD patients in participating movement disorder centers as 'advanced'.

Methods: This is a post-hoc analysis of the clinical and non-clinical characteristics of 'advanced' PD patients judged eligible or ineligible for device-aided treatment by the treating physician. Device-aided treatments included levodopa-carbidopa intestinal gel, also known as carbidopa-levodopa enteral suspension, apomorphine SC infusion, and Deep Brain Stimulation. Patients were analyzed using descriptive statistics.

Results: 66% (n=876) of advanced PD patients were considered eligible for device-aided treatment. Device-aided treatment-eligible patients were on average(SD) 66.0 years(9.2) (mean PD duration: 12.2 years(5.5). Device-aided treatment-ineligible patients had a mean(SD) age and PD duration of 70.6(9.1) and 8.6(5.5) years, respectively. Reasons for lack of device-aided treatment use primarily included: patient needing more decision making time (43%) and patient refusal (28%). No patients stated cost or lack of reimbursement as reasons for lack of use [table1]. Of the 876 'advanced' and eligible PD patients, 383(44%) had ongoing device-aided treatment, 163(19%) began device-aided treatment during the study visit, and 330(38%) had no device-aided treatment planned [table2].

Table 1. Reasons for device-aided treatment (DAT) ineligibility

Reason for DAT-ineligibility	n (% of 460)
Patient needs more time to decide	143 (43%)
Patient refusal	94 (28%)
Cognitive related issues	27 (8%)
Psychiatric related issues	23 (7%)
Comorbidities	20 (6%)
Age	12 (4%)
Lack of caregiver/family support	11 (3%)
Motor function related issues	6 (2%)
Cost/reimbursement	0 (0%)
Other reason	45 (14%)

[a]Multiple entries for each patient were possible

DAT = device-aided treatment

Table 2 Baseline characteristics of DAT-eligible and DAT-ineligible 'advanced' PD patients

Baseline characteristics	Ongoing DAT (N=383)	DAT-eligible (Total N=976) Planned DAT (N=163)	Not Planned (N=330)	DAT-ineligible (Total N=460)
Demographics				
Age, years, mean (SD)	65.1 (8.7)	64.3 (9.0)	67.9 (9.6)	70.6 (9.1)
Gender, female, n (%)[a]	145 (38%)	61 (37%)	132 (40%)	186 (40%)
Caregiver support, yes, n (%)[b]	278 (73%)	109 (67%)	242 (74%)	288 (63%)
Medical history				
PD duration, years, mean (SD)[c]	14.2 (5.8)	10.1 (4.7)	11.1 (5.7)	8.6 (5.5)
Motor fluctuations, yes, n (%)[d]	353 (92%)	154 (94%)	320 (96%)	338 (74%)
Motor fluctuation duration, years, mean (SD)[e]	7.2 (4.3)	4.2 (2.8)	4.4 (3.5)	3.3 (2.9)
Comorbidity, yes, n (%)[f]	327 (85%)	135 (82%)	301 (91%)	431 (94%)
Time since referral to center, years, mean (SD)[g]	5.2 (5.5)	2.7 (3.7)	4.7 (4.9)	4.0 (4.9)

[a]DAT-ongoing N=384, DAT-planned N=164, DAT-not planned N=332; [b]DAT-ongoing N=309, DAT-planned N=162, DAT-not planned N=328, DAT-ineligible N=455; [c]DAT-ongoing N=372, DAT-planned N=160, DAT-not planned N=322; [d]DAT-not planned N=332, DAT-ineligible N=446; [e]DAT-ongoing N=351, DAT-planned N=152, DAT-ineligible N=334; DAT-not planned N=312; [f]DAT-ongoing N=385, DAT-planned N=118, DAT-not planned N=231, DAT-ineligibility N=348, DAT = device-aided treatment

Conclusion: This analysis shows a trend for advanced PD patients judged device-aided treatment-ineligible to be older individuals, with shorter disease duration, however direct statistical comparisons were not performed. Device-aided treatment-ineligibility was primarily related to patient refusal/needing additional time to decide.

Disclosure: This work was funded by AbbVie Inc. AbbVie participated in the study design, research, data collection, analysis and interpretation of data, writing, reviewing, and approving the publication.

EPO2057

Prevalence and Correlates of Anxiety & Depression in Cervical Dystonia

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Background and aims: Non-motor symptoms, anxiety and depression are prominent in Cervical Dystonia and can affect quality-of-life, despite therapy of motor symptoms with botulinum-toxin. Our aim was to assess the prevalence and severity of mood disorder in our Cervical Dystonia population attending the botulinum toxin clinic and to assess their effect on quality-of-life.

Methods: We prospectively collected data on anxiety, depression measures in patients with cervical dystonia attending clinic. Health related quality-of-life (HrQoL) was assessed using the Cervical Dystonia Impact Profile–58 (CDIP-58); mood disorder was assessed using the Beck-Anxiety-Index (BAI-II), Beck-Depression-Index (BDI); Dystonia severity was assessed using the TWSTRS-2 severity-scale and pain-scale.

Results: A cohort of 70 patients (50 women) with cervical dystonia were surveyed; 28/70(40%) reported symptoms of anxiety using the BAI. In 66 patients who completed the BDI-II, 30(45%) reported symptoms of depression; 18/66(27%) had BDI-II scores indicating moderate-to-severe depression. 40/70(57%) patients reported depression and/or anxiety. A weakly significant correlation between anxiety, measured by the BAI and the TWSTRS pain scale ($R^2=0.163$; $p=0.0006$) but no correlation with the TWSTRS–2 severity scale ($R^2=0.024$; $p=0.2$. Similarly depression measured by the BDI–II correlated weakly with the TWSTRS pain scale ($R^2=0.151$; $p=0.001$) but no correlation with the TWSTRS–2 severity scale ($R^2=0.009$; $p=0.44$).

Conclusion: Significant findings of (57%) patients with cervical dystonia have concurrent anxiety and/or depression. The lack of correlation with disease severity, and low correlation with pain suggests non-motor symptoms may have pathogenic mechanisms unrelated to motor-disorder.

Disclosure: Nothing to disclose

EPO2058

Safety and Efficacy of Levodopa-Carbidopa Monotherapy in Patients With Advanced Parkinson's Disease

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Background and aims: To evaluate the efficacy/safety of levodopa-carbidopa intestinal gel (LCIG) daytime monotherapy (with/without nighttime oral carbidopa/levodopa) vs polytherapy (LCIG with >1 adjunctive therapy) in patients with advanced Parkinson's disease (APD).

Treatment of motor complications often requires multiple adjunctive PD therapies. Continuous administration of LCIG reduces motor complications associated with oral levodopa, while potentially simultaneously reducing pill burden.

Methods: LCIG was administered continuously 16 hours/day via percutaneous endoscopic gastrojejunostomy (PEG-J) to patients with APD in two phase 3 studies. In the first study, a 52-week open-label extension of a 12-week double-blind study (patients received either LCIG or oral carbidopa/levodopa), both groups received LCIG, and adjunctive therapies could be tapered off. In the second study, a 54-week, open-label study of LCIG, adjunctive therapies were allowed after week 4.

Results: Study 1 included 30 patients on LCIG daytime monotherapy and 32 patients on LCIG polytherapy. In study 2, of 324 patients with PEG-J placement, 248 (76.5%) were on LCIG daytime monotherapy (of these, 90 patients received no overnight oral carbidopa/levodopa). Total daily levodopa dose increased with LCIG use in all groups. In both studies, patients on daytime LCIG monotherapy experienced similar reductions in "Off" time and improvements in "On" time compared with patients receiving LCIG polytherapy. Adverse events were similar for both groups.

Conclusion: Daytime LCIG monotherapy and polytherapy demonstrated similar efficacy/safety profiles in two phase 3 studies in patients with APD, suggesting that LCIG monotherapy can provide a more simplified treatment option with similar efficacy for appropriate patients.

Disclosure: This work was funded by AbbVie Inc. AbbVie participated in the study design, research, data collection, analysis and interpretation of data, writing, reviewing, and approving the publication.

EPO2059

Effect of levodopa-carbidopa intestinal gel on dyskinesia: Design of an open-label, randomized multicenter 12-week study in advanced Parkinson's disease patients

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Background and aims: To examine the effect of levodopa-carbidopa intestinal gel (LCIG, designated carbidopa-levodopa enteral suspension in the US) treatment relative to that of optimized medical treatment (OMT) on dyskinesia in advanced Parkinson's disease (PD) patients.

LCIG, delivered continuously via percutaneous gastrojejunostomy, reduces wearing off of levodopa therapy in advanced PD patients, but data on dyskinesia are limited. The DYSCOVER (dyskinesia comparative interventional trial on LCIG versus oral medication) study will be the first interventional, randomized study investigating the efficacy of LCIG on dyskinesia in advanced PD patients.

Methods: Sixty LCIG-naïve advanced PD patients with severe motor fluctuations and dyskinesia will be enrolled in movement disorders centers in accordance with local product label. Prior to recruitment, patients will have reached the maximum therapeutic effect of oral anti-PD therapies. Patients will be randomized (LCIG treatment group or OMT group) for 12-weeks of treatment with scheduled study visits. Subjects randomized to OMT will continue their current anti-PD medication regimen.

Results: The primary efficacy outcome will be the mean change from baseline to week 12 in the Unified Dyskinesia Rating Scale (UDysRS) total score. Key secondary endpoints include "On" time without troublesome dyskinesia, the 8-item PD Questionnaire (PDQ-8), the Clinical Global Impression of Change assessment, the Unified PD Rating Scale (UPDRS) part II score, "Off" time, and UPDRS part III score. Adverse events will be monitored.

Conclusion: Robust evidence is lacking for device-aided medical treatments in advanced PD. This study is designed to determine whether LCIG is an effective management strategy for the treatment of dyskinesia in advanced PD.

Disclosure: This work was funded by AbbVie Inc. AbbVie participated in the study design, research, data collection, analysis and interpretation of data, writing, reviewing, and approving the publication.

Movement disorders 3

EPO2060

Regional Diffusion of Botulinum toxin to Contralateral Facial Musculature and its Effects on Neuromuscular Junction after Repeated Injections

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Background and aims: Hemifacial spasm (HFS) is characterized by initially progressive, involuntary, irregular, clonic or tonic movements of muscles innervated by the seventh (facial) cranial nerve on one side of the face. Treatment of this condition primarily includes botulinum toxin injections. It is generally agreed that diffusion of botulinum toxin occurs, but the extent of the spread and its clinical importance are disputed. The twitching on the contralateral facial sides in some of the patients with hemifacial paralysis, whose having treatment of botulinum toxin for years prompted us to investigate the spreading effect.

The aim of the stduy is to investigate the whether there is a regional diffusion and effect on neuromuscular junction in the contralateral facial mucles after repeated injections.

Methods: The study was designed as prospective randomized and were evaluted 19 female, 20 male patients (19-65 years) diagnosed with hemifacial spasm. Parameters of efficacy and diffusion (CMAP; SFEMG; MCD and jitter analysis) in both orbicularis oculi muscles were assessed at baseline, before botulinum toxin injection and 4 weeks following injection.

Results: CMAP of the threated orbicularis oculi muscles was significantly reduced. Contralateral CMAP reduction was observed too. Jitter analysis was performed, in order to assess neuromuscular transmission failure in the contralateral orbicularis oculi, at baseline before botulinum toxin injection and 4 weeks after the injection.

Conclusion: The results showed the mean jitter value was significantly increased. We observed higher jitter values in patients receiving repeated treatment for years.

Disclosure: Nothing to disclose

EPO2061

Longitudinal development of nigral iron load in Parkinson's Disease

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Background and aims: Iron accumulation in the substantia nigra (SN) is discussed to be an important factor in the pathogenesis of Parkinson's disease (PD). We for the first time investigated longitudinal changes of nigral iron load measured by Quantitative Susceptibility Mapping (QSM), a highly iron-sensitive MRI method.

Methods: We included 52 PD-patients (36 male, mean age 62.6 ± 10.7; mean disease-duration 4.1 years) and 29 healthy controls (HC) (13 male; mean age 68.1 ± 9.1). All subjects underwent a clinical examination and a 3T MRI scan at baseline and after a follow-up period of approximately 2 years. For group comparisons we performed ANOVAs, corrected for age, gender and between-scan-time.

Results: QSM values in total SN, SN pars compacta (SNc) and SN pars reticulata (SNr) were significantly higher in PD compared to HC ($p<0.001$) at baseline and follow-up. There were no significant group differences in longitudinal QSM-change. QSM values in PD tented to increase in SNc and decrease in SNr, in HC they tended to decrease in SNc and SNr. There was no significant correlation for QSM change and change in clinical parameters (MDS-UPDRS, FTM-tremor rating scale, Non Motor symptoms questionnaire, MMSE, LED).

Conclusion: We confirmed higher nigral iron load in PD compared to HC. However there was only a not significant trend for stronger shortterm longitudinal increase of iron concentration in SNc in PD compared to HC. This might be due to relatively long baseline disease-duration in our PD subjects and suggests nigral iron accumulation as an early factor in the pathogenesis of PD.

Disclosure: Nothing to disclose

EPO2062

Dysphagia predicts poor outcome in late-stage Parkinson's disease

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Background and aims: Few data exists on the rate of clinical progression of disability milestones and prognostic factors for Parkinson's disease (PD) patients who have entered a very late stage of disease. Our aim was to to evaluate the clinical progression and prognostic factors of a late-stage PD (LSPD) population.

Methods: 50 LSPD patients (Schwab and England ADL Scale <50 or Hoehn Yahr Stage >3 in MED ON) and 17 advanced (AD) PD patients matched for age at disease onset underwent an acute levodopa challenge test and an extensive cross-sectional clinical assessment for motor, non-motor symptoms (NMS), quality of life (QoL) and caregiver burden. LSPD patients were also assessed at one year follow-up.

Results: LSPD patients present a more severe clinical picture, with prominent axial motor and NMS, that negatively influenced QoL. LSPD and ADPD patients' MDS-UPDRS-III score significantly improved after levodopa (p <0.001), respectively 18% and 53% (Table 2). The magnitude of levodopa response significantly correlated with motor complications in LSPD. After one-year, 20% of LSPD patients were dead. Overall, after 1 year follow-up there was still clinical worsening of motor symptoms (worsening of MDS-UPDRS-III mean±SD 7.7±10.3) and NMS although heterogeneous. Nevertheless, motor fluctuations and dyskinesias improved. Functional independence worsened. Dysphagia severity at baseline significantly predicted a poor outcome (death, institutionalization or HY 5).

Conclusion: LSPD patients still present a significant, although heterogeneous, progression in motor and non-motor features. Dysphagia severity influences the progression of additional disability milestones.

Disclosure: Nothing to disclose

EPO2063

Differences between early-onset and "normal"-onset Parkinson's Disease in Greece: Data analysis of the Hellenic Biobank of Parkinson's Disease

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Background and aims: The aim of this study is to compare clinical characteristics and environmental exposures between early-onset (≤50 years) and "normal"-onset (>50 years) PD.

Methods: Our data derived from the Hellenic Biobank of PD, consisting of blood samples, clinical and lifestyle information of PD cases and controls during 2006-2017. Cases with A53T mutation in SNCA or mutations in GBA1 gene were excluded. OR and 95% CI were calculated for each factor. Quantitative variables were analyzed with Mann-Whitney test and Spearman's correlation coefficient.

Results: 98 patients with early-onset and 469 patients with "normal"-onset PD were included. Early-onset PD was associated with family history of PD (OR=1.613, 95% CI=1.019-2.555) and cigarette smoking (OR=2.013, 95% CI=1.240-3.268). Smoking years were not associated with onset age of PD (p=0.182). Dystonia and motor complications were more common in early-onset PD (OR=4.665, 95% CI=2.612-8.329, OR=2,858, 95% CI=1.809-4.514 respectively). The mean disease and dopaminergic treatment duration were longer in early onset PD (p<0.001, p<0.003 respectively). There were no associations between onset age of PD and gender, coffee consumption, pesticide exposure, tremor, bradykinesia, rigidity, gait disturbances, postural instability, autonomic dysfunction, dementia, depression or psychosis.

Conclusion: Family history, cigarette smoking, dystonia and motor complications are more common in early-onset PD in this Greek cohort. The longer disease and dopaminergic treatment duration may explain the more common motor complications in early-onset PD. The stronger genetic influences in younger ages may explain the "loss" of negative association with smoking in early-onset PD.

Disclosure: Nothing to disclose

EPO2064

Symptoms of peripheral neuropathy in Idiopathic Parkinson's Disease: prevalence and impact on quality of life; a case controlled study

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Background and aims: Neuropathic symptoms (NS) are commonly reported in Parkinson's Disease (PD), but robust data on the epidemiology of such symptoms are lacking. The present study sought to investigate the prevalence and determinants of peripheral NS in Idiopathic PD (IPD) and ascertain the effects of such symptoms on the patients' quality of life(QoL).

Methods: Patients with IPD and age- and gender-matched controls were screened for NS, using the Michigan Neuropathy Screening Instrument (MNSI). The impact of NS on QoL was investigated using the 36-Item Short Form Survey(SF-36).

Results: 52 patients and 52 age and gender matched controls were recruited.NS were reported more frequently in patients with IPD than in controls(82.7% versus 44.2%, p<0.001). Mean MNSI total score was 3.2±2.2 for IPD compared to 1.4±1.4 for controls(p<0.001). No significant relationships were found between PD-related clinical characteristics(i.e. disease severity and duration, duration of exposure to levodopa, cumulative levodopa dose etc) and the presence of NS.

Significant correlations were found between the number of NS and emotional role limitations(Spearman's rho -0.484), physical functioning(Spearman's rho -0.473), physical role limitations(Spearman's rho -0.373), energy/fatigue (Spearman's rho -0.299), mental health(Spearman's rho -0.231) and the general health perception(Spearman's rho -0.338).

Conclusion: Our results support the notion of a greater prevalence of NS in IPD patients compared to the general population, which, at least in part, may be secondary to large and/or small fibre peripheral neuropathy. This warrants further investigation in larger studies that include detailed neurophysiological assessments.

Disclosure: Nothing to disclose

EPO2065

Pain in Idiopathic Parkinson's disease: prevalence and impact on quality of life; a case controlled study

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Background and aims: Pain is a frequent non-motor symptom of Idiopathic Parkinson's Disease(IPD). We sought to investigate the prevalence of overall pain and more specifically peripheral neuropathic pain(PNP) in IPD, and ascertain any impact of PNP on quality of life(QoL).

Methods: Patients with IPD and age- and gender-matched controls were screened for overall pain using the King's Parkinson's Pain Scale(KPPS). PNP was assessed using the Michigan Neuropathy Screening Instrument(MNSI). QoL was assessed using the 36-Item Short Form Survey(SF-36).

Results: 51 patients and 51 controls were recruited. The prevalence of overall pain was similar between the two groups(88.2% versus 94.1%, p=0.487). However, patients with IPD presented with higher KPPS scores in fluctuation-related(4.9±6.9 vs 1.1±2.6, p <0.001), nocturnal(6.6±7.5 vs 1.7±4.2, p <0.001) and oro-facial(0.6±2.0 vs 0.0±0.0, p=0.040) domains.

When looking specifically into PNP, patients with IPD were experiencing more PNP compared to controls(35.3% versus 13.7%, p=0.011).

After adjusting for age, gender, disease duration and overall KPSS score, PNP was significantly correlated with physical functioning(Spearman's rho -0.290), emotional role limitations(Spearman's rho -0.319) and general health perception(Spearman's rho -0.342) domains of SF-36.

Conclusion: PNP is very prevalent in IPD and has a significant impact on the QoL. The aetiology of such pain requires further studies. The presence of burning pain is suggestive of small fiber neuropathy, but is not captured by the KPSS alone, and therefore a revision of the KPSS is needed.

Disclosure: Nothing to disclose

EPO2066

SPG15 with Levodopa-responsive parkinsonism and peak-dose dyskinesia

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Background and aims: Hereditary spastic paraplegias are a heterogeneous group of neurodegenerative pathologies clinically classified in pure and complex forms. Recently, cases of SPG11 and SPG15 with parkinsonism have been reported. In juvenile cases with pyramidal and extrapyramidal signs the differential diagnosis remains a challenge.

Results: Two portuguese sisters, with unremarkable family history, developed a spastic paraparesis and akinetic-rigid parkinsonism in their second decade of life. Soon after the introduction, levodopa became essential to maintain their functionality. Their condition progressively worsened, with mental deterioration, marked spastic paraparesis, ataxia, epilepsy and important extrapyramidal signs: moderate-severe bradykinesia, rigidity, tremor and dystonia. Upon levodopa dose escalation, peak dose dyskinesia appeared (after 3 years under 450 mg/day of levodopa) and were managed with dose reduction and amantadine. Metabolic, infectious, neoplastic and immunological investigations were normal/negative. Genetic study for levodopa-responsive dystonia was negative (GCH1 and TH genes) as were the study of Parkin, PINK1 and DJ-1 genes. Cerebral MRI showed symmetrical T2 hypersignal of the periventricular white matter and thinning of the corpus callosum; I-Ioflupane SPECT revealed nigro-striatal degeneration. Broadening the genetic pursue, and after a normal spatacsin gene sequenciation, the molecular study of the ZFYVE26 gene demonstrated a homozygous pathogenic mutation.

Conclusion: There are only two reports of parkinsonism as a feature of SPG15, both with nigro-striatal loss in I-ioflupane SPECT and partially beneficial levodopa treatment. Our case adds to the existing literature the occurrence of levodopa-induced dyskinesia and strengthens the evidence of SPG15 as a cause of autosomal recessive spastic parapaplegia with levodopa-responsive parkinsonism.

Disclosure: Nothing to disclose

EPO2067

Acute sensorimotor neuropathy as a complication of Duodopa® treatment

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Background and aims: Duodopa® is a modern treatment for advanced Parkinson's disease (PD) administrated via PEG-J by means of a tube connected to an external pump. Duodopa® is delivered continuously in small quanta preventing large plasma level fluctuations and thus suppressing disabling motor complications related to oral treatment in advanced stages of PD.

Methods: We describe the case of a 66-year-old female with a 16-year history of PD with progressive severe motor and psychiatric complications. Due to complications and inefficacy of oral dopaminergic treatment, the patient has been treated with Duodopa®.

Results: In October 2016, Duodopa® was initiated with a positive subjective and objective effect. After successful titration, PEG-J was inserted and patient was released home. During two months she observed worsening of Parkinson symptoms, the dose of Duodopa was increased. In January 2017 pains, paraesthesia and weakness of the lower limbs developed. EMG confirmed acute severe sensorimotor polyneuropathy. The level of vitamin B12 and folate were normal. Due to the normal EMG finding prior to the Duodopa® titration, it was thought of acute neuropathy as a complication of Duodopa® treatment. The Duodopa treatment was discontinued, the patient transferred back to oral dopaminergic treatment. However we observed an improvement in sensory and motor symptoms in four weeks, EMG finding had nearly normalized in six months.

Conclusion: Acute polyneuropathy is one of the rare complications of Duodopa® treatment. The pathogenesis is not clear; it may be changes of the metabolism of vitamin B6, B12, homocysteine or methylmalonic acid.

Disclosure: Supported by GAČR 16-13323S and Progress Q27.

EPO2068

Localisation of Deep Brain Stimulation electrodes within Subthalamic Nucleus and its impact on Non-Motor Symptoms in Patients with Parkinson's Disease

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Background and aims: Deep brain stimulation (DBS) has clear effect on motor symptoms of Parkinson's disease (PD). Recently an effect on non-motor symptom (NMS) has been studied. Subthalamic nucleus (STN) is the most common target of DBS. According to experimental studies, STN consists of sensorimotor, limbic and associative part. The aim of our study was to evaluate the impact of localization of DBS electrodes within the STN on improvement of NMS in patient with PD.

Methods: Each STN was divided using software system SureTune to thirds that represent their sensorimotor, associative and limbic part. DBS electrodes were divided into groups according to the localisation of their tip. Electrodes with tip outside STN were excluded. Non-motor and motor symptoms were then evaluated by using 8 standard questionnaires preoperatively, one month and four months after DBS. Finally, the correlation between position of the tip of the electrode and change of NMS and MS for each side was calculated.

Results: From 43 evaluated electrodes, 1 was placed in limbic, 31 in associative and 11 in sensorimotor part. The first two group were integrated. There was no significant difference in NMS change in groups on both sides. After four months there was only significantly bigger improvement in MDS UPDRS in electrodes localised in limbic/associative part than in sensorimotor part on the left side.

Conclusion: Our pilot study has not proven correlation between position of the tip of the electrode and change of NMS, which could be due to low amount of electrodes. Further research with more patient must be done.

Disclosure: Supported by IGA_LF_2017_039

EPO2069

Carrier mediated delivery system bearing Dopamine for effective management of parkinsonism

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Background and aims: Delivery of drug and sustaining it in effective concentration in brain is challenging due to blood brain barrier (BBB). In the present investigation, amino acid coupled liposomes bearing dopamine-HCl were prepared to deliver drug to the brain utilising receptor-mediated transcytosis for effective management of parkinsonism.

Methods: L-lysine stearylamine conjugate (LSC) was synthesized & LSC coupled liposomes bearing dopamine HCl was prepared by lipid cast film method. Formulations were analysed for average vesicle size, drug entrapment, in-vitro drug release and in-vivo efficacy of the formulations was assessed by measuring the reduction in the degree of drug induced catatonia in albino rats.

Results: Average particle size was found in the range of 1.92-0.80mm. There was increase in the size for coupled liposomes due to the inclusion of LSC in liposomal bilayers. The percent encapsulation efficiency decreased from $46.82 \pm 2.17\%$ in uncoupled to $38.13 \pm 1.18\%$ in coupled liposomes. The in-vitro drug release after 24hrs was $58.9 \pm 2.94\%$ with uncoupled while the coupled liposomes showed $43.7 \pm 2.18\%$ drug release. The lower value for coupled formulation could be due to the retardation of drug release caused due to the incorporation of LSC in the liposomal bilayers, which enhanced the structural integrity of the bilayer. In-vivo study reveals that the animals receiving uncoupled liposomes showed partial reduction and animals that received coupled liposomes showed almost complete reduction in catatonia.

Conclusion: Fluoresence study clearly indicates the uptake of 6-CF in blood vessels and accumulated in brain. This could be due to enhanced uptake of Lysine coupled liposomes through amino acid transporters present at BBB surface

Disclosure: Nothing to disclose

EPO2070

Tolerability, pharmacokinetics and pharmacodynamic effects of ODM-104 a Novel Catechol-O-Methyltransferase Inhibitor, after escalating repeated doses in healthy subjects

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Background and aims: ODM-104 is a novel Catechol-O-methyltransferase (COMT) inhibitor aimed at the treatment of Parkinson's disease in combination with levodopa and an aromatic amino acid decarboxylase (AADC) inhibitor. The objectives of this study were to evaluate the tolerability, pharmacokinetics and pharmacodynamic effects (effects on levodopa pharmacokinetics) of ODM-104 following repeated oral doses in healthy male volunteers.

Methods: This was a randomised, double-blind, placebo-controlled, repeated-dose escalation study with parallel group design and crossover comparison to entacapone. At each ODM-104 dose level (10, 25, 50, 100, 200 mg) 6 subjects were on active treatment and 3 on placebo. The subjects received ODM-104 or placebo q.i.d for 7 days. All subjects received levodopa/carbidopa (100/25 mg or 100/65 mg) combined with entacapone (200 mg) q.i.d for 1 day before starting the ODM-104/placebo treatment and with ODM-104/placebo q.i.d during the last treatment day.

Results: ODM-104 was well tolerated at tested dose levels. The maximum concentration (Cmax) and exposure (AUC0-24h) of ODM-104 increased in a dose-dependent manner. The Cmax appeared mainly after the 2nd or 3rd daily dose. The terminal elimination half-life of ODM-104 was 6.6-10 h. ODM-104 accumulated slightly. The increase in levodopa exposure (AUC0-24h) had an ODM-104 dose-dependent trend. 100 and 200 mg doses of ODM-104 produced significantly higher levodopa AUC0-24h than 200 mg of entacapone. The effect was evident with both carbidopa doses.

Conclusion: ODM-104 was well tolerated, presented close to dose-proportional kinetics and slight accumulation during 7 days q.i.d dosing. ODM-104 produced significantly higher levodopa exposure than entacapone.

Disclosure: The study was sponsored by Orion Pharma.

MS and related disorders 3

EPO2071

Oxidative stress parameters in relapsing-Remitting Multiple Sclerosis (RRMS) patients before and after corticosteroid therapy

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Background and aims: Oxidative stress is implicated in the pathophysiology of multiple sclerosis (MS). The aim of our study was to investigate the effect of corticosteroid therapy on oxidative stress parameters in RRMS patients during remission and during relapse (before and after the corticosteroid treatment).

Methods: The study included 60 RRMS patients in relapse and 30 in remission. Prooxidative-antioxidative balance (PAB), nitrate and nitrite as a pro-oxidants and total antioxidative status (TAS), paraoxonase, transferrin, bilirubin and uric acid as antioxidants were measured in plasma in remission (Control), before (Group I) and a day after corticosteroid therapy (Group II).

Results: Statistically significant difference was found among Group I, Group II, Control in PAB values (150.3 vs 133.8 vs 127.4 HKU) and nitrate and nitrite production (4.42 vs 3.93 vs 3.63 µmol/L), having lower levels of pro-oxidants after corticosteroid treatment and in remission. Antioxidants were significantly decreased after corticosteroid therapy-TAS (911.9 vs 810.5 vs 977.2 µmol/L), paraoxonase activity (395.3 vs 368.2 vs 422.4 U/L) uric acid (263.1 vs 206.1 vs 279.2 µmol/L), bilirubin (11.89 vs 10.64 vs 12.07 µmol/L) and transferrine values (2.51 vs 2.41 vs 2.61 g/L), being the highest in a remission.

Conclusion: Our results showed increased levels of pro-oxidants and higher antioxidant activity in relapse, while remission was characterized with lower pro-oxidant and the highest antioxidant activity. Corticosteroid therapy resulted in decreased production of free radicals and consequent lessen antioxidant activity.

Disclosure: Nothing to disclose

EPO2073

Pupillometry enhances the detection of optic nerve damage in multiple sclerosis without a history of optic neuritis: prediction of Visual evoked potential latency

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Background and aims: The present study was conducted to investigate alterations in the pupillary light response measured by automatic pupillometry and to assess its potential associations with latency prolongation of the visual evoked response (VEP) in non-ON RRMS patients.

Methods: We investigated P100 latency and pupillometry parameters including neurological pupil index (NPi), pupil size (PS), minimum size of pupil (MinPS), percentage change of pupil size (CH), Constriction Velocity (CV), Maximum of Constriction Velocity (MCV), Dilation Velocity (DV) and latency (LAT) from 62 non-ON RRMS and 80 control. Independent-samples t-tests were run, first to determine pupillometry differences between the right eye of cases and controls and then, to determinate differences across age-matched controls and cases while p100 latency was in normal range. To assess P100 latency variation in terms of EDSS and pupillometry variables, right eyes of non-ON cases were quantified through multiple regression.

Results: The mean comparison of case and control subjects showed statistically significant differences of -0.56, p=.002; -0.24, p=.01; -3.18, p=.015; -0.53, p=.01 for PS, MinPS, CH, MCV, respectively. And under normal p100 classification,it was revealed that there were statistically significant differences of -0.77, p=.007; -5.38, p=.006; -0.78, p=.015 for PS, CH and MCV, respectively. EDSS and CH statistically significantly predicted P100 p<0.005, R2=18.3%.

Conclusion: Pupillary light response parameters are affected by the pathophysiologic process in MS disease even in the absence of ON and latency prolongation of VEP. CH alongside EDSS can predict p100 latency with a medium effect size.

Disclosure: Nothing to disclose

EPO2074

Evaluation of brain atrophy in early Multiple Sclerosis by corpus callosum index

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Background and aims: Neurodegeneration has emerged as a significant phenomenon in Multiple Sclerosis (MS) even in the earliest stage of the disease. Recently, the corpus callosum index (CCI) has been described as a reliable biomarker correlated with whole brain volume and long-term disability. Our aim is to assess the applicability of CCI in newly diagnosed patients.

Methods: We prospectively enrolled 76 patients who were studied between October 2012 and August 2016 with a new diagnosis of CNS demyelinating disease. The control group consisted of 101 age-matched healthy controls. CCI was obtained in 241 brain MRI by manual measurements (on a conventional best mid-sagittal T1W, T2 and FLAIR).

CCI = A + B + C / anteroposterior diameter of corpus callosum
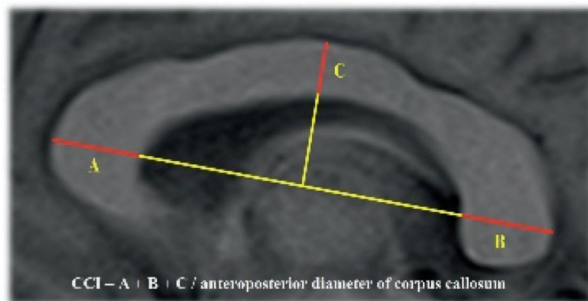
Results: Among the 76 patients in the study (29% males, 71% females, mean age 37.4 years), 82.9% filled the criteria for relapsing-remitting MS (RRMS), 6.6% for primary progressive MS (PPMS) and 10.5% were diagnosed with Clinically Isolated Syndrome (CIS). Their mean CCI was 0.373 (SD 0.05, CI95%). In the control group (64% females, mean age 37.7 years), mean ICC was 0.411 (SD 0.03, CI95%). There was a reduction in mean CCI observed in both groups of MS patients, markedly in PPMS group (0.303), but also among RRMS patients (0.372), when compared to healthy controls. No differences between CIS patients (0.421) and controls (0.411) were observed.
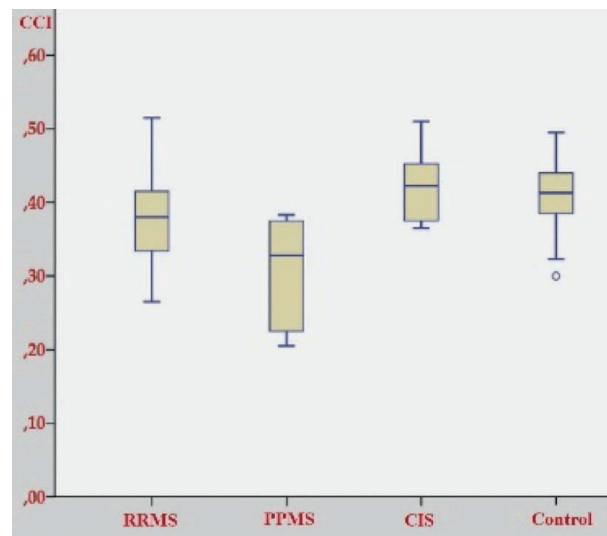
Conclusion: Our study confirms a reduction in CCI in the early stages of MS. This method could be a useful alternative to volumetric measurements, which are almost restricted to clinical trials nowadays

Disclosure: Nothing to disclose

EPO2075

Optical coherence tomography is less sensitive than visual evoked potentials in clinically isolated syndrome suggestive of Multiple Sclerosis

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Background and aims: Visual evoked potentials (VEPs) and optical coherence tomography (OCT) can detect demyelination and neurodegeneration in the visual pathway, with higher sensitivity of VEPs reported in clinically definite MS and first-ever optic neuritis. Our aim was to compare the sensitivity of VEPs and OCT in patients with Clinically isolated syndrome–CIS suggestive of MS.

Methods: 71 patients with CIS (43 females, mean age 34.3 + 9 years) underwent VEPs and OCT with measure of VEP latency and of thickness of the peripapillary retinal nerve fibre layer (RNFL) in both eyes.

Results: Considering all patients, VEPs were abnormal in 43.7% and OCT in 15.5% of patients; 8 patients (11.3%) had both abnormal VEPs and OCT, 23 (32%) had abnormal VEPs only, 3 patients (4.2%) had abnormal OCT only (McNemar's Chi squared 13.885, p=0.0002). Considering optic neuritis at presentation (n=24, 33.8%), VEPs were abnormal in 22 (91.7%) patients and OCT in 7 (29.2%). In patients without ON, abnormal VEPs were found in 9 patients (19.1%) and OCT in 4 (8.5%).

Conclusion: Our findings of a higher sensitivity of VEPs in CIS are consistent with previous literature in MS and isolated optic neuritis. OCT adds little to VEPs in detecting visual pathway involvement, particularly in patients without optic neuritis. Longitudinal monitoring is required to assess comparative value of the two methods in proving optic nerve involvement as an indicator of dissemination in space and their prognostic value on conversion to MS.

Disclosure: Nothing to disclose

EPO2076

Unmet needs of patients transitioning to secondary progressive Multiple Sclerosis: qualitative findings for a resource development

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Background and aims: About 50% of relapsing multiple sclerosis (MS) patients convert to secondary progressive (SPMS) 15 years after clinical onset. Despite the complexity and potential impact of this transition, no targeted interventions to promote patients' wellbeing are available. Managing the Transition to SPMS (ManTra) aims to develop and assess the efficacy of a user-led resource for newly diagnosed SPMS patients. Here, we describe a key project phase: assessment of the experiences and needs of SPMS transition.

Methods: We performed: personal semi-structured interviews with 15 recently diagnosed SPMS patients; three focus groups (with patient significant others, neurologists, and other MS health professionals [HPs] across Italy). Interviews and focus groups were audio-recorded, transcribed verbatim, and analysed (framework method).

Results: Data analysis revealed 62 sub-categories, grouped into 10 categories and four themes: 'Awareness of the transition'; 'Transition'; 'Reaction to disease progression'; 'Resources'. All stakeholders agreed on the following unmet needs: management of SPMS at the MS Centre; psychological support; HP training; communication/information; job/welfare.

Conclusion: We observed a general lack of communication of the transition by neurologists and low awareness by SPMS patients who massively used defensive mechanisms. All stakeholders unanimously asked for improved management at the MS center, provision of psychological support, specific HP training, access to more information, dedicated worker protection policies and job outplacement

in this disease phase. Our findings will be combined with those of the ongoing German qualitative study. An online survey (>400 recently diagnosed Italian and German SPMS patients) will follow to substantiate needs on a large, independent sample.

Disclosure: This study is supported by the Fondazione Italiana Sclerosi Multipla (FISM, grant 2015/R/22 to AS).

EPO2077

Baseline characteristics of the CASTING Study population: a Phase IIIB Trial evaluating Ocrelizumab in patients with relapsing-remitting Multiple Sclerosis and suboptimal response to disease-modifying therapies

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Background and aims: Patients with relapsing-remitting Multiple Sclerosis (RRMS) often experience disease activity despite receiving a disease-modifying therapy (DMT). Ocrelizumab demonstrated superior efficacy versus interferon-beta-1a in two Phase III trials (OPERA I/II [NCT01247324]/[NCT01412333]) in patients with relapsing MS. We report baseline characteristics of RRMS patients enrolled in CASTING, a prospective, multicentre, single-arm Phase IIIb study (EudraCT: 2015-005597-38) evaluating the efficacy and safety of ocrelizumab in patients who had a suboptimal response to an adequate course of a DMT.

Methods: Eligibility criteria included disease duration ≤10 years, ≥6 months prior treatment with one or two DMTs, Expanded Disability Status Scale (EDSS) of 0.0–4.0 at screening, and discontinuation of the most recent DMT due to suboptimal disease control (≥1 relapse, or ≥1 T1 gadolinium-enhancing lesion or ≥2 new/enlarging T2 lesions). Patients receive intravenous ocrelizumab 600mg/24 weeks (≥4 doses [96 weeks]; first dose, 2×300mg separated by 14 days).

Results: In total, 681 patients (64% female) from 16 European countries were enrolled. Mean (SD) baseline age was 34.2 (8.6) years and duration since first MS symptom onset was 5.0 (2.7) years; median (range) EDSS score was 2.0 (0.0–6.0). 61% and 40% of patients had received one versus two DMTs prior to enrolment, respectively. The most commonly used DMT immediately before enrolment was dimethyl fumarate (25%). The most frequent qualifying event for study inclusion was MS relapse while on previous DMT.

Conclusion: The CASTING study will describe the efficacy and safety of ocrelizumab treatment in patients who had ongoing disease activity while receiving another DMT.

Disclosure: Sponsored by F. Hoffmann-La Roche Ltd.

EPO2078

Teriflunomide (Aubagio®) International Pregnancy Registry: enrolment update

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Background and aims: Teriflunomide, approved for the treatment of relapsing forms of MS, is contraindicated in pregnancy based on embryo-foetal toxicity in rats and rabbits. Despite requirements for effective contraception use during teriflunomide clinical trials, a small number of pregnancies occurred. Outcomes of these pregnancies suggested no signal for human teratogenicity. The International Teriflunomide Pregnancy Exposure Registry will record birth defect rates in teriflunomide-exposed pregnancies, and these will be compared with those reported by the European Surveillance of Congenital Anomalies (EUROCAT).

Methods: The International Teriflunomide Pregnancy Exposure Registry is an ongoing, voluntary, multinational, prospective, observational, exposure-registration study. Pregnant women with MS exposed to teriflunomide at any time after Day 1 of their last menstrual period until pregnancy end can enrol. National coordinators liaise with healthcare professionals for data collection and patient enrolment. Target recruitment for statistical analysis: 196 women to achieve 104 live births, providing 80% power to detect a 3.95-fold increase in risk ratio of birth defects associated with teriflunomide exposure vs EUROCAT. Data collected include birth defects and infant characteristics during the first year of life.

Results: As of April 2017, 14 patients have enrolled from 7 European countries; 6 babies have been born with no abnormalities reported; there was 1 elective termination, which was not motivated by results of prenatal tests or concerns for potential birth defect. Updated enrolment data will be presented.

Conclusion: This registry will provide outcomes from teriflunomide-exposed pregnancies; these data will help physicians to provide better counselling for women exposed to teriflunomide during pregnancy.

Disclosure: Study supported by Sanofi.

EPO2079

Clinical profile and treatment pattern of Neuromyelitis Optica Spectrum Disorder (NMOSD) patients in Western India.

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Background and aims: To study clinical profile, treatment pattern and outcomes in NMOSD patients in Western India.
Methods: Clinical profile at onset, follow up and relapses, anti-aquaporin(AQ4) antibody status, imaging were recorded. Relapses on first line immunomodulatory therapy(IMT) and whether relapsed patient was shifted to another IMT after relapse on first agent, was recorded.
Results: 40 NMOSD patients were followed up for a period ranging between 6 months to 5 years. Age ranged between 10-65 years. 6 were males and 34 females. Presentations were longitudinally extensive transverse myelitis(LETM) in 23/40, followed by optic neuritis(ON) in 13/40, area postrema Syndrome(APS) in 1/40, acute brainstem Syndrome(ABS) in 2/40, and one patient had a long lesion extending from medulla to cervical cord(APS+LETM). 37 were AQ4 antibody positive. First line IMT was Azathioprine(Aza) in 30/40, Mycophenolate(MMF) in 7/40 and Rituximab(RTX) in 2/40 patients. One patient did not receive any IMT. So, 37 patients received oral therapy as first line, of which 14 relapsed. 9/14 of the patients who relapsed on oral IMT were switched to RTX.
Conclusion: LETM and ON were the commonest clinical manifestations at onset. We did not come across patients presenting with acute diencephalic syndrome (ADS) and symptomatic cerebral syndrome (SCS). Apprehension towards injection and cost were the factors affecting IMT decision, so majority received oral agents Aza/ MMF as first line therapy. 35% patients relapsed on oral therapy and the trend was to shift from oral therapy to RTX after relapse on oral agent. No relapses were seen once the patient went on RTX.
Disclosure: Nothing to disclose

EPO2080

On the different etiologies of isolated myelitis: a McDonald's 2010 and 2017 criteria comparative study

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Background and aims: Myelitis refers to an inflammatory process of the spinal cord. We present a series of patients with a first episode of myelitis with the aim of describing the clinical and radiological characteristics of its different etiologies and to analyse which of them would meet McDonald's Criteria 2010 and 2017 for a diagnosis of multiple sclerosis.
Methods: Retrospective and descriptive study including all patients with a first episode of myelitis from two tertiary hospitals in Madrid, Spain, between January 2007 and January 2017.
Results: We identified 49 patients with myelitis (22 men/27 women) with an average age of 43. 67% presented sensory and motor symptoms. The lesions were mainly: unaccompanied, with cervical location (51%) and with gadolinium enhancement (63%).The CSF showed inflammation in all cases by the presence of pleocytosis (38%) or oligoclonal bands (53%). Idiopathic myelitis had worse functional outcome at discharge compared to demyelinating (mRS 1.9 vs 1.2).Of all cases of myelitis identified as clinical isolated syndrome or idiopathic etiology (n=41), 7 of them met McDonald's 2010 criteria (17%), 7 met McDonald 2017 criteria (by OCB and typical lesions in brain MRI, 17%), with a change in the previous diagnosis and management.
Conclusion: A higher mean age, in the presence of motor and sensory symptoms, the absence of OCB and a normal brain MRI were significantly related to idiopathic myelitis. In patients with suspected demyelinating etiology, new Mc Donald's 2017 criteria permitted to change the diagnosis in 17% of patients, being able to diagnose multiple sclerosis.
Disclosure: Nothing to disclose

Neurogenetics 1

EPO2081

First clinicogenetic description of Parkinson's disease related to S107L GBA1 mutation

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Background and aims: Mutations in the glucocerebrosidase gene (GBA1) are the most common genetic risk factor for Parkinson's disease (PD). Phenotypic characterisation of GBA1-related PD has been challenging, in part due to differential impact of distinct GBA1 mutations.
The aim is to provide a phenotypic description of two patients with PD heterozygous for the GBA1 mutation S107L. This mutation has not previously been reported in patients with PD.
Methods: Motor and non-motor symptoms (NMS) of PD were evaluated using established rating scales and questionnaires. The genotype was determined by sequencing all exons of GBA1.
Results: Two half-brothers, both heterozygous carriers of S107L exhibited an early PD onset with several NMSs, although rapid progression of motor symptoms was observed in only one.
Conclusion: In these patients, heterozygosity for S107L was associated with an early onset of PD with NMS.
Disclosure: Nothing to disclose

EPO2082

Common and rare genetic variants associated with wearing-off and dyskinesia in Parkinson's disease

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Background and aims: Patients with Parkinson's disease (PD) typically show excellent therapeutic response to dopaminergic medications, but the majority develop late motor complications, including wearing-off and levodopa-induced dyskinesia (LID). Etiology of wearing-off and LID is still unclear. Furthermore, onset time and clinical features of wearing-off and LID are very heterogeneous among patients with PD. Therefore, we aimed to identify the genetic variants that are associated with the occurrence of wearing-off and LID in patients with PD.
Methods: Genomic data was produced using the Korean Chip (K-CHIP), Affymetrix Axiom KORV1.1, which contains imputation genome-wide association study (GWAS) grid and other GWAS loci, functional variants of nonsynonymous exome, pharmacogenetics variants, variants in genes involved in absorption, distribution, metabolism and excretion (ADME) of drugs, and expression quantitative trait loci (eQTL), in 1,070 PD patients.
Results: The SNP rs118109628 showed the most significant association with the occurrence of wearing-off within 5 years after PD onset. The SNP rs144125291 showed the most significant association with the occurrence of LID within 5 years after PD onset. There are several other genomic variants that showed associations with the occurrence of wearing-off or LID within 5 years after PD onset.
Conclusion: This study identified new loci associated with wearing-off and LID within 5 years after PD onset. Further studies are needed to confirm our findings.
Disclosure: This study was supported by a grant of the Korea Healthcare Technology R & D Project, Ministry of Health & Welfare, Republic of Korea (HI17C0328).

EPO2083

Neurocognitive assessment of patients with Chronic Neuronopathic Gaucher's Disease type 3-Norrbottnian form

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Background and aims: The Norrbottnian type of chronic neuronopathic Gaucher Disease type 3 (GD3) worldwide is rare but it is rather frequent in northern Sweden. We aim to describe the neurocognitive profile of patients with Norrbottnian GD3.

Methods: The Repeatable Battery of Neurocognitive Assessment (RBANS) was used to assess cognition in 10 patients (5 males/5 females). Disease severity was assessed with the use of modified Severity Scoring Tool (mSST).

Results: The mean age of our GD3 cohort was 40.9 years (±11.67) and the mean for years of education was 13.25 (±1.83) years. Half of the patients had been diagnosed with epilepsy and were treated with antiepileptic medications. The mean score for mSST was 10.4 (±5.25). Overall, regarding RBANS, the patients scored lower than average in all domains: Immediate Memory (Mean Index Score (MIS) 74.6±15.14), Visuospatial/Constructional (MIS 79.1±20.29), Language (MIS 82±13.78), Attention (MIS 56.4±15.54) and Delayed Memory (MIS 75±21.92). The total average score was also lower than normal (MIS 62.3±15.84).

Conclusion: The group consists of relatively young multisymptomatic patients. The overall assessment of cognition revealed low scores with the group performing worse than the 4% of the healthy population. However, the deficit was even more obvious in attention where the patients scored the lowest and the group value lies below the 2% of healthy population. Memory, both immediate and delayed, was also affected but to a lesser degree and so was visuospatial and constructional ability.

Disclosure: Nothing to disclose

EPO2084

withdrawn

EPO2085

X-linked Charcot-Marie-Tooth disease and multiple sclerosis: emerging evidence for a possible association

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Background and aims: X-linked Charcot-Marie-Tooth disease (CMTX) is a hereditary neuropathy caused by mutations in GJB1, a gap-junction protein expressed in Schwann cells and oligodendrocytes. Subclinical and clinical CNS involvement can be observed in CMTX. To date, three patients developing CNS demyelination compatible with multiple sclerosis (MS) have been individually reported.

Methods: The Neurogenetics Unit, Eginition Hospital, Athens provides genetic testing for Greek patients with suspected CMTX. Over 20 years, 70 patients (36 males) with GJB1 mutations have been identified. These were assessed for clinical features suggestive of MS. Additionally, 16 CMTX patients without suspected MS underwent brain MRI. Serum from available patients with CMTX and MS was tested for anti-AQP4, MOG and ganglioside antibodies.

Results: We identified 3 CMTX index-patients, who developed clinical features suggestive of CNS demyelination and fulfilled MS diagnostic criteria. The resulting MS frequency of 4.3% in the CMTX cohort, significantly differed from the highest background MS prevalence (12/10,000) ever reported in Greece (p=0.00014). Additionally, one patient not fulfilling MS diagnostic criteria had CSF oligoclonal bands. Brain MRI identified 2 patients (12.5%) with lesions highly suggestive of demyelination. Moreover, 6 patients had subcortical lesions, 10 had callosal hyperintensity, and 13 diffuse white-matter hyperintensity. Patients with CMTX and MS tested negative for anti-AQP4, MOG and ganglioside antibodies.

Conclusion: We have demonstrated a higher-than-expected frequency of MS in CMTX patients and a high frequency of demyelinating lesions on brain MRI in CMTX patients without suspected MS. This provides circumstantial evidence for GJB1 mutations acting as a possible MS risk factor.

Disclosure: Nothing to disclose

EPO2086

Interrupted CAG repeats in ATXN2 gene: an expansion of the genetic spectrum of frontotemporal dementias

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Background and aims: Spinocerebellar ataxia type 2 (SCA2) is caused by an expansion of an unstable CAG trinucleotide repeat in the coding sequence of ataxin-2 (ATXN2) gene. Expansions of 33 or more pure CAG repeats are pathogenic and lead to cerebellar ataxia. Expansion of 33 or more CAG interrupted by one or more CAA motifs leads to isolated dopa-responsive parkinsonism, without cerebellar ataxia or any neurological features. We identified an interrupted ATXN2 expansion of 39 CAG in a patient with predominant cognitive disorders diagnosed as a corticobasal syndrome, and pathological hallmarks of frontotemporal lobar degeneration (FTLD) with TDP-43-positive inclusions type A.

Methods: We describe the clinical and pathological characteristics of this patient.

Results: This study provides several important results: 1) interrupted full-length ATXN2 expansions can produce isolated FTLD phenotype; 2) interrupted expansions are associated with phospho-TDP-43 neuronal cytoplasmic and intra-nuclear 'cat eye' inclusions, and p62 neuronal inclusions in neocortex; 3) no mosaicism has been observed in various brain structures;

Conclusion: Finally, this study provides arguments for a common pathological pathway involving TDP-43, not only in the FTLD and ALS spectrum of diseases, but also in several CAG repeat expansion disorders including ATXN2 interrupted expansion diseases. Most importantly, this case establishes a novel genetic link between FTLD phenotype and ATXN2 gene. It expands the molecular spectrum of FTLD-TDP disorders, and shows that ATXN2 analysis should be performed not only in patients with cerebellar ataxia or parkinsonism but also in FTLD patients or, more largely, in cases with TDP-43 pathology after exclusion of the most frequent FTLD genes

Disclosure: Nothing to disclose

EPO2087

Diagnostic yield of Next-Generation Sequencing (NGS) technology applied to Neurological disorders

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Background and aims: The increasing availability of NGS, coupled with the exponential increase in the description of genetic etiologies for neurological diseases, requires neurologists to be familiar with its strengths and weaknesses.

The aim of our study was to assess the diagnostic yield of NGS studies in neurological disorders at our tertiary center.

Methods: Retrospective descriptive cross-sectional study of consecutive neurological patients for whom a NGS study was ordered, for 18 months.

Results: Of 192 patients included, a definitive molecular diagnosis was reached in 35.4%. The main neurological syndromes represented were: intellectual disability/autism (45.8%), epilepsy (12%), dementia (9.9%) and muscle disease (9.4%).

An additional 19.8% of patients had a result of clinical undetermined significance (CUS), meaning either a variant of unknown significance in a phenotypically suitable gene (PSG) or a probably pathogenic variant not previously described in a PSG in a patient in whom the family segregation revealed the same mutation in one of the healthy parents. Results excluded from the CUS definition were: variants in PSG, variants in heterozygosity in recessive conditions and variants in which the bioinformatics prediction was benign or probably benign.

We found a rate of 5.2% of accidental pathogenic findings unrelated to the symptoms that motivated the NGS study.

Conclusion: Our results, derived strictly from clinical practice, show that in approximately one third of patients with neurological disorders of undetermined etiology a definitive diagnosis can be reached when NGS technology is used. Its cost-effectiveness taking into account its impact on patient management, was not addressed.

Disclosure: Nothing to disclose

EPO2088

Novel pathogenic ITM2B mutation or incidental benign sequence variant? Next Generation Sequencing conundrum

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Background and aims: To illustrate the potential difficulties in interpreting results of next generation sequencing (NGS) panels.

Methods: A man in his fifties became increasingly withdrawn, expressed delusional ideas, and psychiatric diagnosis of depression was made. He progressively developed limb tremors, parkinsonism, falls, and loss of spontaneous verbal output. Various neurodegenerative disorders were considered and excluded after extensive investigation, with residual diagnosis of corticobasal syndrome, possibly tauopathy.

Results: Although there was no family history of similar disorder, blood was sent for the dementia/movement disorder NGS panel. This was negative aside from a sequence change in exon 5 of the ITM2B gene (predicted protein change p.Thr228Ala) located on chromosome 13q14.2, not previously described. It was not apparent whether this represented pathogenic mutation or incidental sequence variant: ITM2B mutations are found in familial British and Danish dementias, conditions characterised as cerebral amyloid angiopathies, but missesne mutations have not previously been described to our knowledge. Hence the biological credibility for pathogenicity of this sequence change was uncertain. Subsequent amyloid (18F florbetapir) PET imaging was negative.

Conclusion: NGS panels enhance the potential to define pathogenic mutations in neurodegenerative disorders, but may also reveal incidental sequence variants of uncertain significance. Interpretation of NGS results can be challenging.

Disclosure: Nothing to disclose

EPO2089

Reversible valproate-induced subacute encephalopathy caused by a mitochondrial DNA variant

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Background and aims: There are several reported cases of patients developing motor and cognitive neurological impairment under treatment with valproic acid (VPA). We describe a woman who developed a subacute encephalopathy after VPA intake, harboring a mitochondrial DNA variant, previously described as causing VPA sensitivity in one pediatric patient.

Methods: A 65-year-old woman developed a progressive, severe neurological deterioration after a three-month treatment with valproate sodium, 800mg daily. Magnetic resonance spectroscopy (MRS), muscle histochemical analysis and assay of mitochondrial enzymatic activities, and mitochondrial DNA sequencing were performed.

Results: Neurological examination showed drowsiness, vertical gaze palsy, inability to either stand or walk, diffuse weakness, increased tendon reflexes. Blood lactate was increased, EEG showed diffuse theta and delta activity, MRI subcortical atrophy and leukoencephalopathy, MRS marked reduction of the NAA spectrum, with a small signal compatible with presence of lactate. Muscle biopsy evidenced a significant variability of the fiber caliber with hypotrophic fibers, presence of ragged red fibers (20%) and reduced COX reactivity. Assay of the muscle enzymatic activities showed multiple deficiencies of the electron transport chain. The nt.8393C>T variant in the MT-ATP8 gene was found in homoplasmy. The patient considerably improved after valproate withdrawal.

EEG showing a slow alpha with theta and delta activity

MRI scan showing cortical atrophy with confluent areas of hyperintensity

	Patient	Control values
CI(NADH dehydrogenase)	1.73	1.56-2.6
CII(succinate malonatedehydrogenase)	0.05	0.07-0.11
CI+CIII (NADH cytochrome coxidoreductase)	0.03 (27.3%)	0.11-0.25
CII+CIII(succinate cytochrome coxidoreductase)	0.01 (20%)	0.05-0.08
CIV(cytochrome coxidase)	0.04 (23.5%)	0.17-0.28
CS(citrate synthase)	10.68	7.80-10.90

Respiratory chain enzyme activities in muscle homogenate. The enzymatic activities of the respiratory chain complexes are expressed as mmol/min/gr muscle tissue and normalized to the activity of citrate synthase, a marker of mitochondrial mass. The percentage of mean residual activity of normal controls is shown in brackets.

Conclusion: The mutation we found has been reported both as a polymorphism and related to the valproate-induced encephalopathy. The present case is the first bearing this mutation in homoplasmy. In case of neurological symptoms after starting VPA therapy, once hyperammonemia and liver failure have been ruled out, mtDNA abnormalities should be considered.

Disclosure: Nothing to disclose

EPO2090

Diagnosis of autosomal recessive spinocerebellar ataxia type-10 (SCAR 10): implications for treatment

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Background and aims: Clinical and imaging features are seldom useful in narrowing the differential diagnosis of autosomal recessive cerebellar ataxias. Next generation sequencing (NGS) has proved its usefulness in establishing a definite diagnosis and enable accurate genetic counselling. SCAR10 is associated with CoQ10 deficit and some case reports have suggested clinical stability with oral supplementation.

Methods: Case report

Results: We present two isolated cases of slowly progressive cerebellar ataxia. Patient#1: A 35-year-old woman with dysarthria, diplopia and gait ataxia, since age 23y. Physical examination showed cerebellar nystagmus, dysarthria, gait and appendicular ataxia, hyperreflexia and bilateral extensor plantar responses. Patient #2: A 51-year-old male with dysarthria, dysphagia, gait ataxia and hyperreflexia starting at 36y of age. Brain MRI revealed global cerebellar atrophy in both cases. Treatable causes of ataxia were investigated, but no abnormalities were detected, besides a CoQ10 deficit in patient #2 (not tested in patient #1). Multiple genetic tests were negative in both cases, including MJD/SCA3, CABC1 (causing CoQ10 deficiency), POLG and FRDA.

A NGS panel showed these patients to be a homozygote (#1) and a compound heterozygote (#2) for pathogenic variants in ANO10, confirming the diagnosis of SCAR10 in both. This prompted treatment with high-dose oral COQ10, resulting in relative stability of cerebellar deficits over more than 5 years, and adequate genetic counselling.

Conclusion: This case highlights the usefulness of NGS in achieving a definite diagnosis in "sporadic" cases of cerebellar ataxia. In rare cases, such as those described here, treatment may be available and result in slowing of disease progression.

Disclosure: Nothing to disclose

EPO2091

New genes on infantile epileptic encephalopathies–five years experience of a terciary center review

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Background and aims: The use of Next Generation Sequencing(NGS), exome and panels, in the previous years has allowed major advances on the identification of causative genes of paediatric epileptic encephalopahies(EE).

Methods: Review of clinical files of children with EE due to new genes identified by NGS since 2012.

Results: We present 10 children (7 boys, 17months-21 years), all presenting with seizures refractory to medical treatment in the newborn period and all evolving to global developmental delay without dysmorphic features or organomegalia. A few distinctive clinical features include global severe hypotonia and scarce spontaneous movements in the child with SLC25A22 mutation and spastic tetraparesis related to KCNQ2, GRIN2A and SCNL2A. The child with MEF2C mutation presents continuous stereotypies and the one with SPTAN1 mutation also shows Rett-like stereotypies but also global chorea and dystonia. One of the 2 children with STXBP1 mutation has autism.

All children presented with global lentification of eletrogenesis except ATP1A3 and multifocal paroxystic activity on EEG. SCNL2A mutation was the only associated with neonatal burst –suppression pattern and ATP1A3 with nonconvulsive status epilepticus.

The only consistent positive response to treatment occurred with the use of ketogenic diet on the children with ATP1A3 and GRIN2A mutations.

Conclusion: The recognition of new causative genes of paediatric EE allows the recognition of suggestive phenotypes, more individualized treatment directed to the dysfunction of codified proteins and paves the way to eventual future genetic treatment. All genes involved code for proteins relevant for synaptic function.

Disclosure: Nothing to disclose

Neuro-oncology

EPO2092

Primary CNS Lymphoma presenting as ophtalmoparesis and facial nerve palsy

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Background and aims: PCNSL is an uncommon variant of non-Hodgkin lymphoma confined to the CNS. Leptomeningeal involvement can occur as a manifestation of systemic lymphoma or synchronously with PCNSL and is exceedingly rare to be found exclusively.

Methods: A 65-year-old woman with history of atrial fibrillation, presented at emergency room, with symptoms of headache, diplopia and imbalance for 3 days. On examination, she had a right abducens nerve palsy, right facial nerve palsy and unsteady gait. No adenopathies were present.

Brain CT and nonenhanced MRI were normal. In the following days, she developed bilateral facial nerve palsy, cervical and lumbar radiculopathies.

Results: A contrast-enhanced MRI revealed bilateral enhancement of the internal acoustic canal, and CSF analysis showed lymphocytic pleocytosis and hyperproteinorraquia. A first flow cytometry immunophenotyping was normal, but a second one revealed malignant lymphocytes supporting the diagnosis of diffuse large B-cell lymphoma. Extensive CSF and serum studies were negative for infectious or systemic autoimmune causes. Body CT and bone marrow aspirate were negative. Initially improved with steroids, the patient developed a severe septic shock due to pneumonia and died 1.5 months later. Upon clinical deterioration, a CT scan revealed multiple mass lesions involving the brain lobes, white matter and cerebellum.
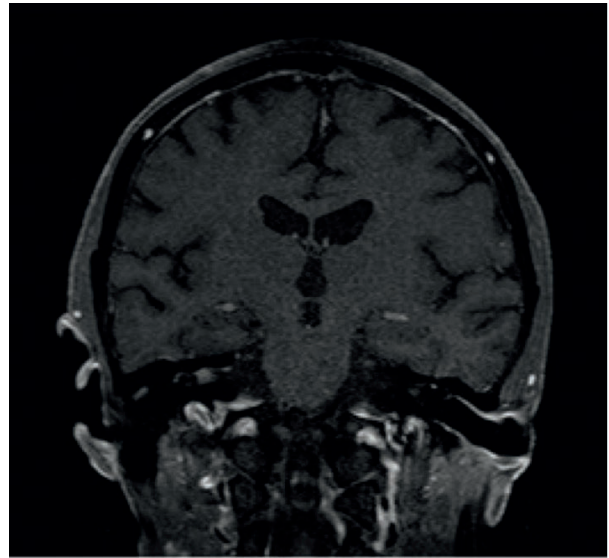
Figure 1: MR imaging with coronal post-gadolinium T1-weighted image with bilateral enhancement of internal acoustic canal.
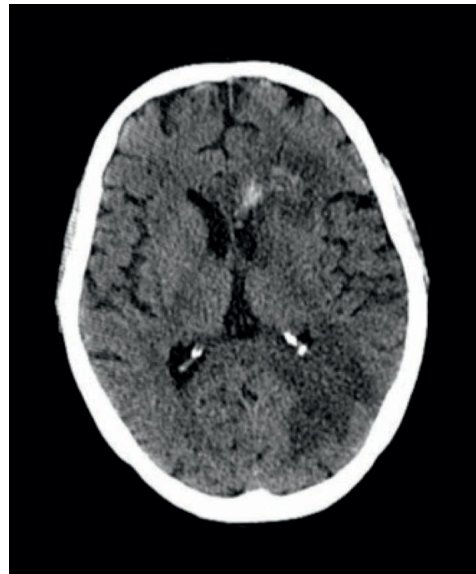
Figure 2: Non-enhanced CT with a hypodense expansive lesion on left striatocapsular region with hyperdense foci compatible with acute intralesional haemorrhage. On left peritrigonal white matter there is a similar lesion, also with haemorrhagic foci (not shown).

Conclusion: Establishing the diagnosis of leptomeningeal involvement from lymphoproliferative disorders can be challenging. In our case, evidence was limited to a subtle contrast enhancement on MRI. Only in a later stage parenchymal lesions could be seen.

We strongly suggest that upon high clinical suspicion, CSF immunophenotyping should be performed and repeated if found negative.

Disclosure: Nothing to disclose

EPO2093

Isolated Castleman's disease affecting the central nervous system presenting as generalized seizure

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Background and aims: Castleman's disease is a rare pathologic process of unknown etiology, characterized by nonneoplastic lymph node enlargement. His clinical features are classified in two categories, localized and generalized, and two distinct histological patterns are also recognized, the hyaline-vascular and the plasma-cells types. Intracranial involvement is extremely rare. We describe a case of localized intracranial Castleman's disease.

Methods: A 30-year-old-man suffered a generalized tonic-clonic seizure that required intravenous administration of benzodiazepines and phenytoin for control. Neurological examination on admission revealed somnolence, disorientation, and mild left hemiparesis.

Results: Seizures were subsequently controlled with oral phenytoin therapy, which was subsequently replaced by lacosamide. A body computerized-tomography (CT) examination and cerebrospinal-fluid (CSF) study found no abnormalities.

Brain magnetic resonance (MR) imaging demonstrated an extraaxial mass in the right temporo-parietal convexity that was homogeneously enhanced with gadolinium. Based on the neuroradiological findings, the presumptive diagnosis was convexity meningo-angiomatosis.

A right temporal craniotomy was performed and the dural-based solid mass was resected. Histological examination of the surgical specimens revealed numerous lymphoid follicles with hyalinized vascular proliferation and the diagnosis was the hyaline-vascular type of Castleman's disease.The patient had an uneventful postoperative course. He was discharged without neurological deficit one week after surgery. After follow up for one year, he remained seizure free without evidence of systemic involvement.
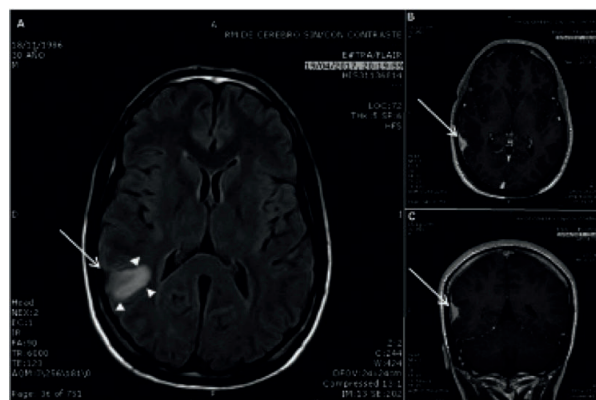
A: FLAIR-weighted magnetic resonance (MR) image showing a mass in the right temporo-parietal convexity (arrow). Brain edema surrounding the mass is extensive in comparison to the size of the mass (arrowheads). B, C: T1- weighted (MR) image after contrast administration showing the mass with homogenous enhancement (arrow).
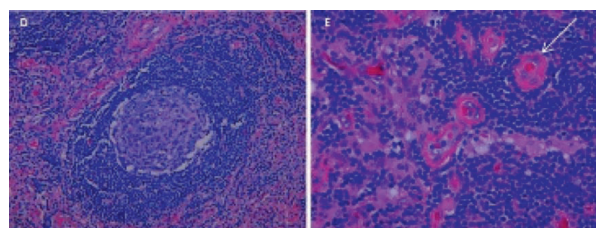
D: Photomicrograph showing rings of lymphocytes surrounding germinal centers. Hematoxylin-eosin stain, original magnification x 80. E: Photomicrograph showing numerous hyalinised vessels (arrow). Hematoxylin- eosin stain, original magnification x 100.

Conclusion: Intracraneal Castleman's is a rare disease that could appear as a solid extracranial mass attached to meninges. It may manifest as seizure or focal signs and it should be considered in the differential diagnosis of meningeal tumors.

Disclosure: Nothing to disclose

EPO2094

Intraspinal intradural nodular fasciitis mimicking glioblastoma metastasis: a case report

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Background and aims: Nodular fasciitis (NF) is a rapidly growing but non-malignant lesion. Due to its rapid growth and unspecific imaging characteristics it is often misinterpreted as a malignant process.

Methods: We report the case of a 78-year-old male patient suffering from a right temporal glioblastoma with radiographic meningeal tumor spread. During the further course of the disease he developed a rapidly progressive paraplegia. An MRI scan showed a contrast enhancing intraspinal intradural lesion with compression of the myelon on segment Th 8/9. With a high suspicion of a spinal metastasis of the known glioblastoma, emergency spinal decompression and resection of the intradural mass was performed.

Results: The resected tissue of the spinal lesion had a total diameter of 1.0cm. There was no specific expression of actin (clone HHF35), calponin, GFAP, STAT6, melan A, pan-CK, EMA, progesterone-receptor and neurofilament. S100 was only focally expressed and CD34 staining was restricted to blood vessels. Thus, a metastasis of the known glioblastoma could be excluded. Additionally, a FISH analysis was performed but failed to show a clear USP6 rearrangement. The lesion was considered to be a reactive proliferation, consistent with a nodular fasciitis.

Conclusion: This patient with a history of a left temporal glioblastoma developed a reactive intraspinal lesion. Although we could not demonstrate an USP6 rearrangement, a characteristic that is often but not always found in nodular fasciitis, we assume nodular fasciitis the most likely diagnosis. To the best of our knowledge, this is the first report of an intraspinal and intradural nodular fasciitis.
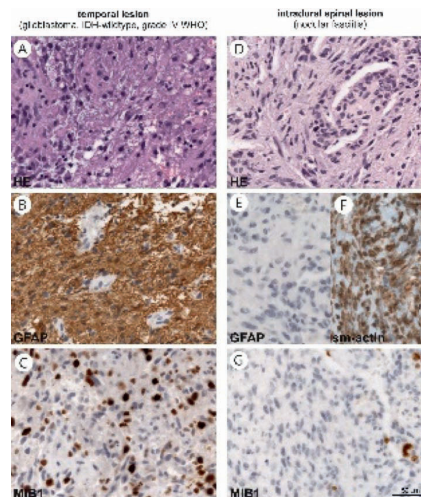
The temporal tumor (A-C) showed cells with an astrocytic morphology, expression of GFAP and numerous MIB1-positive cells. In contrast, the spinal lesion consisted of spindle shaped cells. Epitheloid cells were noted (D). This lesion lacked expression of GFAP (E), was immunoreactive for smooth muscle actin (F) and showed MIB1-positive cells (G).
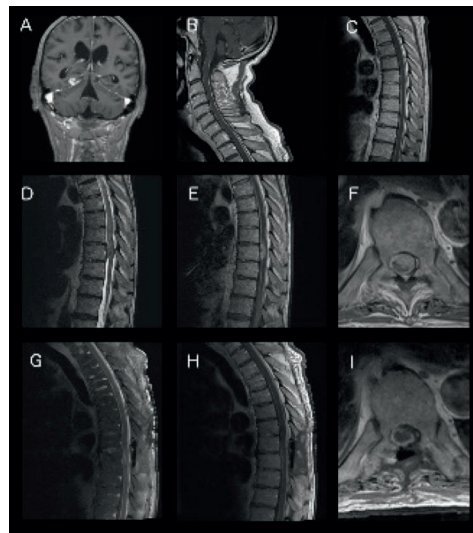
Right-sided multicentric temporomesial contrast-enhancing lesion on postcontrast T1 sequences (A+B) with spinal leptomeningeal tumor spread (C+D). Novel intradural lesion at the level Th8/9 on spinal MRI (E+F). The postoperative images showed a good decompression of the myelon and partial resection in postcontrast T1 and T2 sequences (G+H).

Disclosure: Nothing to disclose

EPO2095

Intravascular Lymphoma of central nervous system – the great imitator

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Background and aims: Intravascular lymphoma (IVL) is a rare variant of extranodal diffuse large B-cell lymphoma restricted to the vascular lumina, affecting preferentially the Central Nervous System and skin, with non-specific clinical manifestations, which pose a diagnostic challenge.

Methods: n/a

Results: Case report: A 59-year-old male with history of stage IV lymphoplasmocytic lymphoma (LPL) 2 years prior to admission, in remission, presented with acute right hemiparesis. After a thorough investigation, he was discharged with a diagnosis of stroke but subsequently progressive gait difficulties and impaired cognitive function ensued. Two months later, general examination was unremarkable and a neurological examination showed multiple-domain cognitive dysfunction, right spastic hemiparesis, and gait instability. The laboratory workup revealed persistently elevated LDH, CPR and ESR. Brain MRI showed bilateral and multifocal (left predominant) hyperintense T2- and T2-FLAIR-weighted white-matter parieto-occipital lesions, also involving the splenium of corpus callosum and right middle cerebellar peduncle, without restricted diffusion or contrast enhancement. CSF examination was negative, including cytological analysis without malignant cells, no intrathecal immunoglobulin synthesis and unremarkable immunophenotyping. Due to clinical progression, brain MRI was repeated 10 days later and revealed bilateral progression of the previous lesions to the temporal and frontal lobes, with diffusion restriction and patchy contrast enhancement. A brain biopsy was performed, confirming the diagnosis of B-cell intravascular lymphoma.

Conclusion: Discussion: It is unclear whether IVL represented a transformation from LPL, or whether it was a de novo lymphoma. Nevertheless, our case should raise awareness for early brain biopsy in cases of progressive neurological deterioration with nonspecific findings in brain MRI.

Disclosure: Nothing to disclose

EPO2096

Lymphoma T type with cerebral presentation: report of 3 cases

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Background and aims: More than 90% of lymphoma witch cerebral présentation are diffuse and large cell B type, and most of them are restrained to the CNS.
Aims : define et description of T-Lymphoma with cerebral présentation.

Methods: Based on prospective cohorte of primary cérébral lymphoma, between 2011 and 2017, in a tertiary health-care derpartement of neuro-oncology, Pitie-salpétrière hospital in paris, that include 212 case of PCL. We aimed to select T-lymphoma define by histology analysis and double-analyzed with two différents pathologists.
3 cases have been identified (1.4% of all cases of PCL), 1men/2females, aged between 57 and 77 yo. All of them were immunocompetents.

Results: 1 case had caeliaque disease. 2 of them had a typical radiologic presentation, the third had a lymphomatosis cerebri présentation. None of them had ophtalmologic or LCS dissemination. One of them had an extra-cerebral lesion (surrenal gland localization), the others had no extra-neurologic dissemination.
All have been treated with chemotherapy based on methotrexate high dose : 1 patient presented a complete response, one presented partial response and progression that was prevent by second ligne (Ifosfamide Etoposide carboplatine) completed by autologous cell graft. The third one died after partial response. Complete and sustained response was achieved in 2 cases with a mean follow-up of 26 months (12-40 months).

Conclusion: T-lymphoma with cerebral présentation are rare and seems to share the same prognosis and response to standard treatment, as in primitive cerebral B-lymphoma, but more than in B-lymphoma most make investigate an extra-neurological dissemination.

Disclosure: Nothing to disclose

EPO2097

Epithelial-Myoepithelal Cell Carcinoma (EMCC) arising from salivary glands heterotopia in Meckel's cave

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Background and aims: EMCC is a rare malignancy comprising 1% of all salivary gland tumor generally arising from parotid gland. The histological hallmark is the bi-layered epithelial-myoephitelial phenotype.

Methods: A 36-year-old woman presented with subacute right eye ptosis and unreactive mydriasis. A high-dose corticosteroids (CCS) cycle was tempted without significant clinical improvement. After few days, the patient developed right lateral gaze diplopia and trigeminal V2 hypoesthesia.

Methods: Cerebrospinal fluid (CSF) examination, optical coherence tomography (OCT), brain MRI with/without contrast, orbital CT scan with 3D reconstruction, endoscopic endonasal biopsy.

Results: CSF analysis resulted normal. OCT revealed right eye papilledema. Brain MRI showed slightly T2-hyperintense tissue enlarging Meckel's cave and following as a sheet the course of the carotid artery. After gadolinium (Gd) administration, it presented intense and homogenous enhancement. The orbital CT scan confirmed the right superior orbital fissure enlargement. The second MRI (after CCS cycle) showed right eye muscle cone and trigeminal nerve involvement through the oval foramen. Microscopically, the mass was composed of nests of neoplastic cells with central glandular spaces, surrounded by an inner layer of eosinophilic cells immunoreactive with CK17 and CD117 and by multiple outer layers of clear cells positive with smooth muscle actin. Ki67 immunostaining was positive in 20% of the neoplastic cells.
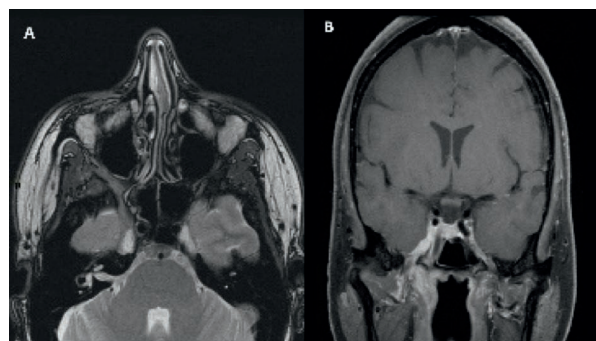
Figure 1. Brain Mri Before (A) And After (B) Gadolinium Administration
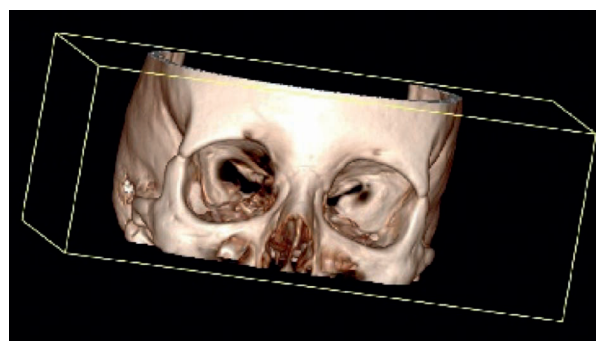
Figure 2. Orbital Ct (3D Reconstruction) Showing Right Superior Orbital Fissure Enlargement
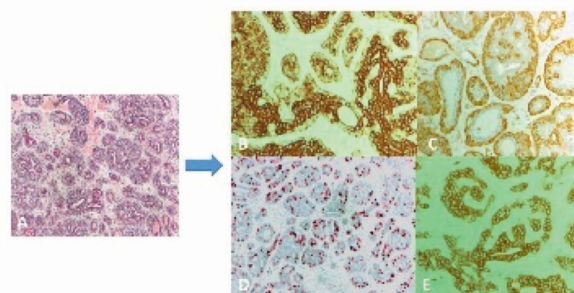
Figure 3. H&E Stain (A) And Immunostaining (B=CK7, C=SMA, D=CD117, E=Ki 67)

Conclusion: Salivary glands heterotropia has been described in various head and neck districts and peripheral organs. On the basis of neuroradiological and clinical features, we described the first case of EMCC originated from salivary gland heterotopia in Meckel's cave.

Disclosure: Nothing to disclose

EPO2098

Multiple sleep latency test and symptoms of paraneoplastic lesion of the limbic system in patients with breast cancer

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Background and aims: Paraneoplastic limbic encephalitis is a rare condition and some difficult to diagnose. The symptoms of paraneoplastic lesions of limbic system occur only in 8% patients with breast cancer, include sleep disorders, anxiety, depression, cognitive impairment, and they are associated with onconeural antibodies. Debut of neurological symptoms of paraneoplastic limbic encephalitis precedes clinical manifestation of breast cancer from 3-5 months to 4 years.

Objective: To detect and analyse the clinical, neurophysiological and neyroimmunological markers paraneoplastic lesions of limbic system in patients with breast cancer.

Methods: 7 women with breast cancer II-IV stages were examined; mean age: 45.28±8.13 years. Detection onkoneural of antibodies in the serum of patients were carried out using Neuronal Antigen Profile EUROLINE (IgG) in vitro by immunoblotting. Was used valid tests and scales: MoCA, HADS, BDI, HDRS. The average time of falling asleep (MSLT) was performed by standard technique on the apparatus firm "Nicolet". Control group: 7 healthy women were matched for age.

Results: Onkoneural antibodies were found in the sera of 100% of patients (anti-Hu-43%; anti-Yo-57%). In patients were revealed high levels of anxiety (BDI: 17.14±9.35; HADS: 12.14±3.53), depression of moderate severity (HDRS:15.14± 5.49) and mild cognitive impairment (MoCA: 21.28±3.14)-memory disorders. Average sleep latency in the group of patients (17.12min) was significantly higher than the average latency in the group of healthy (9.3min) p=0.006012.

Conclusion: Neurophysiological, laboratory and clinical evidences are confirmed paraneoplastic lesions of the limbic system of the brain in pations with breast cancer.

Disclosure: Nothing to disclose

EPO2099

Retracing the steps of melanocytic dissemination: from venous infarctions to cerebral metastases

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Background and aims: The incidence of brain metastases arising from melanoma is approximately 10% and leptomeningeal metastases occur in 5-7%. Primary central nervous system melanoma is fairly rare, accounting for 1% of all cases of melanoma and 0.07% of brain tumours.

Methods: We report the case of a 65-year-old man presenting with a haemorrhagic venous infarction of the left temporal lobe, conducive to motor aphasia and right-sided hemiparesis. The brain magnetic resonance imaging also revealed peculiar supratentorial cerebral and meningeal lesions suggesting neoplasia or vasculitis. Stigmata of another similar hemorrhage were found in the left frontal lobe. Extensive blood testing and cerebrospinal fluid analysis were unremarkable. The patient declined undergoing brain biopsy at the time. Over the next months the symptoms worsened and progression of lesions with necrosis and surrounding vasogenic oedema was found on computed tomography. A brain biopsy was performed for histological and immunohistochemical assessment.
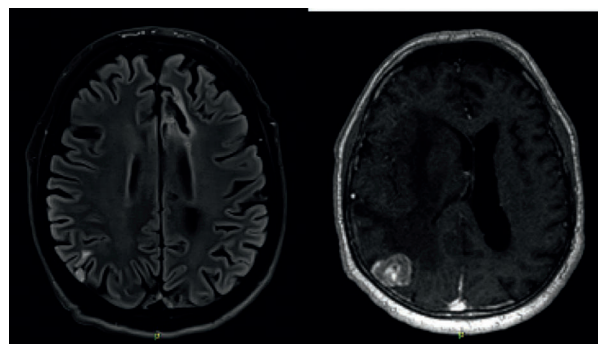
Brain MRI. Axial fluid attenuation inversion recovery-weighted image (left) showing right parietal mass of probable meningeal origin and left-sided frontal lesion bearing stigmata of haemorrhage. Axial T1-weighted image performed 7 months later (right) showing the same right parietal contrast-enhancing mass, larger, with surrounding oedema
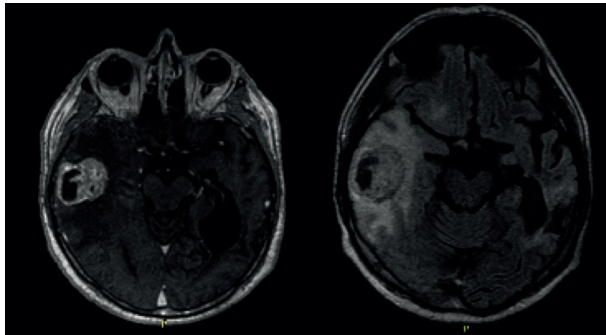
Brain MRI. Axial T1-weighted sequence (right) and fluid attenuation inversion recovery-weighted scequence (left) showing a right temporal lesion with an inner necrotic area and surrounding vasogenic oedema

Results: Histopathological and immunohistochemical evaluation were consistent with cerebral metastasis from malignant pigmented melanoma. There were no suspicious primary lesions, but the patient recounts having had a thoracic lump excised some years prior, allegedly benign, unfortunately unavailable for second opinion. The meningeal lesion prompts considering a leptomeningeal metastasis, yet a primary meningeal melanoma, albeit less likely, might also be entertained.
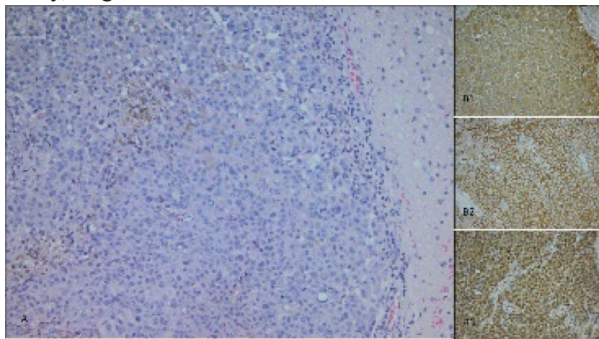
A. Histopatological specimen hematoxylin and eozin stained, 200 times enhanced, showing malignant melanocytic proliferation (left) and immunohistochemical stains 400 times enhanced (right) confirming the melanocytic origin through S100 positivity (B1), HMB45 positivity (B2) and MITF positivity (B3)

Conclusion: The co-existence of cerebral venous infarctions with melanoma is a particular finding and its differential diagnosis will be further discussed. Prompt histopatologic reevaluation of previously excised suspicious lesions should be strongly considered especially if brain biopsy cannot be performed.
Disclosure: Nothing to disclose

EPO2100
Adult ependymoma: experience in our hospital

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Background and aims: Ependymomas are tumors that grow from the ependymal epithelium of the ventricular system; rarely from the brain parenchyma or from other tissues. They represent less tan a 10% of brain tumors and 25% of medullary tumors (60% of intrmedullary ones). We review our experience.
Methods: Retrospective revision of adult ependymoma cases in our hospital from January of year 2012 to May of 2017. We analysed demographic data, location of the tumor, histological type and clinical features.
Results: Forty patients are included, 18 women/22 men, with an average age of 47 years old (from 17-75). There were 20 brain tumors (7 of them of supratentorial location, 13 infratentorial) and 20 medullary (13 in the terminal filum and the rest of them cervicodorsal). 2 of the patients were twins and surgically treated of the same infratentorial tumor type. The most common histological type was classic ependymoma, grade II of the OMS (38% were located in brain, 31% medullary) and the myxopapillary (grade I) represented a 62% of the filum ones. The main symptoms were headache (43%), disbalance (43%) in brain tumors; and pain (58%) in spinal. A fillum ependymoma first symptoms were those of superficial siderosis.
Conclusion: In our series, the number of brain ependymomas is lightly higher than published in medical literature; age and histological types are similar to described. We point out some atypical cases: the presentation in twins and the debut as superficial siderosis of the central nervous system.
Disclosure: Nothing to disclose

Neurorehabilitation

EPO2101

Central hypoventilation syndrome in posterior circulation stroke: a case report.

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Background and aims: Central hypoventilation syndrome is a rare condition characterized by the failure of automatic breathing, which can result from various central nervous system disorders. Several cases have been reported, most of which resulted in death. We report the case of a patient with central hypoventilation syndrome caused by a posterior circulation stroke, which was improved by respiratory rehabilitation.

Methods: A 59-year-old woman had experienced a hemorrhagic stroke of the bilateral cerebellum, and had suffered from recurrent respiratory distress and aspiration pneumonia since the stroke occurred. The brain MRI showed encephalomalacic changes in bilateral cerebellar hemispheres, the left middle cerebellar peduncle, the left pons, the left anterior, and the right lateral medulla (Fig.1).
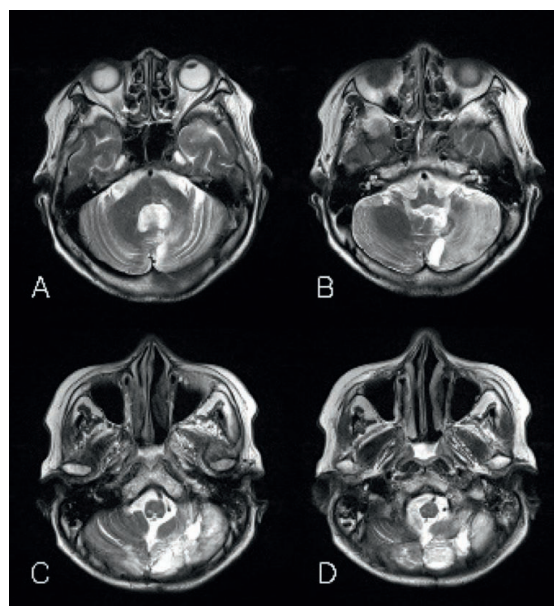
The brain MRI showed encephalomalacic changes in both cerebellar hemispheres, left middle cerebellar peduncle, left pons, left anterior and right lateral medulla.

Results: With a portable ventilator applied via tracheostomy, a respiratory rehabilitation program including intercostal muscle strengthening and diaphragmatic breathing exercises proceeded. After 4 weeks of rehabilitation, a pulmonary function test showed improvements in respiratory parameters (Fig.2). Consequently, the portable ventilator was applied for 8 hours only during night time to prevent sudden apnea.
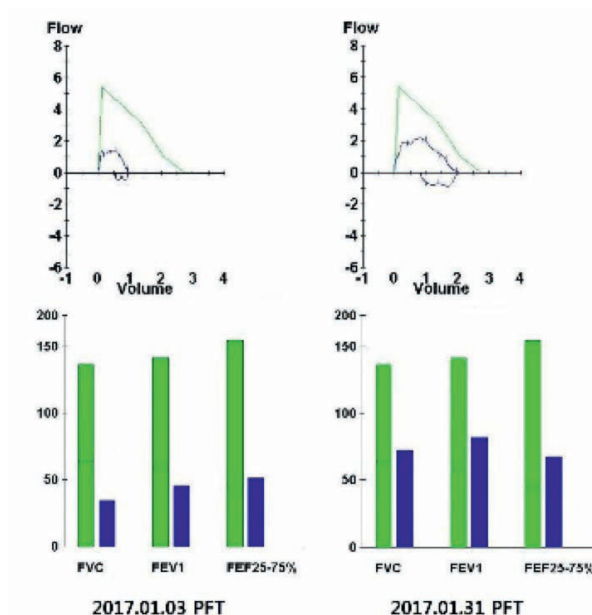
The changes of pulmonary function test. The left showed initial pulmonary function test, and the right showed follow-up pulmonary function test. The results showed improved respiratory parameters after respiratory rehabilitation.

Spirometry	2017.01.03		2017.01.31	
	Pre	%Ref	Pre	%Ref
FVC (Liters)	0.95	35	1.99	73
FEV1 (Liters)	0.92	46	1.65	82
FEV1/FVC (%)	97		83	
FEF25-75% (L/sec)	1.26	51	1.65	67
FEF50% (L/sec)	1.34	42	2.07	68
PEF (L/sec)	1.40	26	2.15	40

The changes of pulmonary function test parameters. After 4 weeks of respiratory rehabilitation, FVC and FEV1 were improved as double.

Conclusion: In this case, the lesions in the pneumotaxic center of the pons and the ventral repiratory group in medulla seem to attribute to reduced chemosensitivity and impaired breathing coordination. There is no consensed diagnostic criteria for central hypoventilation syndrome, and the clinical courses are unpredictable. Several therapeutic options are available, including pharmacological approaches and the use of mechanical ventilators, and diaphragmatic pacemakers. Our case was the first to suggest that respiratory rehabilitation can contribute to favorable outcomes in the treatment of central hypoventilation syndrome.

Disclosure: Nothing to disclose

EPO2103

A preliminary study on the performance of one-leg versus two-leg symptom-limited exercise test in individuals with subacute stroke

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Background and aims: Based on previous studies, healthy individuals have shown to reach higher maximal oxygen consumption and greater workloads in a two-leg maximal cycling exercise test than in a one-leg test. However, for individuals with low aerobic capacity, such as subacute stroke patients, whether the above-mentioned physiological differences between two types of exercise tests still exist is unknown. Therefore, this preliminary study was to investigate physiological performances of one-leg versus two-leg symptom-limited cycling test in individuals with subacute stroke.

Methods: Ten people with subacute ischemic stroke were recruited. A stationary bike (Corival, Lode, Finland) was used to perform one-leg and two-leg symptom-limited exercise tests. Two tests were conducted on separate days within one week. The test order was randomized. Oxygen consumption and heart rate were continuously monitored by a metabolic cart (Metamax 3B system, Cortex, Germany) and data were analyzed breath-by-breath. Peak power (Powerpeak), oxygen consumption (VO2peak), and heart rate (HRpeak) were used for statistical analyses.

Results: Powerpeak, VO2peak, and HRpeak for one-leg versus two-leg tests were 50 vs. 54 watts, 0.617 ± 0.010 mlO2/kg/min vs. 0.651 ± 0.038 mlO2/kg/min, and 119.1 ± 19.7 vs. 117.4 ± 20.3 beats/min, respectively. No statistical significances ($p>0.05$) were found on all physiological responses for one-leg versus two-leg symptom-limited cycling tests.

Conclusion: This pilot study reveals that one-leg and two-leg symptom-limited cycling exercise induce similar physiological responses in individuals with subacute stroke. Future studies recruiting more individuals with subacute stroke are needed to further confirm this finding.

Disclosure: This study is partly supported by a grant from Ministry of Science and Technology, Taiwan (MOST 103-2314-B-037-003-MY3).

EPO2104

The assessment of balance function using the game system "virtual reality"

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Background and aims: Balance disorders are common symptoms in patients with diseases of the central nervous system, visual and vestibular analyzers. Assess the condition of balance function (BF) in patients with peripheral vestibular syndrome (PVS) and healthy persons using the game system "Virtual reality" (VR).

Methods: There were investigated 20 healthy persons (mean age 26.22 ± 9.14 years), 10 patients (mean age 29.22 ± 11.04 years) with PVS. There was used the equipment for applications Unity3d with VR "HTC Vive" with optical method of tracking body position. There were designed such parameters as average speed of postural axis (PA), the area of the support contour PA, which were measured in a standing position for 20 s, without using the VR and standing using VR for 20 s. There were calculated the coefficients S and K.

Results: In the group of healthy: 15 S=$1.03\pm0,21$; K=0.97 ± 0.29, what characterizes a sustainable BF. 5 S=0.97 ± 0.23, K=$0,49\pm0,41$ that reflects of a sustainable BF. In the group of patients with PVS: 5 S=0.77 ± 0.22 and K=0.19 ± 0.19 and reflect latent violations of BF, 2 S=0.91 ± 0.27 K=0.51 ± 0.44, which reflects the phenotypic features of sustainable BF, 3 patients; S=0.90 ± 0.11; K=0.93 ± 0.22 what characterizes a sustainable BF.

Conclusion: The method can be used to reveal disorders and features of the BF in healthy and patients with PVS on the basis of quantitative indicators of the postural movement of the axis in VR that will allow you to develop an individual program of rehabilitation of BF.

Disclosure: Nothing to disclose

EPO2105

Features of the bioelectric motor activity of the cerebral cortex in patients with upper limb motor disorders following a stroke

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Background and aims: The use of non-invasive neurocomputer interfaces based on EEG data in a rehabilitation is a promising strategy for improving the quality of life of patients after a stroke. However, there are still very few studies that have shown the features of EEG in healthy people and in patients with upper limb motor disorders following a stroke.

Methods: 5 healthy subjects and five patients with I63.3 Cerebral infarction due to thrombosis of cerebral arteries (the middle cerebral artery (MCA) infarction) underwent tasks with movements and subsequent movement imagination. The Encephalan-131-03 encephalograph (EEGA-21/26, Russia) with built-in software for data analysis was used for EEG registration. The electrodes were placed according to the scheme of 10-20%.

Results: The alpha-rhythm predominated during the study (8.00-13.00Hz) in healthy subjects. The theta rhythm (4.00-8.00Hz) in zones F3-C3, F4-C4 was registered for movements and the subsequent imaginary movements. While the examination of patients after a stroke has demonstrated beta-1 rhythm to be predominated (13.00-24.00Hz). Also there were theta rhythm (4.00-8.00Hz) in zones F3-C3, F4-C4 and beta-2 rhythm (24.00-35.00Hz) in the zones corresponding to MCA. Similarly, in both groups, alpha rhythm (8.00-13.00Hz) was registered in the P3-PZ-P4 zones during imaginary movements.
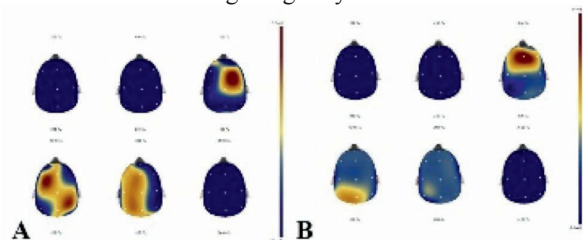
Fig. 1. Topographic mapping of spectral EEG characteristics of a healthy subject
(A) Activity during the execution of the block of tasks of real movements.
(B) Activity during the execution of the block of tasks on the imagination of movements
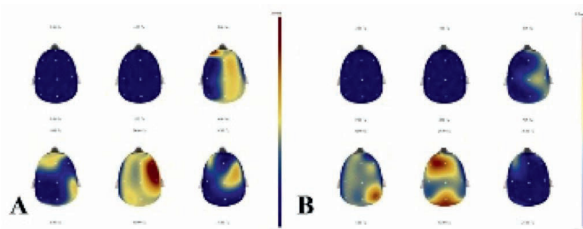
Fig. 2. Topographic mapping of spectral EEG characteristics of the patient after a stroke
(A) Activity during the execution of the block of tasks of real movements.
(B) Activity during the execution of the block of tasks on the imagination of movements

Conclusion: This study confirms the presence of bioelectrical features in patients with upper limb motor disorders following a stroke manifested by differences in the prevailing rhythm, localisation of excitation, the appearance of beta-2 rhythm during motor activity.

Disclosure: Nothing to disclose

EPO2106

Efficacy of training in virtual environment in patients with balance disturbances

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Background and aims: In the recent meta-analysis, it has been shown that the use of VR in combination with conventional therapy and as an alternative technique leads to a more significant recovery. The aim of our research was to study the efficacy of VR training in patients with balance disturbances.

Methods: 25 patients were included in the study, (mean age 67 [49; 72], median Berg balance scale 50 [42, 54]) with static and dynamic balance problems following chronic cardiovascular disease. Main group (n=15), received two weeks (30 min, 5 days\week) of virtual biofeedback training on Kinect based system «Rehabunculus» and conventional therapy. Control group (n=10) received equal time conventional therapy. Evaluation methods: Barg Balance Scale, objective Romberg test on Kinect based system.

Results: The preliminary data showed significant improvement in static and dynamic balance measured with BBS & Romberg test (p>0,05) in the main group. Also is clearly demonstrated improvement of single support phase during forward stepping. 5 patients (33%) increased their ability to walk without cane outdoor. In control group significant changes were observed only in static balance measured with BBS, Romberg test shoved only trend to improvement.

Conclusion: Preliminary data evidence that Rehabunculus VR system can be used for more intensive and effective stationary rehabilitation in combination with conventional therapy than conventional therapy alone.

Disclosure: Nothing to disclose

EPO2107

The impact of stroke severity on the outcome of clinical trials

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Background and aims: Using the results of two identical stroke studies with highly deviating baseline severity the discriminative power of common clinical outcome scales is evaluated in a meta-analytic framework in order to learn for future study designs and to avoid unnecessary loss of test power. Both studies had a prospective, randomized, double-blind, placebo-controlled design.

Methods: Treatment with 30ml Cerebrolysin once daily for three weeks was started 24-72 hours after stroke onset. In addition, patients participated in a standardized rehabilitation program for 21 days that was initiated within 72 hours after stroke onset. For both studies the original analysis data were used for meta-analysis (individual patient data analysis).

Results: Outcome at day 90 shows considerable heterogeneity due to marked ceiling effects in the population with mild baseline severity, while the analysis of early benefit (day 14, day 21) by means of the National Institutes of Health Stroke Scale, which is regarded as most sensitive to early improvements, showed high discriminative power in both study populations despite different baseline severity levels.

Conclusion: These new results strongly support the earlier findings of DeGraba (1999) who highlighted the importance of baseline stroke severity in stroke trials for discriminative power at different selected points in time. Despite heterogeneity of study populations the meta-analysis was able to well demonstrate beneficial effects of Cerebrolysin on motor function and neurological status in early rehabilitation patients after acute ischemic stroke.

Disclosure: Nothing to disclose

EPO2108

Pilot study of visual biofeedback and stabilometric platform use in home therapy of balance impairment in people with Multiple Sclerosis

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Background and aims: Balance impairment in people with multiple sclerosis (MS) is common. Gaming systems (Nintendo, Kinect.) have been tested for home therapy, however, cannot be properly individualised. Therefore a small portable system that includes stabilometric platform with visual biofeedback (Homebalance). Aim of this study is to evaluate the use of portable system for balance training in the home setting.

Methods: Home training was performed daily 20 minutes for 4 weeks The following assessments were performed at baseline and after 4 weeks of the training: Timed 25 foot walk test (T25FW), Timed Up and Go test (TUG), Berg balance test and mini BEST test, MS Walking Scale-12 and Falls Efficacy Scale.

Results: There were enrolled 10 people with MS, mean age 38.4 years (SD 6.7 y), mean disease duration 14.4 years (SD 6.8 y) with EDSS 1.5 to 6,. All participants completed 4 weeks training. Mean T25FW improved from 16.5 to 11.6 sec, TUG improved from 19.5 to 13.5 sec and TUG with a cognitive task improved from 22.3 to 15.2 sec. BEST test changed from 18.4 to 19.6 and Berg test score from 38.8 to 40.2.

Conclusion: Our pilot study showed feasibility of this type of training in group of people with MS. Audiovisual biofeedback helps to control exercise performance at home. Homebalance training was effectively used with people with mild balance and problems as well as with people with severe disability.

Supported by the project Progres Q27/LF1

Disclosure: Nothing to disclose

EPO2109

Clinical effectiveness of Botulinum Toxin (BoTN) injections in patients with sialorrhea and drooling

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Background and aims: Sialorrhea and drooling are common symptoms of many different neurological diseases and can increase the risk of aspiration. It affects the normal chewing mechanism and has a significant negative effect on social function. The objective of this study is to evaluate the effectiveness and safety of Botulinum Toxin A (BotoxR) injections in patients with drooling and sialorrhea and to assess the safety and adverse effects of Botulinum Toxin A (BotoxR) injections in the major salivary glands as there is a lack of NICE guidance.

Methods: We assessed the notes of patients treated with Botulinum Toxin A (BotoxR)* injections for sialorrhea and drooling in the Botox clinic (University Hospitals of Leicester) between 01st July 2015 and 31st December 2015.

Results: In our Botox cohort improvement in the drooling scales (more than 25% improvement) was found in 71% of the patients; no improvement (<25% improvement) in 29% of the patients; which is similar to published data in other studies. 14% of the patients reported mild adverse effects (dry mouth, odd taste).

Conclusion: BoTN injections are a useful option in the symptomatic control of sialorrhea and drooling. The BoNT injections for sialorrhea and drooling improve the quality of life of the patients with mild and infrequent side effects BoNT injections without ultrasound guidance (US) are effective, but the US guidance may improve the safety of the injections, especially in the submandibular salivary glands (Egevad et al.).

Disclosure: Nothing to disclose

EPO2110

The IRCCS Network of Neuroscience and Neurorehabilitation: the Italian platform for care and research about neurodegenerative disorders

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Background and aims: The IRCCS Network of Neuroscience and Neurorehabilitation is mainly focused on the sharing of knowledge, protocols and data, in order to promote the standardization and optimization of patients' clinical-care and therapeutic strategies.

Methods: Involving 24 highly specialized IRCCSs, the Network is providing several improvements to the research on neurodegenerative disorders, allowing:
- the centralization of genetic analyses
- the sharing of analytical and instrumental data
- the sharing of interpretation guidelines for genetic and instrumental data
- the characterization of sub-phenotypes of disease
- the development of standardized protocols
- the creation of a database of genomic variants
- the multidisciplinary evaluation of VoUS (variants of uncertain significance) from genomic analyses

Results: Furthermore, the development of the Network allowed the creation of a multidisciplinary platform for consultation between physicians and telecounseling, in order to improve the medical care of patients. Moreover, the integration of clinical and genomic data lead to a better characterization of patients. This innovative approach lays the foundations for the development of personalized medicine strategies based on a deep characterization of patients. In fact, one of the most innovative aspects of the network was the recording of dynamic data, collected not only at the time of the enrollment, but also in the follow-up evaluations.

Conclusion: It is expected that the collaboration between members of the IRCCS Network will support research programs on neurodegenerative disorders. The platform will support the sharing of genomic, epigenomic, pharmacogenomic data as well as traditional clinical measurements as family history, clinical outcomes and instrumental data.

Disclosure: On behalf of the Genomic and Proteomic Network of the Italian Institutes for Research and Care (IRCCS)

Peripheral nerve disorders

EPO2112

Bifacial weakness with paresthesias: a case associated with Campylobacter jejuni infection and electrophysiologic evidence of axonal loss in facial nerves

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Background and aims: Bifacial weakness with paresthesias (BFP) is a rare variant of Guillain-Barré Syndrome. Patients present with rapidly progressive bilateral facial weakness, distal limb paresthesias, and hyporeflexia, without ataxia, limb weakness or other cranial neuropathies. It is typically a demyelinating neuropathy. Here we report a case of BFP with electrophysiologic evidence of axonal degeneration in facial nerves and Campylobacter jejuni infection.

Methods: Case report

Results: A healthy 39-year-old Native American woman presented with a 10-day history of lower back pain, paresthesias in all limbs, followed by facial diplegia. A week before these symptoms she had fever and myalgia. Examination showed facial diplegia (Figure 1), absent lower extremity reflexes, and otherwise normal neurologic functions. CSF showed albuminocytologic dissociation. Antibody titers to Campylobacter jejuni were elevated. Anti-ganglioside antibodies and other infectious and inflammatory studies were negative. MRI studies of the brain and entire spine were normal. At presentation, facial motor responses were present and blink reflex responses were absent suggesting possible proximal conduction block in the facial nerves. Electromyography showed low amplitude motor unit potentials with reduced recruitment in orbicularis oris. She was treated with IVIG. Electrophysiology studies one week later showed absent facial motor responses, absent blink reflexes, and denervation in orbicularis oris, indicating axonal degeneration. Six months later, she had resolution of paresthesia, and clinical and electrophysiological improvement of bilateral facial neuropathies.

Figure 1: Bilateral lower motor neuron facial nerve weakness. Patient asked to (A) "close eyes", (B) "smile", (C) "kiss", (D) "puff up your cheeks". The photographs are reproduced with the patient's permission.

Conclusion: The patient's clinical presentation is typical of BFP. This is the first report of BFP associated with Campylobacter jejuni infection and electrophysiologic documentation of axonal loss affecting the facial nerves.

Disclosure: Nothing to disclose

EPO2113

Iatrogenic medial antebrachial cutaneous neuropathy – an uncommon complication of a common procedure

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Background and aims: Medial antebrachial cutaneous nerve can be involved in brachial plexopathy especially involving the medial cord but isolated medial antibrachial neuropathy can occur as a complication of ulnar nerve surgery at the elbow or rarely, as in our case, with hormonal contraceptive implant insertion in distal medial arm.

The aim of this case is to highlight an uncommon complication of a comon procedure. We present a case of iatrogenic antebrachial cutaneous neuropathy seconadry to Implanon® insertion.

Methods: We report a case of medial antebrachial cutaneous neuropathy in a 19-year-old female after insertion of an implantable hormonal contraceptive containing etonogestrel (Implanon®). The symptoms started with pain at the site of insertion in the medial arm and left elbow soon after insertion associated with dysaesthsia and reduced sensation in the medial forearm. The implant was removed 4 months later due to ongoing symptoms. Whilst her symptoms have slightly improved, she is left with a reduced/altered sensation in the distribution of left medial antebrachial cutaneous nerve of the forearm.
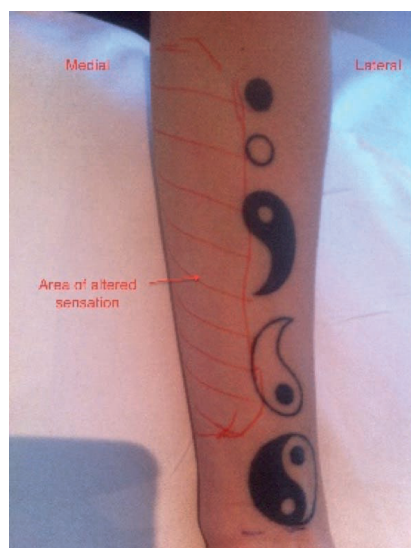
Picture displaying the approximate area of reduced sensation and dysaesthesia in the distribution of medial ante-brachial cutaneous nerve
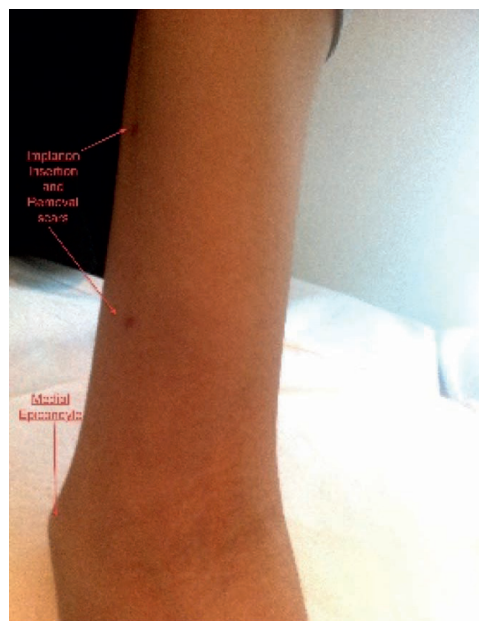
Picture showing the scars of Implanon® insertion and removal

Results: The electrophysiological study of the left upper limb were within normal limits except for a reduced left medial antebrachial sensory nerve action potential (SNAP) amplitude–being less than 50% compared to the right indicating an isolated left medial antebrachial cuatenous mononeuropathy.

Conclusion: One needs to be aware of this rarely reported complication of medial antebrachial cutaneous neuropathy due to insertion or removal of hormonal contraceptive implant in the arm. Electrophysiological studies can be useful in the diagnosis. Early recognition and managgment may lead to better outcome.

Disclosure: Nothing to disclose

EPO2114

What may be hidden under the most common forms of polyneuropathy: keep your mind open

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Background and aims: Over the last decade the early diagnostic of TTR-FAP became very important due to an available pathogenic therapy. The challenge of diagnostics is caused by non-specific symptoms of the disease on it's early stage and mimicking for other more common forms of polyneuropathy.

We aimed to report a case of familial amyloid polyneuropathy which was misdiagnosed with toxic polyneuropathy.

Methods: Nerve conduction study and DNA sequencing were performed. A right sural nerve biopsy specimen was obtained for histological investigation.

Results: We observed a 57-year-old caucasian man who complained of a progressive numbness and decreasing of temperature sensation in the feet and hands, which started 6 years ago. Also he presented distal and proximal weakness in the legs, severe fatigue and 10 kg lost within the last year. A history of severe alcohol consumption made the diagnosis of toxic polyneuropathy. Detailed interview revealed problems with urination and diarrhea, which started 6 month ago. There was a positive family history of weakness in the legs. NCS showed signs of sensorimotor axonal and demyelinating polyneuropathy, which fulfilled the electrodiagnostic criteria of probable CIDP. The sural nerve biopsy specimen showed focal edema and very small amyloid deposits in the subperineural tissue. DNA-sequencing of the TTR gene identified a rare c.157T>C (Phe53Leu) mutation, associated with FAP, which is the first case in Russia.
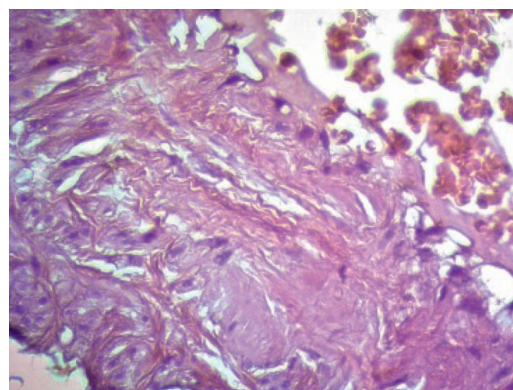
Right sural nerve biopsy, Congo red stain
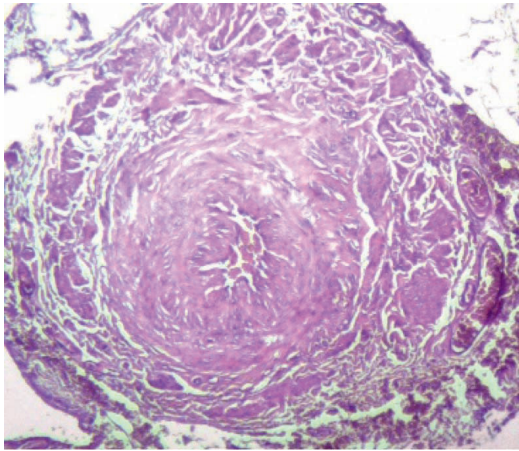
Right sural nerve biopsy, hematoxylin and eosin stain

Conclusion: "Red flags" of the amyloid polyneuropathy may absent in it's early stage leading to a misdiagnosis. Presented case shows that TTR-FAP is a mimicking disease, requiring complex diagnostics with an obligatory genetic testing.

Disclosure: Nothing to disclose

EPO2116

A case of Facial Onset Sensory and Motor Neuronopathy Syndrome (FOSMN) with familial history of Amyotrophic Lateral Sclerosis (ALS) and sensory symptoms

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Background and aims: FOSMN is a rare neurological syndrome characterised by slowly progressive sensorial disturbs and motor weakness, spreading craniocaudally from the face to the limbs. Only 38 cases were described up to 2016. We report on a case of a 79-year-old man, whose brother died at the age of 57 year of ALS, after 2 years of disease.

Methods: The patient underwent complete neurological examination, brain Magnetic Resonance Imaging (MRI), extensive neurophysiological assessment and muscular biopsy. Information about his brother's neurological history was recollected.

Results: Dysesthesia and burning paraesthesia of the facial area were the initial symptoms, first experienced 20 years ago and slowly spreading to the limbs. Motor involvement came later in the course of the disease. He has no other relevant comorbidity. The last neurological examination showed bulbar involvement and diffused muscular hypotrophy, with spontaneous fasciculations and symmetrical hyporeflexia on all limbs. Brain MRI showed cortical, mesencephalic and pontine atrophy. Neurophysiological assessment confirmed abnormalities in sensory nerve conduction, chronic neurogenic changes with fasciculation but no active denervation, as well as the pathognomonic absence of bilateral blink reflex. The muscle biopsy described typical chronic neurogenic changes. The revision of all available information about his brother was compatible with the clinical diagnosis of ALS: he developed a classical rapidly progressive motorneuron disease, but interestingly also reported hypoesthesia in the right trigeminal region and in the areas innervated by L2-L5 in the right limb.

Conclusion: This is to our knowledge the first description of a case of FOSMN syndrome with familial history of ALS.

Disclosure: Nothing to disclose

EPO2119

Cholesterol level increases in patients with Complex Regional Pain Syndrome

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Background and aims: Based on anecdotal observations, we hypothesized that cholesterol levels increase in patients with Complex Regional Pain Syndrome (CRPS). Our goal was to test this hypothesis, in consecutive patients diagnosed with CRPS in our clinic.

Methods: Serum cholesterol levels (total and LDL) were measured in three patient groups: CRPS in acute phase (< 6 months from start), CRPS in chronic phase (> 6 month from start) and patients with chronic neuropathic pain syndromes, other than CRPS.

Results: Nine patients had CRPS in the acute phase, 33 patients had CRPS in the chronic phase, 24 patients had chronic neuropathic pain, other than CRPS. Patients with chronic CRPS had significantly higher total cholesterol levels as compared with patients with patients with chronic neuropathic pain other than CRPS (p=0.023). A similar trend was observed for LDL cholesterol, but it did not reach the level of significance (p=0.07). The occurrence of abnormally high level of cholesterol (both total and LDL) was significantly higher in the group of chronic CRPS patients, as compared with the patients with chronic neuropathic pain (p=0.04 and 0.01 respectively).There was no difference in gender and age between these groups.

Conclusion: Our results suggest that cholesterol levels increase in the chronic phase of CRPS. However, further data analysis on larger patients, inclusion and follow-up of more patients with acute CRPS is needed to further elucidate this.

Disclosure: Nothing to disclose

EPO2120

Pain and fatigue in PMP22 related neuropathies: comparison of HNPP and CMT type 1A with healthy controls

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Background and aims: Neuropathic pain and fatigue are debilitating symptoms with prominent impact on quality of life. Both of these are recognized in Charcot-Marie-Tooth (CMT) 1A patients; pain is reported as common as 71% of the patients and fatigue rates up to 64%. There are case reports and retrospective studies mentioning pain in hereditary neuropathy with liability to pressure palsies (HNPP). To our best of knowledge, there are no studies investigating fatigue in HNPP patients.

The main purpose of the study is to determine the frequency of the pain and fatigue in HNPP and CMT-1A patients, and establish the type of pain.

Methods: Patients and healthy controls were recruited from social media and Hereditary Neuropathy Foundation. The survey consisted of demographical questions, the duration of fatigue and pain, localization of the pain, disease and medication history, checklist individual strength (CIS), 0-10 numeric pain scale (NPS), ID-Pain, Beck depression inventory and short form-36 questionnaires. The questionnaire was reachable from 24th of May 2015 to 30th June 2017. Only patients with genetically confirmed diagnosis of HNPP or CMT-1A were included. Patient recruitment is demonstrated in figure 1.
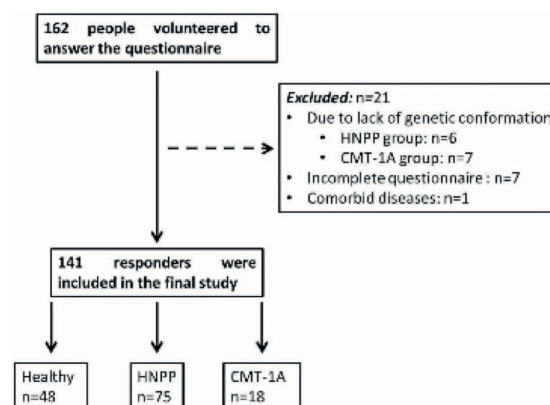
Figure 1

Results: Demographic aspects and detailed findings are summarized in table 1. NPS, total CIS scores and CIS subscales were similar between HNPP and CMT-1A patients and both were significantly higher than healthy controls (p<0.001).

Table 1	N (%)	Age (SD)	Gender (m/f)	Disease duration (SD)	Time to diagnosis (SD)	Pain (n)	Fatigue (n)
Healthy controls	48 (34%)	50.63 (15.22)	13/35	N/A	N/A	39.6% (19)	31.4% (17)
HNPP	75 (53.2%)	42.11 (12.54)	18/57	23.90 (14.34)	15.51 (14.08)	96% (72)	76% (57)
CMT-1A	18 (12.8%)	48.50 (21.59)	4/14	35.89 (17.20)	12.39 (15.47)	94.5% (17)	94.5% (17)
p value		0.105	0.894	0.007	0.476	<0.001	<0.001

Table 1

Conclusion: According to our findings, pain that is mostly neuropathic, and fatigue appear to be major components of HNPP and CMT-1A.
Disclosure: Nothing to disclose

EPO2121

Post bariatric surgery polyneuropathy: gastric banding vs. gastric bypass

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Background and aims: Bariatric Surgery (BS) has gained popularity in order to treat morbid obesity. As post-operative neuropathies (PO-N) are increasingly recognized, our aim was to examine incidence, clinical presentation, and outcomes of PO-N secondary to BS.
Methods: Patients who underwent BS between the years 2012 and 2015 at Parma University were included in this survey, and assessed before (T0) and 1 year after surgery (T1). Baseline characteristics and medical comorbidities, type of surgery, and PO complications were retrieved. Patients with a previous history of peripheral neuropathic disease were excluded from the analysis. If a patient presented with a new onset neurologic symptom including extremity numbness, paresthesia, muscle weakness, the status was considered PO-N+.
Results: Data from 61 patients were retrieved (n=30 Roux-en-Y Gastric bypasses, RYGP; n=31 Gastric banding, GB; 81.0% females). Of them, 7 (11.4%) developed some signs of PO-N, that eventually disappeared at T+24 months. The most common manifestations were paresthesia (n=6) and muscle weakness (n=4), similarly distributed in RYGP (n=4) and GB (n=3) groups. Although PO-N patients exhibited higher SF-36 score at T0 (p=0.018), no significant differences were found regarding BMI (T0, T1), percentual weight loss, serological data (ie vitamin B1, B2, B6, B12: in all cases p>0.05).
Conclusion: Neuropathy after BS is usually associated with lower levels of vitamin B1, B2, B12. However, we found no differences in PO-BMI, excess weight loss, and metabolic data levels . Larger data and more extended follow-up are required to validate our results.
Disclosure: Nothing to disclose

EPO2122

NK cells as surrogate marker for predicting efficacy of IVIg in CIDP

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Background and aims: Natural Killer (NK) cells are part of our innate immune system with regulatory and effector functions. Different studies suggest that the treatment with intravenous immunoglobulins (IVIg) has an immunomodulatory effect on NK cells. IVIg is a first-line treatment for various autoimmune diseases in particular in chronic inflammatory demyelinating polyneuropathy (CIDP). The lack of a predictive marker for IVIg responsiveness in CIDP avoids the early preservation of non-responding patients.

Methods: Using semi-quantitative PCR and flow cytometry in the peripheral blood of patients with CIDP, we analysed the effects of IVIg on the NK cell population before treatment initiation and 24h after first dose and correlated the changes with the reponsiveness to IVIg.

Results: IVIg administrations induced a reduction in the expression of several typical NK cell genes. Interestingly, this IVIg-induced reduction of NK cells was reversible four weeks after the IVIg treatment. Flow cytometry data revealed that IVIg reduced the cytotoxic CD56dim NK cell population, while regulatory CD56bright NK cells remained almost unaffected or were even increased. Interestingly, we found that the observed effects on NK cells almost exclusively occurred in CIDP patients who responded to IVIg therapy.

Conclusion: Correlation between the changes in the NK cell population and treatment efficiency suggests a crucial role for NK cells in the immunomodulatory mechanism of IVIg. Further studies are warranted to investigate whether the differences in the NK cell status of patients with CIDP represent a reliable surrogate marker in predicting the outcome of IVIg therapy.

Disclosure: Nothing to disclose

EPO2123

Isolated lesion of the lateral pectoral nerve due to repeated trauma

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Background and aims: The lateral pectoral nerve (LPN) subserves the proximal two thirds of the pectoralis major muscle. It does not contain cutaneous sensory fibers. Clinical findings of lateral pectoral nerve injury include asymmetry of chest wall associated with atrophy and weakness of the pectoralis major muscle. Mononeuropathy of the lateral pectoral nerve occurs less frequently [1,2,3,4]. In this report we present two cases of progressive atrophy and weakness of the clavicular part of pectoralis major muscle innervated by lateral pectoral nerve.

Methods: We present two cases of progressive isolated damage to the lateral branch of the pectoral nerve with marked atrophy of the clavicular portion of the major pectoral muscle.

Results: In our patients, the mechanism of isolated lesions of lateral pectoral nerves have been attributed to repetitive external microtraumas and pressure on the nerve trajectory between the chest and shoulder during sports or occupational activities.

Conclusion: Isolated injury of lateral pectoral nerve is unusual. In the literature there are cases described and attributed to nerve damage as a result of traction injuries, seat belt trauma and as a complication of mastectomy. Our cases were exposed to external forces on the nerve between chest and shoulder while using a tool, or repetitive fists in a certain manner for a long period.

Disclosure: Nothing to disclose

EPO2124

6 minutes walking test as outcome measures in CIDP patients

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Background and aims: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a disabling disease with monophasic, chronic or relapsing course. CIDP patients frequently complain about fatigue during a relapse or progressive deterioration of their clinical condition, together with sensory and motor symptoms. Moreover, clinical evaluation and clinimetric tests are based on qualitative evaluation or self-administered scale, not so sensitive in capturing minimal variations. Our aim was to find a quantitative measure of clinical improvement and correlate it to those commonly used in clinical practice

Methods: We performed an extensive assessment on 34 CIDP patients before and after therapy (first or second-line) through a large battery of outcome measures both routinely used as modified version of the Inflammatory neuropathy cause and treatment (INCAT) scale, Overall neuropathy limitations Scale (ONLS), Rasch-built overall disability scale (RODS), modified Rankin scale (mRS), Medical research Council (MRC) scale, 10 meters walking test both more rarely used too, as 6 minutes walkin test (6MWT). Response to therapy was evaluated through patients interview and by performing Wilcoxon signed-rank test. Logistic regression model was applied to evaluate the correlation among outcome measuring tools.

Results: We found a significant relationship between total walked meters and ONLS, RODS, mRS and MRC score ($p > 0.000$), not with INCAT scale. Mean velocity significantly increased at each time point before and after therapies ($p > 0.000$).

Conclusion: Our data suggest that 6 minutes walking test is a useful, reliable, objective scale, letting clinicians able to measure in a quantitative way patient's improvements, and their recovery from fatigue

Disclosure: Nothing to disclose

Monday, 18 June 2018

Cerebrovascular diseases 3

EPO3001

Role of pretreatment blood pressure on outcome of patients with nontraumatic intracerebral Haemorrhage

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Background and aims: Acute intracerebral haemorrhage (ICH) is mostly accompanied by increase in blood pressure (BP). Lowering BP is one of the basic treatment strategies of ICH. Although high BP is suspected to be associated with poor outcome of ICH patients, some results, especially in the very acute stage of ICH, are still controversial.
Aim of our study was to assess the effect of admission BP on 3 months functional outcome and hematoma progression.
Methods: 110 patients with acute nontraumatic ICH were included in the study. The first in hospital measured BP value was evaluated. Primary outcome was 3 months functional outcome classified as good (modified Rankin Scale (mRS) 0-3) and poor (mRS 4-6) and the presence of hematoma enlargement within 24 hours.
Results: A logistic regression was performed. BP above 160 mmHg systolic was associated with poor outcome, OR=4.168 (5% CI 1.135-18.792, p=0.033). There was no association with poor outcome for cut off level of 140 mmHg systolic BP. We did not found any relation between admission BP and hematoma enlargement.
Conclusion: Our data support hypothesis that high BP in the very acute stage of ICH, even if early treated, is associated with poor prognosis. In correspondence with some previous studies, we did not found any association between BP increase and hematoma volume progression. This finding may suggest that early correction of BP prevents the hematoma expansion as well as that the poor outcome of patients with high baseline BP is caused by other factors (e.g. edema or larger baseline hematoma volume).
Disclosure: Nothing to disclose

EPO3002

Influence of platelet indices on response to intravenous thrombolysis in acute ischaemic stroke-preliminary data

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Background and aims: Mean platelet volume (MPV), platelet distribution width (PDW) and platelet-to-large cell ratio (P-LCR) are easy and inexpensive indices reflecting platelet activation that can be derived from routine blood analysis in the emergency setting. In previous studies increased MPV has been associated with a higher risk of myocardial infarction and ischaemic stroke as well as worse prognosis. Alteration in platelet indices may be linked to worse response to IV thrombolysis (IVT). To our knowledge no one has yet addressed this issue. Aim of our study was to assess whether easily available platelet indices can predict response to IVT in patients with acute ischaemic stroke.
Methods: We enrolled 55 patients (mean age 66.96±15.33, range 18-88) with acute ischaemic stroke treated with IVT (Alteplase 0.9 mg/kg) over a period of 24 months. Patients who underwent endovascular treatment were excluded. Mean NIHSS at presentation was 8.16±5.09. Efficacy of IVT was assessed by reduction in NIHSS score at 24 hours and 7 days from treatment.
Results: No correlation was found between MPV, PDW and P-LCR values before IVT and NIHSS reduction at 24 hours. On the contrary, all indices showed a statistically significant negative correlation with NIHSS reduction at 7 days (Pearson's correlation, MPV r=-0.28, p=0.043; PDW r=-0.27, p=0.047; P-LCR r=-0.29, p=0.038). Significance was maintained after controlling for possible confounders. Furthermore, no correlation was found with haemorrhagic transformation.
Conclusion: MPV, PDW and P-LCR may represent useful markers to predict outcome after IVT in acute ischaemic stroke.
Disclosure: Nothing to disclose

EPO3003

Female survivors of first-ever small subcortical stroke have an increased risk of long-term cognitive decline compared to men

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Background and aims: Sex is a significant determinant of functional outcome and survival after stroke. Cognitive aspects of long-term outcome after small subcortical stroke (S3) of lacunar type have been rarely analyzed in the light of sex differences.

Methods: A cohort of small vessel disease (SVD) patients presenting with first-ever S3 has been evaluated 4 years after qualifying event for the presence of depression and cognitive decline (CD).

Results: Study group comprised 136 female and 158 male patients who all underwent neuropsychological assessment and brain MRI. No difference was detected between the groups in regard to age ($p=0.709$) or frequency of vascular risk factors (RF) ($p>0.1$ for all). At baseline, women had more disability compared to men with mean modified Rankin scale (mRS) score 2.6 (1.4 in men, $p<0.0001$). All MRI SVD parameters were more severe in females, including measures of white matter lesions and total number of lacunar infarcts (tLI) ($p<0.0001$ for all). Follow-up data indicated that CD was more frequently detected in women than men (78.7% vs. 51.2%, $p<0.0001$), which was not the case for depression ($p=0.654$). Multivariate regression analysis showed that severity of MRI lesions (HR 1.38, 95%CI 1.17-1.62; $p<0.0001$), CD (HR 1.85, 95%CI 1.06-3.24; $p=0.032$), tLI (HR 0.74, 95%CI 0.59-0.92; $p=0.008$) and mRS (HR 8.35, 95%CI 5.04-13.84; $p<0.0001$) were independently associated with female sex.

Conclusion: On long-term follow-up female sex was associated with more frequent CD after first-ever S3, probably secondary to more severe brain SVD lesions compared to male sex. This finding could not be explained by RF or age differences.

Disclosure: Nothing to disclose

EPO3004

Viral infections as a cause of ischemic stroke

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Background and aims: Viral infections can cause the infective vasculitis with high inflammatory markers and coagulation that can become the risk of ischemic stroke.

Methods: Totally 82 ischemic stroke patients investigated, 45 males, 37 females aged 50 to 70 with anamnesis of herpes simplex ½ and cytomegalovirus infection 3 months previously of stroke. Major risk-factors including atherosclerosis, diabetes mellitus, arterial hypertension, cardiac diseases, smoking have been researched. Stroke severity assessed by NIHSS. Ischemic lesion ascertained on Brain MRI (1.5 Tesla). Blood researched for Antinuclear antibodies (ANA) and Antineutrophil cytoplasm antibodies (ANCA) by enzyme –linked immunosorbent assay (ELISA), coagulation test and serology for Herpes simplex virus (HSV 1/2) and cytomegalovirus was done. Statistics performed by SPSS -14.0. Pearson correlation and Multivariate logistic regression (entered stepwise model) were done.

Results: From 82 stroke patients 42 patients found were for HSV1, 25 patients –for HSV2 and 15 patients –for cytomegalovirus. Blood ANA was elevated in 72% of patients (11.5U± 4.6)and Anti PR 3 (c-ANCA) in 28% of patients (0.96U±0.05). Positive correlation found between blood ANA and ANCA levels with Blood INR in stroke patients (R=+0.47 and R=+ 0.25 respectively, P<0.05). Multivariate logistic regression revealed the significance of blood high ANA and ANCA in conjunction with smoking for severity of stroke measured by NIHSS ($p<0.01$). There was not significant correlation between ANA and ANCA levels and ischemic lesion size on MRI.

Conclusion: Herpetic infections can cause the infectious vasculites and by increasing the inflammatory reaction might help to the ischemic stroke development.

Disclosure: Nothing to disclose

EPO3005

Accuracy of identification of acute cerebrovascular accidents at pre-hospital setting in Latvia

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Background and aims: To determine diagnostic quality of acute cerebrovascular incidents in pre-hospital setting in Latvia.

Methods: Retrospective descriptive data analysis was performed including data from Emergency Medical Service (EMS) and hospital records from five hospitals in Latvia. All 8969 adult patients, delivered to stroke-ready hospitals by EMS during 2015 with diagnosis of stroke or TIA, respectively I60-64 or G45, according to ICD-10 were included in the study.

Results: Out of 8969 patients 67.2% were female and 32.8%-male. Median age was equal to 73 years. Overall pre-hospital diagnostic accuracy of cerebrovascular accidents was 44.9%. TIA accounted for 37.4% of all pre-hospital diagnoses but the diagnosis of TIA was proved only in 14.4% of delivered patients. Stroke, without specifying between hemorrhagic and ischemic (I64) accounted for 56.7% of all delivered cases and diagnoses were correct more frequently-in 64.0% of cases. Accuracy of diagnosis were associated (p <0.001) with a reason of calling EMS (e.g., paralysis) and patient age. There were no observed associations with EMS team profile, hour of day or day of the week.

Conclusion: In Latvia accuracy of pre-hospital diagnosis of acute cerebrovascular accidents is relatively low. In particulary, the accuracy is low in diagnosis of TIA. It is necessary to increase EMS staff training, with particular emphasis on the diagnosis of TIA, in order to better select the patients who need urgent treatment and further investigation in stroke unit.

Disclosure: Nothing to disclose

EPO3006

Our experience of using implantable loop recorder devices to specify stroke etiology in Pauls Stradins clinical university hospital, Riga, Latvia from 2014 to 2017

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Background and aims: Identifying atrial fibrillation (AF) is essential as AF-related strokes are associated with an increased risk of disability and death, and they tend to recur when anticoagulation is not implemented.

To evaluate the incidence of AF among cryptogenic stroke survivors using implantable loop recorders.

Methods: Retrospective study included cryptogenic stroke survivors who had implantable loop recorders (ILR) implanted between the years 2014 and 2017. The data was collected from electronic database, medical histories, and via phone. The analysis of data was carried out using IBM SPSS 23.0.

Results: The study included 22 cryptogenic stroke survivors. The patients were aged from 42 to 74 (mean 55.18) years. There were 5 (23%) women and 17 (77%) men. In 7 (31.82%) patients atrial fibrillation was found, time ranges from 2 to 8 months (mean 4.8). Out of all revealed AF patients, 5 (71.4%) were under anticoagulant therapy. Out of all patients, 2 had a recurrent stroke and 1 was diagnosed with AF and did not use any anticoagulants, and the other one has never checked loop recorder data and was not under any anticoagulant therapy.

Conclusion: Among patients with cryptogenic stroke, AF was detected in 31.82% (n=7). These results suggest that the implantable loop recorder is an effective way of finding subclinical AF. Loop recording monitoring is superior to conventional monitoring and may be considered after a cryptogenic stroke for patients who are good candidates for anticoagulation.

Disclosure: Nothing to disclose

EPO3007

Admission neutrophil to lymphocyte ratio as a possible marker for distinguishing between atherothrombotic and cardioembolic ischemic strokes

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Background and aims: Neutrophil to lymphocyte ratio (NLR) is an important measure of systemic inflammation and was shown to predict prognosis and haemorrhagic transformation in ischemic stroke patients. Since a high NLR value was associated with an increased risk of atrial fibrillation occurrence in previous studies, our aim was to assess the utility of admission-NLR in distinguishing between atherothrombotic and cardioembolic strokes.

Methods: We performed a cross-sectional study including 244 patients hospitalized for acute ischemic stroke and treated with intravenous rtPA. Stroke etiology was established according to ASCOD criteria. Atherothrombotic strokes were defined as A1 or A2 and cardioembolic strokes as C1 or C2. Complete blood count was obtained at admission. NLR was calculated as absolute neutrophils count divided by lymphocytes count.

Results: The median age of the patients was 71 years (25-75 IQR 61-79), 52.1% being male. The median NIHSS score at admission was 14 points (25-75 IQR 9-18). According to ASCOD criteria, 17.6% of strokes were classified as A1, 4.09% as A2, 49.18% as C1 and 6.96% as C2. NLR values were significantly higher in patients with cardioembolic strokes compared to patients with atherothrombotic strokes (median NLR value for cardioembolic strokes 2.84 (25-75% IQR 1.88-3.74) versus 2.19 (25%-75% IQR 1.62-2.87) for atherothrombotic strokes, p=0.02).

Conclusion: Neutrophil to lymphocyte ratio could be a valuable tool in differentiating between atherothrombotic and cardioembolic strokes in the emergency department setting. Further studies including larger number of patients are needed to confirm the present results.

Disclosure: Nothing to disclose

EPO3008

Intravenous fibrinolytic therapy in Centenarians

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Background and aims: Early intravenous thrombolysis (IV-rtPA) within 4,5 hours after onset is the standard treatment for ischemic stroke (IS). Currently elderly patients are treated with IV-rtPA safely although benefit may be inferior to younger patients. Experience beyond 100 years is anecdotical.

Methods: Prospective registry (2010-2017) of patients treated with rt-PA in our tertiary university hospital stroke unit (SU). Patients 100 years or older with IS treated with IV-rtPA were selected. Demographic and clinical variables, IS severity as measured by NIHSS, hemorrhagic complications and functional outcome at 3 months (modified Rankin scale, mRS) were registered.

Results: Three patients, all women, of 101, 103 and 104 years, were treated in our SU. All were functionally independent (mRS ≤2) and presented with cardioembolic stroke due to atrial fibrillation without previous anticoagulant treatment. Their Chad2vasc2 sacle was≥4 and IS was severe with NIHSS of 15, 21, and 23 respectively. Treatment with IV-rtPA was applied within 4,5 hours of stroke onset, with a median time from the onset of symptoms of 235 minutes (-). Two patients were asymptomatic (mRS ≤2) at discharge and at 3 months, while the third had a mRS of 3 at 3 months. No serious hemorrhagic or systemic adverse events were registered. All three were prescribed direct oral anticoagulants at discharge.

Conclusion: In our experience, centenarians with IS treated with IV-rtPA had severe cardioembolic strokes, which were successfully treated without serious adverse events. When functional basal status is good, age per se should not be regarded as a contraindication for IV-rtPA.

Disclosure: Nothing to disclose

EPO3009

The change in antithrombotic medication profile of cardioembolic stroke prevention in Latvia from 2014 to 2016

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Background and aims: Current studies show that NOACs are non-inferior to VKA in stroke prevention and present fewer bleeding complications. But there are no guidelines that suggest that NOACs should be preferred over VKA for stroke prevention. We wanted to evaluate if the preferred antithrombotic medication has changed over the recent years.

Methods: All cardioembolic stroke patients admitted to P. Stradins Clinical University hospital, Riga, Latvia during 2014-2016 were included in the study. The use of antithrombotic medication was evaluated- before stroke onset, on discharge and one year after discharge.

Results: A total of 1485 patiens were included in the study, 531 in 2014, 507 in 2015 and 447 in 2016. The results are shown in the added charts.

Primary prevention

	2014	2015	2016
NOACs	0.19%	2.96%	6.04%
VKA	8.66%	8.68%	5.82%
Antiplatlet agents	37.66%	31.16%	29.08%
No prevention	54.48%	57.20%	59.06%

On discharge

	2014	2015	2016
NOACs	30.97%	36.33%	59.63%
VKA	29.42%	22.13%	17.68%
Antiplatlet agents	34.96%	32.36%	20.32%
No prevention	4.65%	9.19%	2.37%

One year after discharge

	2014	2015	2016
NOACs	29.78%	49.38%	69.30%
VKA	42.22%	32.51%	17.67%
Antiplatlet agents	26.22%	15.64%	10.23%
No prevention	1.78%	2.47%	2.79%
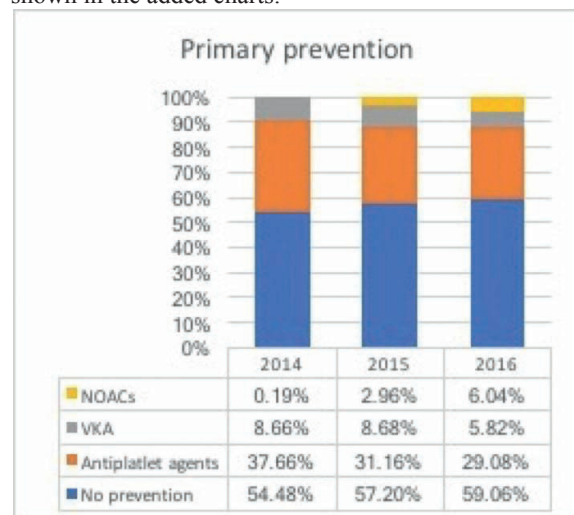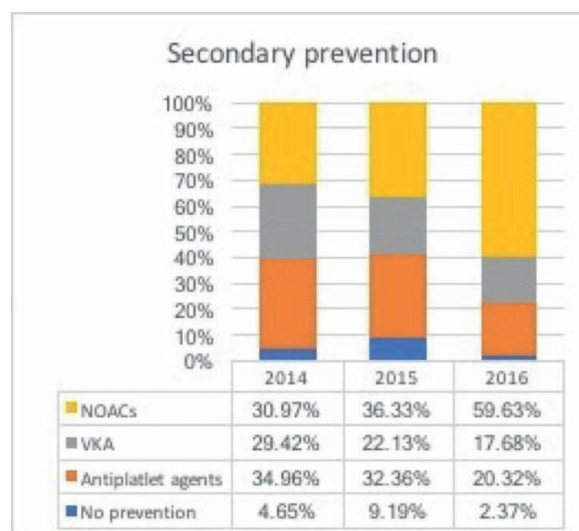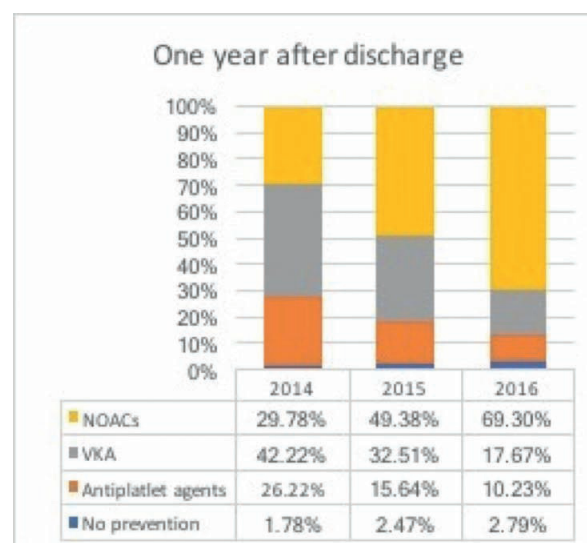
Conclusion: The preference of NOACs over VKA in secondary stroke prevention is significantly increasing over the years.

Disclosure: Nothing to disclose

EPO3010

Marital status and in-hospital mortality of ischemic stroke

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Background and aims: Social isolation is a factor with important influence on the outcome of ischemic stroke. The aim of this study was to investigate the influence of marital status on in-hospital mortality of ischemic stroke.
Methods: We have analyzed 1591 consecutive patients with ischemic stroke hospitalized at the Clinic of Neurology in Nis, Serbia. Binary logistic regression was performed in order to measure the influence of multiple factors on the stroke in-hospital mortality. This model contains the following independent variables: sex, age, National Institutes of Health Stroke Scale (NIHSS) on admission and marital status (married, divorced, widowed or never married).
Results: It was shown that the model as a whole was statistically significant $\chi2$ (df=8, N=1591)=480.367, p<.001), and that it successfully discriminates stroke survivors and patients who died during hospitalization. The model explains 37% (r2, Nagelkerke) of the variance in stroke mortality and successfully classifies 77% of cases. The influence of age, NIHSS and marital status were statistically significant. The strongest predictor of stroke mortality was NIHSS on admission (odds ratio 1.165). Our results showed that marriage is a strong independent protective factor for stroke in-hospital mortality, with odds ratio of 0.266 for currently married patients (p=0.001), 0.34 for divorced patients (p=0.027) and 0.33 for widowed patients (p=0.009).
Conclusion: In conclusion, marriage or history of marriage is a protective factor for in-hospital mortality of ischemic stroke.
Disclosure: Nothing to disclose

EPO3011

Evaluation and outcome of triage for patients with transient ischemic attack: a two-year analysis of the TIA Clinic of the University Hospitals Leuven

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Background and aims: Urgent evaluation of transient ischemic attack has shown to lower the risk of recurrent cerebrovascular events. We present the results of the TIA clinic model in UZ Leuven, Belgium, during its first two years (2015-2016).
Methods: We prospectively collected data including the rate of recurrence at 90 days, hospitalization rate, patient characteristics and patient assessment, and compared the results with a historical cohort.
Results: Fifty-six patients were included and compared to 75 historical controls. Ninety-day recurrence rate was 3.6% for TIA Clinic patients (versus 6%, p=0.70). No low-risk TIA clinic patient had a recurrent cerebrovascular event at 90 days follow up, compared to two patients in the high-risk group. The rate of hospital admissions was similar during TIA Clinic period compared to the 2013-2014 period (67.9% vs 72%; p=0.61). There was faster access to MRI scans (p=0,001), more usage of MRI brain scans (p=0.0017) and CT angiography (p=0.0058), less CT whole brain scans (p<0.001), more prescriptions of statin therapies at discharge (p<0.0001) and more follow-up visits (p=0.0085) in comparison to the historical data.
Conclusion: The TIA Clinic model resulted in low rates of recurrent cerebrovascular event at 90 days after TIA. It is a safe and efficacious model for management of low risk TIA patients. The TIA Clinic model improved patient assessment and resulted in equal percentage of recurrence at 90 days.
Disclosure: Nothing to disclose

EPO3012

Non-aneurysmal basal cistern haemorrhage: does initial blood distribution influence presentation and outcome?

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Background and aims: Non-aneurysmal subarachnoid haemorrhage (SAH) is divided into perimesencephalic SAH (PM-SAH), usually a benign entity, and non-perimesencephalic SAH, a heterogeneous group ranging from CT-negative to diffuse SAH (D-SAH), with a wide range of outcomes. The authors evaluated the presentation and outcome of these entities.

Methods: Retrospective review of records of patients admitted between 2008-2016 with angiogram-negative SAH and haemorrhage centered to the perimesencephalic cisterns, classified as PM-SAH and D-SAH according to Rinkje criteria.

Results: Of 283 patients with SAH, no etiology was found in 46 and 23 patients were included, with a mean age of 57 years. PM-SAH was present in 13 patients and D-SAH in 10 patients. On admission, all PM-SAH patients scored <3 on the World Federation of Neurosurgical Societies (WFNS) scale and one patient had focal neurological deficit. In the D-SAH group three patients had a WFNS >3, all of whom had hydrocephalus and one seizures. During the in-hospital stay, vasospasm occurred in one PM-SAH patient and two D-SAH. One PM-SAH patient had new-onset seizures. At discharge, all patients with PM-SAH had <3 in the mRankin scale, while three in D-SAH group scored ≥3, corresponding to the patients with WFNS >3 at admission. Past medical history revealed hypertension in 13 patients (56.5%) and anti-thrombotic use in 5 (27.2%).

Conclusion: In our sample D-SAH has a poorer outcome, which is associated with worse clinical status at admission. The finding of a high number of patients with hypertension and anti-thrombotic therapies suggests an increased risk for these pathologies.

Disclosure: Nothing to disclose

Epilepsy 3

EPO3013

The efficacy of an online learning tool in improving EEG analysis and interpretation skills of neurology registrars, neurologists and technologists

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Background and aims: Web-based, distance learning programs may provide effective electroencephalogram (EEG) training in resource-poor settings. EEGonline is an interactive, web-based, 6-month multi-modality, learning program designed to teach basic principles and clinical application of EEG. This study aimed to determine the effectiveness of EEGonline in improving EEG analysis and interpretation skills.

Methods: Fifty-three participants (19 neurologists, 28 neurology residents and 6 medical technologists) from 13 mostly African countries registered on EEGonline from 19th June to 17th December 2017, were enrolled. Pre- and Post-course multiple-choice question (MCQ) test results and EEGonline user logs were analysed. Differences in pre- and post-test performance were correlated with quantified exposure to various EEGonline learning modalities. Participants' impressions of EEGonline efficacy and usefulness were assessed through Pre- and Post-course perception surveys.

Results: Forty-two participants attempted both pre- and post-course tests. Mean scores were 49.0% and 66.8% respectively (t=7.2156, df=41, p<0.0001) [Figure 1]. Median percentage improvement was 37.8% (Range -35.5 to 262.5) with 77% of participants showing improvement. Post-course test performance was better in participants accessing interactive EEG-activities versus didactic lecture-notes. Further analysis will correlate post-course test performance with overall use of EEGonline and its various learning modalities.

Over eighty percent of post-course survey respondents felt their EEG analysis skills had improved, that EEGonline was a useful learning tool (Figure 2) and should be recommended as part of EEG training curricula.
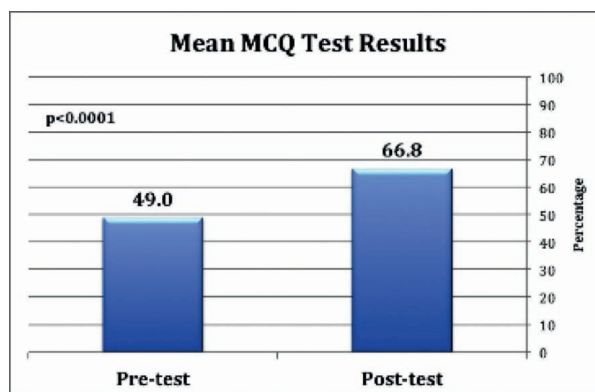
Figure 1
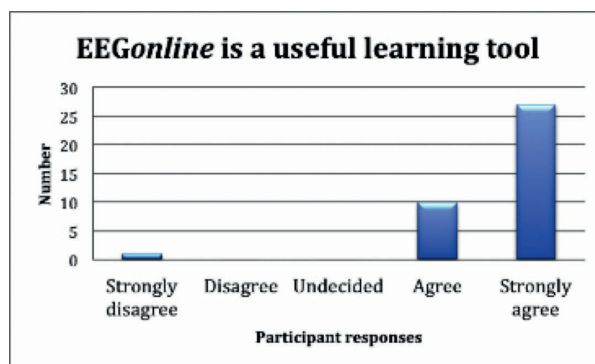
Figure 2

Conclusion: Preliminary results confirm that EEGonline, a web-based, multi-modality learning tool is effective in improving EEG analysis and interpretation skills and may be useful in resource-poor settings

Disclosure: Nothing to disclose

EPO3014

The neuroprotective effect of Hericium erinaceus in the mouse hippocampus after pilocarpine-induced status epilepticus

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Background and aims: Hericium erinaceus (HE), an edible mushroom in Asia, has been used in traditional medicine for treating various diseases. However, roles of HE in epilepsy remain to be investigated. Thus, we evaluated HE-induced neuroprotective effects in the hippocampus after pilocarpine-induced status epilepticus and its underlying mechanisms.

Methods: Male 6-week-old C57BL/6 mice were administered HE crude extracts (60mg/kg, 300mg/kg, p.o.) from 14 days before pilocarpine injection to 6 days after the onset of status epilepticus (SE). At 30 min after atropine methyl nitrate and terbutaline hemisulfate injection (2mg/kg, i.p.), pilocarpine hydrochloride (280mg/kg, i.p.) was treated to induce SE. Seizure stages were determined by Racine scale. At 2 h after SE onset, diazepam (10mg/kg, i.p.) was administrated to terminate seizures. All experimental animals were sacrificed at 1 week post-SE. The neuroprotective effects by HE treatment were determined by cresyl violet and NeuN staining. COX-2 expression and seizure-induced gliosis were analyzed by immunohistochemistry.

Results: Cresyl violet staining and immunohistochemistry to NeuN showed prominent cell death in the pyramidal cell layers of the hippocampal CA1 and CA3 subfields in vehicle-treated group. However, neuronal cell damage in the hippocampal CA1 subregion was significantly reduced by HE treatment (60mg/kg). HE did not affect SE-induced reactive astrocytosis or microglial activation in all groups. Interestingly, HE (60mg/kg) decreased the number of COX-2 expressing cells, which were mostly astrocytes and a few microglia.

Conclusion: Chronic administration of Hericium erinaceus showed neuroprotection against pilocarpine-induced status epilepticus, possibly via COX-2 inhibition in the hippocampus.

Disclosure: Nothing to disclose

EPO3016

Adherence to treatment in epileptic patients attending the emergency department: analysis of causes and associated factors.

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Background and aims: Several studies show that patient non-compliance as a cause of treatment failure in epilepsy. Our purpose was to analyse the causes of poor therapeutic adherence in epileptic patients as well as possible related factors.

Methods: An observational retrospective study was carried out on epileptic patients who were evaluated by the neurologist in the emergency department for seizure recurrence during 2016. We analysed demographic and clinical information on these patients and describe the main causes of lack of adherence.

Results: Of a total of 255 patients included, poor adherence was the main seizure trigger in 13.3% (34 patients). In non-adherent patients the mean age was 41.9 ±18.5 years (mean ±SD), 67.6% were male, 17.6% had a history of drug abuse, 23.5% of excessive alcohol consumption and 32,4% of psychiatric disease. 58.8% of on-adherent patients were receiving monotherapy, 8,8% bitherapy and 14.7% polytherapy. 17.6% had dropped out the treatment. Among the patients with poor adherence, 44,1% were not taking properly their prescribed medication by choice, 42.1% of patients forgot to take medication and 5,9% dropped out because of poor tolerance. Non-adherence was positively and significantly correlated with history of drug abuse (p=0.018) and excessive alcohol consumption (p<0,005). Differences were not significant in age, gender or history of psychiatric disorder.

Conclusion: In our study, the main cause of lack of adherence was voluntary decision. Poor adherence was significantly associated to history of drug abuse and excessive alcohol consumption. It is important to develop strategies to enhance patient adherence.

Disclosure: Nothing to disclose

EPO3017

Cessation of seizures following endoscopic third ventriculostomy and septostomy

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Background and aims: Chronically increased intracranial pressure is not recognized as a cause for seizures. We report three patients with medically refractory seizures who became seizure-free following their treatment of chronic hydrocephaly via endoscopic third ventriculostomy and septostomy without any antiepileptic medication modifications.

Results: We report a 21-year-old female, a 36-year-old male and a 30-year-old male with medically refractory focal epilepsy. First and second cases had asymmetric triventricular hydrocephaly and third case had an enlarged lateral ventricle with transependymal oedema. None of them were suitable for resective surgery due to multiple epileptogenic foci. First patient has undergone septostomy and third ventriculostomy due to a new onset progressive headache and MRI findings. For second and third patients, operation decision was based mainly on imaging findings and lack of alternative solutions. Preoperative seizure frequencies were 8, 2 and 1 seizures per month, respectively. All patients were seizure free at the follow ups (2 months, 5 months and 7 months respectively). Case 1 and 2 reported rare auras without propagation to seizures.

Conclusion: Refractoriness of the seizures in chronic hydrocephaly patients might emanate from increased pressure leading to relative ischemia and changes in the microenvironment of the tissues that are already under stress. Surgical treatment for chronic obstructive hydrocephaly might aid in seizure control in selected refractory epilepsy patients.

Disclosure: Nothing to disclose

EPO3018

Preliminar study on BDNF regulation by DNA methylation in Mesial Temporal Lobe Epilepsy

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Background and aims: Brain-derived neurotrophic factor (BDNF) is a neurothrophin associated with a wide range of neurophysiological processes, such as neurogenesis, gliogenesis, synaptogenesis and neuroprotection. BDNF has been described as overexpressed in hippocampus of both animal models and Mesial Temporal Lobe Epilepsy (MTLE) patients. Gene expression may be modulated by DNA methylation of the respective promoter regions. We sought to analyze, the DNA methylation of the BDNF exon I promoter, a region associated with neuronal imbalance.

Methods: DNA methylation levels were evaluated by Quantitative Methylation-Specific PCR (QMSP) in hippocampus and adjacent neocortex of 23 MTLE patients and 10 healthy controls.

Results: No statistically significant differences in DNA methylation levels of BDNF exon I promoter were found between MTLE patients and controls

Conclusion: MTLE has been associated with alterations in the DNA methylation profile. Our preliminary results suggest that these methylation changes do not affect globally the promoter regions but may be gene / promotor region specific. BDNF gene presents a complex structure with multiple promotor regions that allows to fine-tune transcriptional regulation and may be responsible for the variety of BDNF neuronal functions. Different promotor regions have been analysed in experimental and clinical studies with conflicting results. We suggest that to a better comprehension of BDNF dysregulation in MTLE it is necessary a study of DNA methylation of all promoter regions of this gene. This is particularly important as BDNF can orchestrate different cellular processes involved in epiletogenesis.

Disclosure: Supported by a BICE Tecnifar Grant

EPO3019

Cognitive disorders in idiopathic generalized epilepsies

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Background and aims: The aim of our study was to determine whether there is cognitive impairment in patients with IGE, to analyse the cognitive profile of patients with Idiopathic generalized epilepsies (IGE) and compare it with the cognitive profile of patients with temporal lobe epilepsy (TLE).

Methods: A comprehensive battery of neuropsychological tests was used to analyse 27 patients with IGE and 26 patients with TLE, treated and evaluated at the Centre for Epilepsy Clinic of Neurology, Clinical Centre of Serbia, as well as 25 healthy controls. In all patients, the diagnosis of epileptic syndromes was established according to the current criteria of the International League Against Epilepsy. The following cognitive functions were analysed: intelligence, attention, speech, frontal (executive) functions, memory and visuospatial construction skills. The control group was older and had a higher level of education compared to the groups with epilepsy, while did not differ in terms of sex and manipulative dominance. Global cognitive screening (MMSE) was significantly lower in IGE.

Results: The results showed that the patients with IGE had significant global cognitive impairment. It was also found that patients with TLE had significant impairment that was not different compared to the group with IGE. In patients with IGE intelligence, attention, speech and frontal functions were predominantly impaired.

Conclusion: Our study showed that patients with IGE had significant global cognitive decline, but absence of any meaningful difference in the cognitive profile compared to the patients with TLE.

Disclosure: Nothing to disclose

EPO3020

Withdrawal antiepileptic drug: is it safe?

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Background and aims: Epilepsy is a chronic disease of the central nervous system, affects 1% of the population. Patients who are seizure-free, want to continue with antiepileptic drugs (AEDs), despite financial burden, side effects and stigmatisation, due to the risk of seizures. Theobjective of thisstudy; is to estimate the risk of recurrence after withdrawal of AEDsand to determine risk factors in patients who are seizure free on monotherapy.

Methods: Eighty eight patients, who were seizure free for at least 2 years were included in the study. The patients were divided into two groups as relapse or remission status.

Results: Forty-six of the patients were female (52.3%), 42 were males (47.7%) and the mean age was 28.8±12.3. 71 patients (80.7%) were at remission and 17 patients (19.3%) had seizure recurrence after clinical follow-up. Late onset drug initiation age of relapse group was significantly higher than remission group. It was determined that the relapse rates were increased in patients who had pathologic findings in the EEG examination after withdrawal of AEDs.

Conclusion: Well-defined individual risk factors will protect patients from side effects of AEDs, stigmatisation and risk of recurrence.

Disclosure: Nothing to disclose

EPO3021

300 consecutive cases of status epilepticus: a retrospective study

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Background and aims: Status epilepticus (SE) is defined as a condition of abnormally prolonged seizures or as a condition with two or more discrete seizures between which there is incomplete recovery of consciousness. SE a life threatning emergency with significant mortality and morbidity. Reported annual incidence is 9.9-41.0/100.000. If SE continues despite treatment with adequate dosage of first and second-line drugs, it is defined as refractory SE (rSE). Super-refractory status epilepticus (srSE) is rSE that continues or reoccurs 24h after the onset of adequate anaesthetic therapy. Objective of our study was to evaluate clinical data of 300 consecutive cases of SE patients treated in our department of neurology in 2014-2017.

Methods: Medical records of 300 consecutive patients treated for SE in 2014-2017 were reviewed. We colected data on age, sex, pre-existing neurological disorders, aetiology and type of SE, use of antiepileptic drugs before and after admission, clinical course, EEG and outcome.

Results: Out of 300 patients treated for SE, 136 were women. In 248 cases SE was symptomatic (103 acute, 90 remote and 55 progressive), etiology was unknown in 52 cases. 96 cases of rSE and 9 cases of srSE were identified. Further data and statistical analysis of the above mentioned clinical variables will be presented.

Conclusion: According to our data the calculated annual incidence in the area covered by our department is 8.7-14.7/100,000 and the overall mortality of SE is 6.7%. We dicovered underuse of EEG and suboptimal adherence to SE treatment protocol.

Disclosure: Nothing to disclose

EPO3022

Etiology of interictal periodic epileptiform discharges on ambulatory scalp EEG

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Background and aims: Periodic discharges (PEDs) are frequently seen in several acute / subacute structural and metabolic brain disorders. Interictal PEDs in chronic seizure disorders are rare and their occurrence in patients with refractory epilepsy has been associated with cortical dysplasia. We aim to review the etiology of interictal PEDs on ambulatory scalp EEGs of epileptic patients.

Methods: EEG reports from 1991 to 2017 were screened for PEDs and its variants. Clinical records were reviewed and patients were included if they met the following criteria: a diagnosis of epilepsy; evidence of an epileptogenic lesion on imaging or a normal 3T MRI. Inpatient EEGs or EEGs performed in patients with acute cerebral lesions were excluded.

Results: From a total of 18667 EEGs, 40 patients met the selection criteria. Mean age was 40 years (8-81 years) and 60% were female. PEDs were most frequently unilateral (85.0%) and frontotemporal (45.0%). Maximal frequencies ranged from 1 to 4Hz (median 1Hz). The following etiologies were found: hypoxic/ischemic (n=6, 15.0%); unidentified epileptogenic lesion (n=6, 15.0%); hippocampal sclerosis (n=5; 12.5%); malformations of cortical development (n=4; 10.0%), including focal cortical dysplasia (n=3) and periventricular heterotopia (n=1); immune (n=4; 10.0%); infectious (n=2; 5.0%); miscellaneous etiologies (n=7; 17.5%). Three patients had more than one epileptogenic lesion, namely tuberous sclerosis, hypoxic-ischemic encephalopathy and cortical atrophy, coexisting with hippocampal sclerosis in all cases.

Conclusion: Interictal PEDs on ambulatory EEG are rare. In our sample PEDs were unspecific for an etiological diagnosis, in contrast to the documented association in refractory epilepsy.

Disclosure: Nothing to disclose

Headache and pain 2

EPO3023

Pressure pain sensitivity in extracephalic regions after Onabotulinumtoxin: a therapy in Chronic Migraine

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Background and aims: One of the pathophysiological hallmarks of migraine is a lower threshold to pressure pain sensitivity. It has been related not only with the peripheral sensitization when it happens in the cephalic area but also with central sensitization when it occurs in extracephalic regions. Previous data showed changes in the cephalic region after OnabotulinumtoxinA (OnabotA). We aimed to evaluate changes in pressure pain sensitivity in extracephalic regions in patients with Chronic Migraine (CM) after therapy with Onabot A.

Methods: We considered CM patients with indication to be treated with OnabotA (PREEMPT paradigm) according to local guidelines. We evaluated pressure pain thresholds (PPT) in the cervical region, metacarpal and pretibial, taking the mean value out of three determinations, one week before and one month after the first OnabotA injection. We compared the change in PPT in responders and non-responders. We considered responders patients with a reduction of at least 50% in the number of migraine days after OnabotA.

Results: We included 20 patients, 18 of them female, with a mean age of 45.4 years (20-65). The responder rate was 50%. There was no difference in the PPT pre-treatment. The change in the PPT after the treatment in the responders and non-responders group was 0.71 vs. -0.185 in cervical region; 0.988 vs. 0.09 in metacarpus and 1.31 vs. 0.13 in pretibial region.

Conclusion: CM patients responding to a first OnabotA procedure exhibited an increase in PPT in extracephalic regions, which might represent changes in central sensitization.

Disclosure: Nothing to disclose

EPO3024

Long-term adverse effects of Onabotulinumtoxin A: experience in a series of 34 chronic migraine patients

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Background and aims: Efficacy and safety of OnabotulinumtoxinA (OnabotA) in Chronic Migraine (CM) have been established both in controlled trials and real-world data. It has been described local muscle atrophy in cases treated during more than five years. We aimed to evaluate long-term adverse effects of OnabotA in a series of patients.

Methods: CM Patients treated with OnabotA during 10 or more procedures. Treatment was offered to non-responders to topiramate and at least one other oral preventative, according to local guidelines. We prospectively gathered efficacy and adverse effects.

Results: We included 34 patients (29 women) treated during 10–18 procedures. Age at first injection was 41.4±12.6 (16-69) years. In 22 cases (64.7%) dose was increased accordingly to "follow the pain strategy", and in 9 (26.5%) the maximum dose of 195 IU was reached. In 10 patients (29.4%) an adverse effect appeared throughout the observation period; in 9 musculoskeletal pain or stiffness, mainly in occipital location, and in one fronto-temporal atrophy. Pain was initially managed with anesthetic blockades before injection and, in 4 cases was finally necessary to reduce the dose of OnabotA. None of the clinical or demographic variables analyzed, nor the maximum dose of OnabotA used, showed differences when comparing groups of patients with and without adverse effects.

Conclusion: Long-term adverse effects of OnabotA in patients with CM were not rare in our series of patients. Their appearance do not depend on the maximum dose of OnabotA and, generally, they can be avoid with modifications of the procedure.

Disclosure: Nothing to disclose

EPO3025

A sleep study in cluster headache: polysomnography of episodic cluster headache patients and healthy controls

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Background and aims: Cluster headache (CH) is characterized by extremely severe, unilateral attacks of pain and by a high nocturnal attack burden. The primary aim was to compare the macrostructure of sleep in episodic CH (eCH) patients in bout with in remission and secondly to compare eCH patients with controls.

Methods: ECH patients, aged 18-65 years, diagnosed according to the International Classification of Headache Disorders 2nd edition, were admitted for polysomnography at the Danish Center for Sleep Medicine, preferably both in bout and in remission. The macrostructure of sleep including arousals, breathing parameters, limb movements (LMs) and periodic limb movements (PLMs) were compared with 25 age-, sex- and BMI-matched healthy controls.

Results: There were no differences in any of the sleep parameters for patients in bout (n=32) compared with patients in remission (n=25). Only 14 out of 32 patients in bout (43.8%) suffered from attacks during the polysomnography and their attacks were not related to specific sleep stages. Interestingly, eCH patients had longer latency (18.9 vs. 11.7 minutes, p<0.05) and lower efficiency (84.4 vs. 86.5, p<0.05) and compared with controls, but fewer PLMs (0.67 vs. 1.30 hour-1, p<0.05). Finally, the sleep apnea index was similar in both groups (9.63 vs. 7.76 hour-1, p=0.7674).

Conclusion: This is the first study that systematically investigates eCH patients with polysomnography in both bout and remission and the largest study comparing eCH patients with controls. The observed sleep disturbances were not associated with the bout but rather seem to be the manifestation of a persisting, underlying pathology.

Disclosure: The study was funded by the Danish Tryg Foundation.

EPO3026

The effects of combined supplementation of Coenzyme Q10 with L-carnitine on mitochondrial metabolic disorders marker and migraine symptoms among patient with migraine: a parallel clinical trial

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Background and aims: Coenzyme Q10 and L-carnitine supplementation have been reported to favorably affect migraine headache. However, we are aware of no study examining the effect of combined supplementation Coenzyme Q10 with L-carnitine on migraine headache.

Methods: In this randomised, double-blind, and controlled-placebo clinical trial, 56 migraine patients aged 20-40 y participated. Subjects were randomly assigned to either intervention or control groups. Subjects in the intervention group were received 30mg/day Coenzyme Q10 with 500mg/day L-carnitine at the same time for 8-weeks and subject in the control group also were given the placebo tablets for 8-weeks.

Results: Mean ±SD age of study participants in intervention and control groups was 31.7±6.6 and 33.2±6.3 years, respectively. Mean weight and BMI of subjects was 68.5±13.7kg, 25.3±4.5kg/m2 in intervention group and 64.3±10.7kg, 23.6±4.3kg/m2 in control group, respectively. Supplements intake led to a significant reduction in serum levels of lactate (changes from baseline in intervention group: -1.37 vs. 0.82mg/dl in control group, P=0.001) and migraine symptoms: severity (changes from baseline in intervention group: -3.45 vs. -0.88 in control group, P=<0.001), duration (changes from baseline in intervention group: -8.35 vs. -3.01 in control group, P=0.006), frequency (changes from baseline in intervention group: -5.87 vs. -1.43 in control group, P=<0.001) and HDR (changes from baseline in intervention group l: -115.82 vs. -39.45 in control group, P=0.003) after 8-weeks.

Conclusion: This study provides evidence supporting the beneficial effects of Coenzyme Q10 and L-carnitine supplementation on serum levels of lactate and migraine symptoms.

Disclosure: Isfahan University Of Medical Sceiences

EPO3027

Response to lacosamide in patients with chronic migraine

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Background and aims: Chronic migraine (CM) is a frequent and difficult to manage pathology since patients often require frequent visits and numerous medication adjustments. Sometimes the usual treatments do not work so we should look for new therapeutic alternatives.

Methods: We conducted an experimental study of lacosamide response in a patient with CM. Demographic and clinical characteristics of his disease were collected.

Results: We recruited 27 patients with CM. The average age was 45.52 years. The average time of evolution was 151.96 months (12.66 years). By sex, 77.8% were women and 22.2% were men. The number of monthly crisis was around 20.85 days/month. 85.2% had taken 2 or more preventive treatments. There were 2 (7.4%) dropouts, the cause was abdominal discomfort. There was a decrease in the number of crisis in 74.1%. Of these, 70% decreased the consumption of analgesics. 81.5% responded to a dose of 100mg/every 12 hours. The average duration of treatment was 4.03 months.

Conclusion: In our series, lacosamide has been shown to be effective for the treatment of CM because it can be used as an alternative to conventional treatment that no longer interacts with other medications and without side effects.

Disclosure: Nothing to disclose

EPO3029

Lacosamide treatment in status migrainosus: could it be the solution?

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Background and aims: Status migrainosus (SM) is defined as a migraine lasting longer than 72 hours. A combination therapy seems to be the best option in order to have a synergistic effect. Some antiepileptic drugs have been used in SM such as valproic acid or levetiracetam. Lacosamide as a sodium blocker may also be useful.

Methods: We selected patients with SM refractory to usual acute treatment during 2017. We proposed to them a short hospitalization (3 days) with a protocol based on a combination of standard treatments (corticosteroids, metoclopramide, chlorpromazine and nonsteroidal anti-inflammatory drugs) plus lacosamide. We analyzed the clinical outcome 1 and 3 months after the treatment.

Results: We identified 7 patients (2 men/5 women, mean age 46), with a diagnosis of chronic migraine and most of them also with a diagnosis of medication overuse headache (4/7). All patients were taking preventive treatment including onabotulinumtoxin A in high doses (200 units, PREEMT protocol). Lacosamide total daily doses were 100 mg for 1 patient, 200 mg for 3 and 400 mg for 3 patients. One month after hospitalization, 6 patients had improved their migraine control, with less medication abuse and better response to abortive and preventive treatment. Unfortunately, 3 months later, 5 of them reverted back to their previous situation.

Conclusion: Lacosamide may be useful as an acute treatment for SM in combination with other drugs with a different mechanism of action. In our experience, lacosamide was not effective in the long-term for patients with refractory chronic migraine.

Disclosure: Nothing to disclose

EPO3030

Cognitive performance in familial hemiplegic migraine with ATP1A2 mutation

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Background and aims: Familial hemiplegic migraine (FHM) is an autosomal-dominant form of migraine with aura, characterized by the occurrence of a transient hemiplegia during the aura. Most studies have focused on its genetic features, but less attention has been paid to the cognitive function of these patients.

Here, we report the neuropsychological performance of two Portuguese FHM families with mutations in the ATP1A2 gene that affect sodium-potassium pump function.

Methods: Twelve symptomatic and asymptomatic subjects belonging to the same family performed an extensive neuropsychologic assessment, which focused on attention, memory, language and executive functions. Validated questionnaires were also used to evaluate trait and state of anxiety. Genetic tests were performed in 9 subjects and 7 of them were positive.

Results: Neuropsychologic assessment revealed that 5 patients (3 with and 2 without the genetic mutation) had at least one cognitive test significantly below average when adjusted to age and education. Across the subjects with impairments, deficits in episodic verbal learning and memory domains were the most consistent. All but 1 patient showed high anxiety scores.

Conclusion: Selective cognitive impairments were found in this FHM family in those with and without the ATP1A2 mutation. We are currently performing a cognitive revaluation after 10 years of follow-up to assess the long-term progression; and such preliminary data will also be presented.

Disclosure: Nothing to disclose

EPO3031

Evaluating the impact of migraine on work productivity in Switzerland using self-reported data from the Migraine Buddy (c) application

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Background and aims: The primary purpose of the study was to evaluate the impact of migraine on work productivity (absenteeism). A secondary purpose was to evaluate the prevalence of self-reported indication of anxiety and/or depression across migraine chronicities, along with the impact this has on medication usage for these groups.

Methods: A retrospective, cross-sectional analysis was conducted using self-reported data collected from Migraine BuddyÓ users (90 CM, 775 EM 4-14 and 635 LFEM individuals) in Switzerland. The most recent 28-days period for each user was selected as the observation period from registration date on the app through Dec 31, 2017.

Results: Migraine records were retrieved from 90 CM, 775 EM 4-14 and 635 LFEM individuals. Among users who reported being employed (n=700), an average of 56.49, 33.09 and 15.43 work days missed per year were reported by CM, EM 4-14 and LFEM patients, respectively. On average, individuals in Switzerland reported missing 31.91 work days per year due to migraines. Individuals who declared either 'anxiety' or 'depression' in 'symptoms' or 'triggers' at least once during the observation period were steadily increasing in number with increasing migraine days, and consumed more migraine medication per migraine recorded over the 28-days observation period

Conclusion: Migraines have a considerable impact on the lives of affected individuals, with work productivity of employed migraineurs impacted across all chronicities, majorly so for chronic migraineurs. Further, the self-reported incidence of anxiety and/or depression also consistently increases with an increase in migraine days, along with consistently higher medication usage across chronicities.

Disclosure: This study was sponsored by Novartis Pharma Schweiz AG, Basel, Switzerland.

Miscellaneous 2

EPO3032

Optic coherence tomography and optic nerve echography in MS patients

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Background and aims: Optic coherence tomography (OCT) is a surrogate marker of neurodegeneration in patients with multiple sclerosis (MS) and has been correlated with disability and brain atrophy. Ultrasonography can easily assess the optic nerve (ON) and might give comparable results in terms of disability and brain atrophy in MS patients.

Methods: We studied 54 MS patients with OCT and orbit echography. We measured ON diameter and ON area as well as haemodynamic parameters of the ophthalmic artery (OA), central retinal artery (CRA) and posterior ciliary arteries (PCA).

Results: We studied 54 recurring-remitting (RR) MS patients, age: mean 39.7 (SD 10). EDSS: mean 1.7 (SD 1.3). Time from diagnosis (years): 6.4(SD 6.9). Nine patients had suffered an optic neuritis at any time before inclusion in the study. OCT and ON echography values were lower on eyes with optic neuritis (OCT: 83 vs 87.8, ON area echography 9.3 vs 10.5mm2, optic nerve diameter echography 3.06 vs 3.6), although these differences were not statistically meaningful. We did not find any correlation between OCT values and either ON area or diameter, but there was a slight positive correlation between OCT values and PCA velocities (OCT-PCA systolic velocity r=0.247, p=0.046; OCT-PCA diastolic velocity r=0.254, p=0.44). Time from diagnosis showed a negative correlation with OCT (r=-0.483, p=0.001) but not with any ON echography values.

Conclusion: OCT but not ON echography can be used as a marker of disease progression. ON area and diameter were lower after optic neuritis.

Disclosure: This study has received funding from Novartis

EPO3033

Reduced cerebral blood flow in untreated middle-aged patients with grade 1-2 essential arterial hypertension compared to normotensive controls

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Background and aims: Arterial spin labeling (ASL), a prospective noninvasive perfusion sequence, may allow to detect early changes in cerebral blood flow (CBF) in patient with essential arterial hypertension (EAH). The aim of this study was to examine whether the CBF values were reduced in untreated middle-aged patients with uncomplicated grade 1-2 EAH compared to controls.

Methods: 82 middle-aged adults (41 healthy volunteers, mean age 46.2±4.6 years and 41 untreated hypertensive patients, mean age 50.3±6.7 years) were recruited. All subjects underwent brain MRI (MAGNETOM Skyra 3.0T, Siemens AG, Germany). Fazekas scale was used to quantify the amount of white matter hyperintensities (WMH). ASL CBF maps were used to calculate the perfusion defects.

Results: Hypertensive patients with and without WMH had significantly lower CBF compared to controls (p<0.0001). WMH were found in 9,7% healthy controls (Fazekas 1) and in 53.7% hypertensive patients (Fazekas 1 in 48.8% and Fazekas 2 in 4.9% patients, p=0.0005). CBF in the cortical plate of both frontal lobes of the brain was significantly lower in hypertensive patients compared to controls (37.3±6.7 vs 45.3±3.5ml/100g/min; 38.02±6.2 vs 45.8±3.2ml/100 g/min, p<0.0001).

Conclusion: CBF in the cortical plate of the frontal lobe can be used as an early marker of brain damage in patients with EAH.

Disclosure: Nothing to disclose

EPO3034

Are recurrent myelitis a prodromic phase of inflammatory diseases or a distinct inflammatory condition?

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Background and aims: Recurrent myelitis (RM) can be the only neurological manifestation of some patients, thus not allowing the diagnosis of a specific inflammatory condition. We evaluated whether patients with RM show differences in lesion distribution and white matter (WM) tract involvement compared to those with neuromyelitis optica (NMOSD) and relapsing-remitting multiple sclerosis (RRMS).

Methods: Brain WM lesion distribution was obtained from the T2-lesion masks of 17 RM subjects, 20 NMOSD and 20 relapsing-remitting MS age- and disease-duration- matched patients. Lesional volumes (LV) were split among WM tracts of the JHU atlas. Intragroup and intergroup analyses of LV distribution and WM tracts involvement (cut-off >5 lesional voxels) were performed.

Results: RM patients had a selective damage of the motor pathways: superior corona radiata (CR) 18% of LV, middle cerebellar peduncle (MCP) 13%, cortico-spinal tract (CST) 12% (p vs other tracts=0.03). MS and NMOSD patients showed a higher involvement of the optic radiations (OR) and of the CR (p=0.04, p=0.03 respectively than other regions). The intergroup comparison of LV distribution confirmed the preferential involvement of MCP (p=0.007) and CST (p=0.04) in RM vs MS, no difference emerged between RM vs NMOSD. Lesions occurred more frequently in the OR and CR in NMOSD and MS (p=0.03, p=0.02, vs other tracts), while RM patients had a preferential involvement of posterior CR (78.6%, p=0.01 vs other tracts).

Conclusion: RM patients evidenced a preferential involvement of the motor pathway also in the brain, suggesting a different pathogenetic mechanism from other WM diseases.

Disclosure: Nothing to disclose

EPO3035

Charles Bonnet syndrome in a patient with Leber's Hereditary Optic Neuropathy (LHON) and sensorineural hearing loss: a functional MRI study

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Background and aims: Charles Bonnet syndrome (CBS) is characterized by simple or complex visual hallucinations (VH) due to damage along the visual pathways.

Methods: A 60-year-old man was diagnosed with LHON (11778/ND4 mtDNA mutation) after subacute visual loss in left eye (right eye amblyopic). One month later, he experienced VH of a few seconds consisting in "moving red and blue miniature cartoon". One year later VH content changed in colored mosaic (10-15 seconds duration), usually stress-related, and blue and white flashes (2-5 seconds), triggered by unexpected auditory stimuli. Audiometry revealed mild sensorineural hearing loss. Three block design functional MRI paradigms were administrated: 1) random "clap", 2) "checkerboard", and 3) non-random "bip".

Results: 1) "Clap" stimuli evoked simple flashes with bilateral activation of primary and secondary visual cortex, cuneus, precuneus and insula, consistent with previous findings. 2) Neither hallucinations nor visual cortices activation (related with the severe loss of visual acuity) were registered after "checkerboard". 3) Primary and secondary auditory cortex were "bip"-activated, without eliciting VH.

Conclusion: CBS in LHON has been reported only once, possibly triggered by brimonidine. The peculiarity of our case is VH triggered by the auditory stimuli, possibly due to a cross-modal plasticity between visual and auditory networks, probably influenced by sensorineural deficit. Functional alterations of both networks in resting conditions have been demonstrated in LHON patients, even without an auditory deficit. The absence of VH triggered by expected stimuli is consistent with the "expectation suppression theory", based on increased neural activations after surprising but not by predicted events.

Disclosure: Nothing to disclose

EPO3036

Autoimmune encephalitis: clinical, laboratory and imaging data comparison between antibody-positive and antibody-negative patients.

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Background and aims: Autoimmune encephalitis (AE) is an emerging and potentially treatable group of encephalitis. Over the years, new subtypes of AE have been described and linked to specific autoantibodies (Ab). However, according to recently published criteria, Ab detection is not strictly necessary for the diagnosis of AE. In this work we compare two groups of AE patients, with or without detectable Ab, in order to explore their features and clinical course.

Methods: We retrospectively analysed demographic, clinical, CSF, EEG and imaging data of two groups of patients admitted to our department between September 2010 and April 2017. We included 19 patients with AE with definite autoantibody (AE+) and 13 patients discharged with diagnosis of autoantibody-negative AE (AE-), who fulfilled recently published criteria for probable autoantibody-negative AE. In AE+ group, 4 patients had anti-NMDAR-Ab, 8 patients VGKC-Ab, 1 patient anti-GAD-Ab, 3 patients Hashimoto encephalitis, 2 patients anti-Ma-Ab and 1 patient anti-Hu-Ab.

Results: We found no relevant differences between the two groups of patients. Clinical picture was homogenous between AE+ and AE-, as well as MRI features, EEG, CSF data and administered treatments.

	Ab+ (n=19)	Ab- (n=13)
Demographics		
Number	19	13
Male (n, %)	11 (58%)	6 (55%)
Age at onset (yrs; mean, range)	54.6 (15-85)	60.2(17-79)
Clinical features (n, %)		
Psychiatric symptoms	12/19 (63%)	9/13 (69%)
Epilepsy	11/19 (58%)	9/13 (69%)
Fever	6/19 (32%)	2/13 (15%)
Memory impairment	10/19 (53%)	9/13 (69%)
Confusion	15/19 (79%)	13/13 (100%)
Hyponatremia	6/19 (32%)	3/13 (23%)
Autonomic disorders	3/19 (16%)	3/13 (23%)
Movement disorders	5/19 (26%)	5/13 (39%)

Table 1. Demographic data, clinical features and association with neoplasm. N=number; Yrs=years; IQR=interquartile range.

	Ab+ (n=19)	Ab- (n=13)	
Altered EEG	16/18 (89%; 1 N/T)	10/13 (77%)	
General organization	12/18 (75%)	9/13 (90%)	
Epileptiform activity	7/18 (44%)	1/13 (10%)	
Slow abnormalities	9/18 (56%)	5/13 (50%)	
Seizures	6/18 (38%)	1/13 (10%)	
Cerebrospinal fluid	18/19 (1 N/T)	13/13	
Proteins (mg; median, IQR)	42 (34-60)	55 (29-101)	p=0.974*
No. of cells (n; median, IQR)	1 (1-4)	7,5 (1-27)	p=0.061*
IEF pattern 1	8/17 (47%)	8/10 (80%)	
IEF pattern 2 or 3	13/17 (18%)	0/10	
IEF pattern 4	6/17 (35%)	2/10 (20%)	
Magnetic Resonance Imaging			
Altered MRI	14/19 (74%)	7/13 (54%)	
Limbic system	11/14 (79%)	5/7 (71%)	
Basal ganglia	4/14 (29%)	2/7 (29%)	
Contrast enhancement	3/14 (21%)	3/7 (43%)	

Table 2. N/T=not tested. *=Mann-Whitney two-tail test. IEF (isoelectrofocusing) patterns: 1=no OCBs seen; 2=OCBs in CSF only; 3= Identical bands in both serum and CSF with extra bands in CSF; 4=mirror pattern.

	Ab+ (n=19)	Ab- (n=13)
First line treatment	19/19	12/13
IVIG	8 (42%)	6 (50%)
IV steroid	8 (42%)	6 (50%)
Oral steroid	3 (16%)	0
Second line treatment	12/19	9/12
IVIG	6 (50%)	2 (22%)
IV steroid	5 (42%)	2 (22%)
Oral steroid	1 (8%)	5 (56%)

Table 3. Treatment courses. IVIG = Intravenous Immunoglobulins.

Conclusion: Autoantibody detection is not mandatory for the diagnosis of AE. From a clinical point of view, autoantibody-negative AE appears quite similar to autoantibody-positive AE. Therefore, alongside from autoantibody testing, recognition of a clinical syndrome suggesting autoimmune encephalitis is the mainstay for timely diagnosis and treatment.

Disclosure: Nothing to disclose

EPO3037

Oligoclonal bands in cerebrospinal fluid in Guillain-Barré Syndrome

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Background and aims: Oligoclonal bands (OB) are an indicative of activation of humoral immunity. OB in cerebrospinal fluid (CSF) in Guillain-Barré Syndrome (GBS) have been poorly described. We studied the presence of OB in patients with GBS and explored their correlation with neurophysiological studies and clinical findings.

Methods: We selected all patients with diagnosis of GBS by Brighton criteria (level 1 and 2) between 2000 and 2016 in our center. We analyzed the association among the presence of IgG OB in CSF and sex, clinical severity, electrophysiological pattern and response to intravenous immunoglobulins (IVIGs).

Results: 45 patients were studied. Medium age was 57.7 years and 62% were males. Twenty three (51%) meet criteria for acute inflammatory demyelinating polyneuropathy, 18 showed the axonal variant, 14 a mixed pattern and 80% were treated with IVIGs. IgG OB were demonstrated in 28 (62.2%) patients of our sample. 25 of them (89.3%) presented an identical pattern in CSF and serum, only 3 (10.7%) had an extra IgG OB CSF pattern. Presence of OB in CSF was not statistically associated to sex, a concrete neurophysiological pattern, clinical severity or IGIVs response.

Conclusion: Presence of IgG OB in CSF is common in patients with GBS, mostly showing an identical pattern compared to serum suggesting a systemic immune activation with lymphocyte B transmission to the nervous system. Presence of OB did not correlate with neurophysiological findings, clinical severity or treatment response.

Disclosure: Nothing to disclose

EPO3038

AQP4-positive longitudinal extensive transverse myelitis associated with Takayasu arteritis: a case report

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Background and aims: Neuromyelitis optica spectrum disorder (NMOsd) is an aggressive autoimmune condition characterized by optic neuritis and longitudinally extensive transverse myelitis (LETM). In 75% of the cases specific autoantibodies against aquaporine 4 (AQP4) are present. Associations with various systemic autoimmune diseases have been reported (mostly lupus erythematosus or Sjögren syndrome). Takayasu arteritis is a rare vasculitis occurring predominantly in young females of Asian origin causing granulomatous inflammation of large-vessels. The exact pathophysiological mechanisms remain unknown.

Methods: A 40-year-old female laboratory assistant of Korean descent consulted for rapidly progressive paraplegia, urinary retention and belt-shaped waist pain. On the bases of a LETM from C6 to the conus medullaris (Figure 1) and of the presence of anti-AQP4 antibodies NMOsd was diagnosed (Wingerchuk criteria 2015). CT scanning revealed bilateral pulmonary embolism. In addition, mural thickening of the left carotid artery, brachiocephalic trunk, right renal artery, and superior mesenteric artery was found, the latter also showing stenotic and aneurismal lesions (Figure 2). Taken together with elevated inflammatory markers, a diagnosis of Takayasu arteritis was made. The patient was treated by anticoagulation and immunomodulatory agents (corticosteroids, followed by IVIG, and rituximab). After 3 months she returned home, able to walk with a cane.
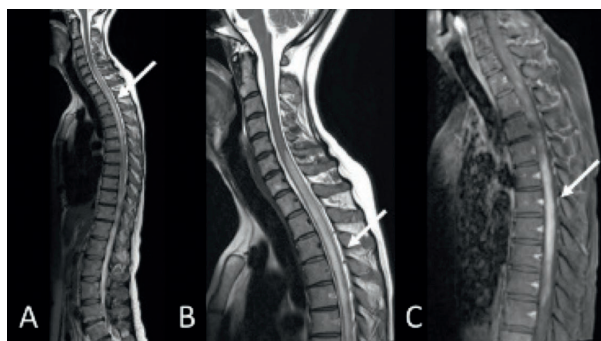
Figure 1 (A) spinal sagittal T2-weighted magnetic resonance image (MRI) demonstrate high signal from C6 to the conus medullaris and (B) cervical sagital T2-weighted MRI demonstrate longitudinal myelitis in the cervical spine. (C) Post gadolinium T1 sequence with heterogeneous contrast enhancement from Th3 to Th8.
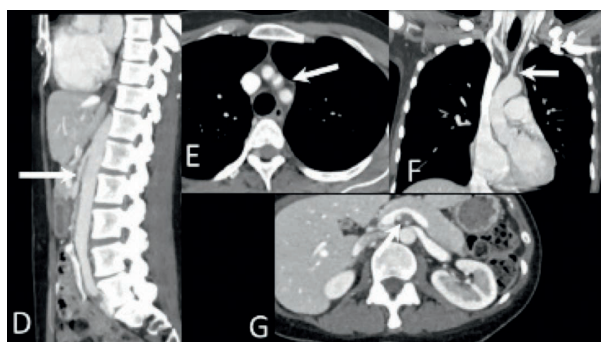
Figure 2 thoracic-abdominal computed tomography shows mural thickening (D) the mesenteric superior artery, (F) brachiocephalic trunk, and (G) right renal artery.

Results: To our knowledge; this is the first case report of Takayasu arteritis associated with NMOsd.

Conclusion: In patients with NMOsd concurrent Takayasu arteritis should be considered and, as is evidenced by our patient's presentation and the course of her disease, aggressive immune therapy started early.

Disclosure: Nothing to disclose

EPO3039

Retrospective analysis of the sensitivity and specificity of a diagnostic algorithm for autoimmune encephalitis

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Background and aims: The patient with suspected autoimmune encephalitis poses a dilemma: an early initiation of treatment is associated with a more favourable prognosis, but the definitve proof via antibody detection is time-consuming and sometimes impossible. Hence there is an urgent need for diagnostic algorithms acting independently of antibody detection. We aim to retrospectively apply the algorithm published by Graus et al to those patients treated at our departement during a 10-year-period to determine its sensitivity and specificity for the diagnosis of autoimmune encephalitis during the early stages of the disease.

Methods: The medical data of all patients with the diagnosis of "encephalitis" treated at our department between 2007-2017 will be retrospectively analysed. The initial diagnosis will be reevaluated by the author-excluding patients in whom it cannot be classified as either "confirmed" or "possible" -and will serve as a reference against which the diagnosis resulting from the algorithm shall be compared to determine its sensitivity and specificity.

Results: Main target criteria:sensitivity, specificity, negative and positive predictive values of the diagnostic category "possible autoimmune encephalitis" at the time of hospital admission

Subordinate target criteria: sensitivity, specificity, negative and positive predictive values of all other diagnostic categories of the algorithm and of all categories during later stages of the disease.

Conclusion: We expect this study to yield information on the value of the diagnostic algorithm in the early stages of encephalitis. This is significant as a reliable algorithm would enable an early diagnosis and initiation of treatment-thereby improving the patients' chances of recovery.

Disclosure: Nothing to disclose

EPO3040

Autoimmune Encephalitis in central Slovenia

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Background and aims: Autoimmune encephalitis (AE) is nowadays recognized as an important cause of subacute encephalopathies with various accompanying conditions (epilepsies, psychosis) previously diagnosed as idiopathic. Since AE is a relatively new and possibly underdiagnosed entity a study on AE prevalence in Central Slovenia was performed.

Methods: We performed a retrospective analysis of the patients (n=466) admitted to the University Medical Center Ljubljana between 1. 1. 2012 and 31. 12. 2016 which were tested (blood or/and cerebrospinal fluid) for anti-neural antibodies. The subjects with paraneoplastic syndromes other than AE were excluded. We defined seropositive and seronegative AIs (strong suspicion of the diagnosis, positive response to immunotherapy).

Results: We identified 23 patients (12 female, 11 male) with AE, resulting in an estimated incidence of 0.46/100.000. The mean age of patients was 54.9 years (22–79y), with anti-N-methyl-D-aspartate-receptor (anti-NMDAR) encephalitis patients being significantly younger (mean 38y). Six patients (26.1%) were seronegative, half of them had a carcinoma. The majority of seropositive AEs were anti-Ma2 positive (8; 34.8%), followed by anti-NMDAR (5; 21.7%), anti-Yo and anti-Hu (both 2; 8.7%). Malignancy was found in nine (75%) patients with intracellular directed antibodies and in one (20%) patient with cell-surface directed antibodies. The majority improved after immunotherapy; however two patients died due to complications, both having paraneoplastic cerebellar syndromes.

Conclusion: The results are comparable to those in the literature by both the phenomena and the presence of anti-neural antibodies. However, AEs are underdiagnosed in Slovenia and should be included into the differential diagnosis of patients with subacute encephalopathies more often.

Disclosure: Nothing to disclose

EPO3043

The impact of a realistic-simulation course on the self-perception of confidence of healthcare professionals when treating CVA

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Background and aims: Acute CVA is a neurological emergency which demands quick attention. Simulations are becoming widely used in medical education. However, there is few evidence of its utility on neurocritical care education. We, therefore, aim to assess the impact of a realistic-simulation course on healthcare professionals' self-perception of confidence when treating acute CVA.

Methods: We conducted a three-scenario realistic-simulation course "SR.AVC" to seventeen subjects randomly chosen, during the XI Brazilian CVA Congress. All participants responded pre and post-test questionnaires evaluating the self-perception of confidence on acute CVA care. Other 38 participants, randomly chosen amongst the trainees of ENLS (18) and Neurossonology (20) courses were submitted to the same questionnaires. We evaluated the variations between pre and post-tests results, to assess the change on trainee's self-perception of confidence.

Results: 46 (83.63%) subjects completely answered the questionnaires. ENLS and Neurossonology groups had mainly neurologists (7 and 11) while on SR.AVC® were non-neurologists (11). Friedman's two-way analysis of variance determined that, compared with Neurossonlogy (p=0.739) and ENLS (p=0.317), the change on SR.AVC®'s group was statistically significant (p=0.033). Wilcoxon's signed-rank test, found out that post-test scores statistically higher than pre-tests (p=0.048).

Comparative pre/post-test scores: ENLS
P=0,317

Comparative pre/post-test scores: Neurossonology
P=0,739

Comparative pre/post-test scores: SR.AVC
P=0,033
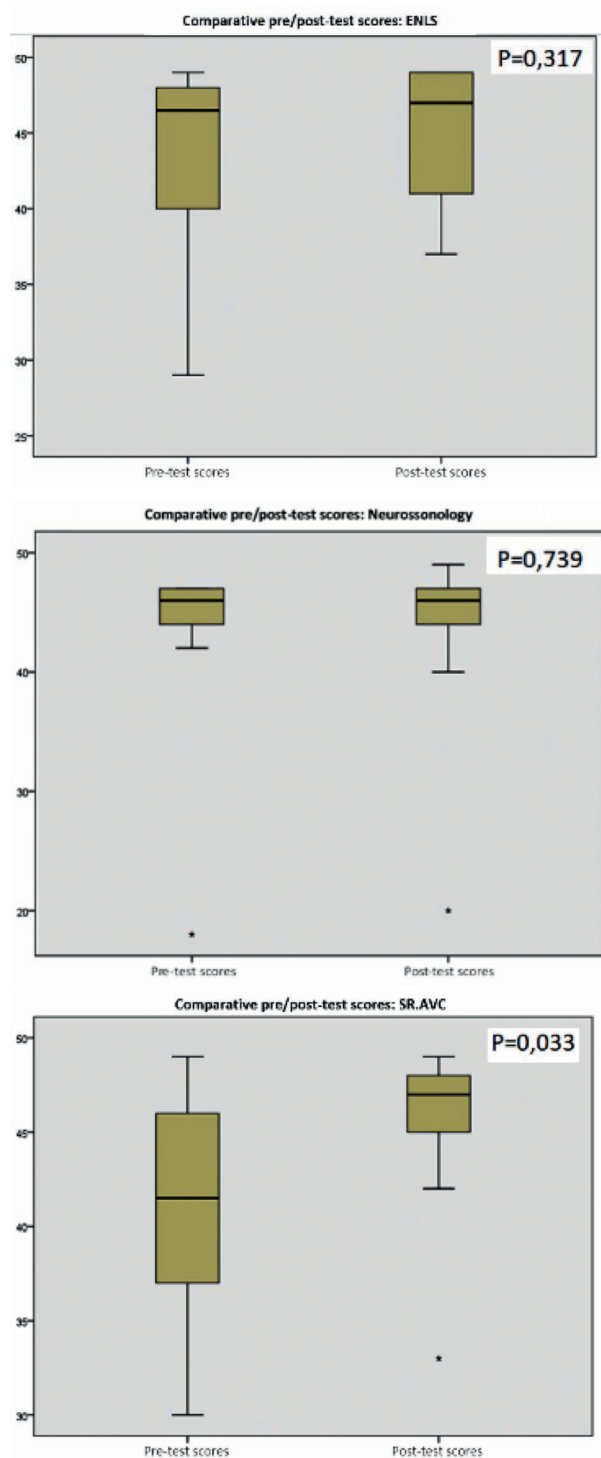
Conclusion: The realistic-simulation course is an effective tool on the training of the skills required for the management of acute CVA. The simulations provided a safe and controlled environment which made possible a significant improvement on trainees' self-perception of confidence, evidenced by a significant variation of scores when comparing pre and post-tests.

Disclosure: Nothing to disclose

Motor neurone diseases; Cognitive neurology/neuropsychology

EPO3044

Fluctuation in behavioral responsiveness in severely brain-injured patients

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Background and aims: To characterize fluctuation in behavioral responsiveness in patients with severe brain injury within a short time period.

Methods: 15 patients (8 females, 9 traumatic, median age: 48 [19-78]; median time since insult:13 [6-59]) were assessed by trained examiners four times with the Coma Recovery-Scale Revised (CRS-R), once a day, twice in the morning, twice in the afternoon, within a 7 days period. A Wilcoxon was used to assess the difference in mean CRS-R total scores between the morning and the afternoon assessments. Descriptive statistics were used to further describe the patient's profiles.

Results: Patients were diagnosed as unresponsive (n=4), minimally conscious minus (MCS-; n=4); minimally conscious plus (MCS+; n=6) or emerged from the MCS (n=1). We did not find a difference between mean CRS-R total scores when the assessments were performed in the morning or in the afternoon. All patients showed variability in CRS-R scores across the 4 assessments, with differences ranging from 0 to 12 (median=2) within morning or afternoon sessions. 53% of the patients (6MCS+; 2MCS-) showed unstable diagnoses across the 4 assessments.

Conclusion: Our data suggest a high heterogeneity in daytime behavioral fluctuation in patients with severe brain-injury. They also support previous literature highlighting the necessity to use multiple assessments within a short time-period in these patients to get a reliable diagnosis. Future studies on a bigger cohort should focus on better characterizing day-time fluctuation within patients.

Disclosure: Nothing to disclose

EPO3045

Metamemory in Mild Cognitive Impairment: relation with progression to Alzheimer's disease

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Background and aims: Mild Cognitive Impairment (MCI) is often used to describe the transitional stage between normal ageing and dementia. Metamemory refers to the subjective knowledge, beliefs and attitudes towards one's own cognitive capacities and tends to decline with the progression of Alzheimer's disease (AD). Our aim was to evaluate the variation of metamemory over time in a population with MCI and determine its relation with progression to dementia.

Methods: Longitudinal study of a cohort of MCI patients who underwent thorough cognitive, functional, psychopathology and subjective memory complaints (SMC) assessment. We analyzed data from the first and final patient's assessment (operationalized as the patients' assessment at conversion or their most recent assessment).

Results: We included 78 participants, 51.3% female, with a mean age of onset of 67.4 years and 6.29 years of education. At follow up (median 3 years), 46.2% converted to dementia; 58.3% were apoE4 carriers and 44.4% had a positive family history of dementia. There were high significant positive correlations between the patients' metamemory and psychopathological symptoms (depression and anxiety); the caregivers' SMC correlated with their general cognitive and functional status. Comparing the first and last assessment, there were no differences between the patient's memory complaints but the caregiver's SMC score was significantly higher at follow up.

Conclusion: Our results suggested that the caregivers' metamemory reflected more accurately the alterations in the patients' cognitive and functional abilities then their own. Furthermore, greater patient memory complains were associated with higher levels of psychopathological symptoms and did not reflect their cognitive performance.

Disclosure: Nothing to disclose

EPO3046

Cerebrospinal fluid biomarkers in patients with mild cognitive impairment

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Background and aims: The usefulness of cerebrospinal fluid (CSF) biomarkers (beta amyloid, total tau and phosphorylated tau) in Alzheimer's disease (AD) is well known, however it remains uncertain in mild cognitive impairment (MCI).

Methods: We studied 105 patients with MCI or subjective memory complaints, 51.4% men, with a mean follow-up of 4.2 years ($\pm$ SD 2.1). Clinical and functional parameters, CSF levels of beta amyloid-42 (AB42), total tau (TT) and phosphorylated tau (PT) and the progression to dementia were analysed. We studied the sensitivity (S) and specificity (E) of the three biomarkers individually and the combination of the three for the development of any type of dementia and specifically for clinical phenotype of dementia of Alzheimer's type (DAT) (hippocampal memory deficit).

Results: 59.1% developed dementia during follow-up, 38.1% fulfilled clinical criteria of DAT. AB42 CSF levels predicted dementia with a S=65% and E=69%, with S=75.6% and E=65.07% for DAT. For TT, S=39% and E=90% for dementia and S=41% and E=82% for AD. For PT S=52% and E=81% for dementia and S=63% and E=77% for DAT. A combination of the 3 biomarkers, S=63% and E=88% were obtained for dementia and S=73% and E=77% for DAT.

Conclusion: The determination of biomarkers in CSF is useful to predict the progression to dementia, specially AD, but it should not be used individually as a screening test.

Disclosure: Nothing to disclose

EPO3047

Alpha-synuclein in CSF of mild cognitive impairment patients: a preliminary study

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Background and aims: Objectives: To quantify α-synuclein in cerebrospinal fluid (CSF-AS) in mild cognitive impairment (MCI) patients, and to compare the results of that protein considering the clinical evolution after a 5 years clinical follow-up.

Material and methods: We included 55 MCI patients. After a minimal follow-up of 5 years 22 of them were diagnosed with psychiatric illnesses (CT), 17 developed over time Alzheimer's disease (AD) following NIA-AA criteria (2011) and 16 succumbed to Lewy body disease (LBD) following McKeith criteria (2005). We measured CSF-AS using Covance reagents and Aβ, T-tau and p-tau proteins by means of Fujirebio reagents at inclusion.

Results: The CSF-AS levels were found to be higher in LBD patients in comparison with CT group. In addition, AD patients showed essentially higher CSF-AS than LBD and CT. We excluded the possible relation between CSF-AS and the classical CSF biomarkers, by performing a Spearman correlation test. The alpha-synuclein protein was found to be present in a higher correlation with p-tau protein. But, when we differentiate between the various groups the higher correlation was observed to be predominant with T-tau. However the correlation coefficient has never been 1 with the classical biomarkers.

Conclusion: In this preliminary study, the results suggested that CSF-AS levels were increased in MCI patients who would develop LBD, and specially, in those who would develop AD. Adding alpha synuclein to the classical CSF biomarkers may be worthwhile to predict the evolution of MCI patients. A larger study is guaranteed to confirm these results.

Disclosure: Nothing to disclose

EPO3048

Chromogranin A in the cerebrospinal fluid of patients with Amyotrophic lateral Sclerosis

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Background and aims: Chromogranin A (CgA), a major constituent of secretory large dense-core vesicles of neuroendocrine cells and neurons, is mainly involved in secretion regulation. Previous preclinical data suggest that CgA could play a role in amyotrophic lateral sclerosis (ALS), and, recently, higher levels of CgA have been reported in the cerebrospinal fluid (CSF) of ALS patients relative to controls.

Methods: We measured CSF levels of CgA and phosphorylated neurofilament heavy chain (pNFH), an established ALS biomarker, in 32 ALS patients (17 (53.1%) males and 15 (46.9%) females; median age, 64.5 y) and 32 disease controls (16 (50%) males and 16 (50%) females; median age, 66.5 y) without degenerative or inflammatory CNS diseases.

Results: ALS patients displayed slightly lower CSF CgA levels than controls (median, 70.8 ng/mL and 86.7 ng/mL, respectively; Figure 1), with low statistical significance ($p=0.0265$), wide overlap between patients and controls, and consequent low diagnostic performance (area under the ROC curve (AUC), 0.6616; 95% CI, 0.5294 to 0.7938; $p=0.0263$; Figure 3). This contrasted with the clear increase in CSF pNFH levels in ALS patients relative to controls (median, 1857.1 pg/mL and 172.9 pg/mL, respectively; $p<0.0001$; Figure 2), with AUC of 0.9316 (95% CI, 0.8688 to 0.9944; $p<0.0001$; Figure 3). CgA levels among ALS patients were not associated with any clinical parameters.
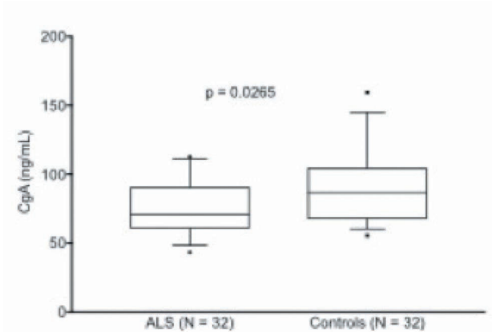
CSF CgA levels in ALS patients and disease controls (linear scale). Boxes represent interquartile ranges (25%-75%) with median values, whiskers represent values between 5% and 25% and between 75% and 95%, and points represent outliers. CgA, chromogranin A.
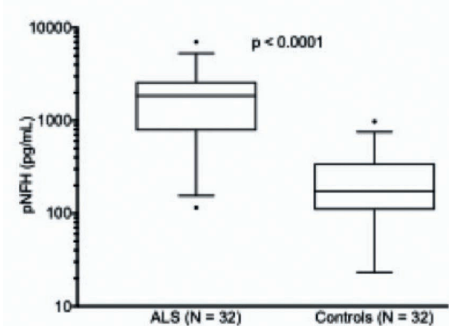
CSF pNFH levels in ALS patients and disease controls (Log-10 scale). Boxes represent interquartile ranges (25%-75%) with median values, whiskers represent values between 5% and 25% and between 75% and 95%, and points represent outliers. pNFH, phosphorylated neurofilament heavy chain.
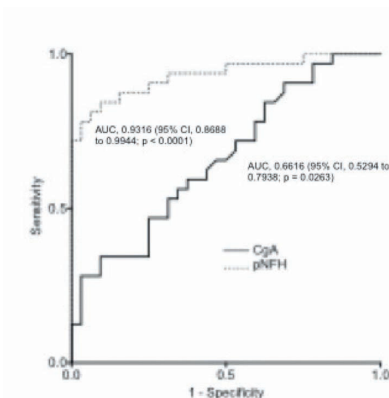
ROC curves of CgA and pNFH for discrimination between ALS patients and disease controls. CgA, chromogranin A. pNFH, phosphorylated neurofilament heavy chain

Conclusion: Given the considerably lower diagnostic performance in comparison to pNFH and the lack of association with disease parameters, CgA does not appear to be a promising clinical ALS biomarker.

Disclosure: The study was supported by grants from the German Federal Ministry of Education and Research (project FTLDc 01GI1007A, MND-Net 01GI0704), the EU Joint Programme-Neurodegenerative Diseases network PreFrontAls (01ED1512), the Foundation of the state of Baden-Wuerttemberg, the Thierry Latran Foundation, and Boehringer Ingelheim Ulm University BioCenter.

EPO3050

Phrenic nerve motor amplitude predicts function decline in amyotrophic lateral sclerosis

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Background and aims: Phrenic nerve motor amplitude (DiaphrAmpl) has been previously shown to predict hypoventilation and survival in amyotrophic lateral sclerosis (ALS). However, no studies have shown its predictive value in detecting functional decline, which is the aim of our study.

Methods: We prospectively included 39 ALS patients (62.3 ± 10.3 years, 20 males, 18.6 ± 13.1 months from symptom onset, 13 bulbar-onset). Patients were evaluated at baseline and at 2-6 months (mean=3.8 ± 0.9 months) with the functional ALS scale score (ALSFRS), the predicted forced vital capacity (%FVC) and the DiaphrAmpl. The change from baseline on the ALSFRS was analysed with a linear mixed-effects model for repeated measures, taking into account clinical characteristics, DiaphrAmpl and %FVC at baseline.

Results: At baseline, no significant correlations ($p > 0.05$) were observed between ALSFRS mean=31.7 ± 4.3), DiaphrAmpl (right/ left mean=0.50 ± 0.16/ 0.56 ± 0.19,) and %FVC (mean=89.7 ± 14.9). We found a significant decline ($p < 0.05$) from baseline in ALSFRS (mean=-2.9 ± 2.1), %FVC (mean=-6.9 ± 10.1) and DiaphrAmpl (right mean=-0.06 ± 0.11, left mean=-0.07 ± 0.12). There was no significant difference between DiaphrAmpl (right:-11.1%; left:-12.1%) and %FVC (-7.5%) percentage of change from baseline ($p > 0.05$). When testing the longitudinal effects in functionality, a greater change in ALSFRS was observed if the initial score was higher and the baseline DiaphrAmpl was lower ($p < 0.05$); but no influence of baseline %FVC ($p > 0.05$).

Conclusion: In addition to its known predictive value in hypoventilation and survival, DiaphrAmpl also relates to longitudinal functional decline and should be considered in clinical trials.

Disclosure: Nothing to disclose

EPO3051

Increased risk of melanoma in c9orf72 expansion carriers

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Background and aims: Some types of cancer have increased prevalence in Amyotrophic Lateral Sclerosis (ALS) patients. There is mounting evidence of an increased risk of ALS in patients who have had melanoma. The inverse relationship has also been suggested.

We aimed to study the hypothesis that c9orf72 expansion is linked to the risk of melanoma development.

Methods: We describe 2 families of interest in which the coexistence of FTLD-ALS spectrum disorders and melanoma are relevant. To investigate a possible link between specific mutations and melanoma, we further compared the risk of melanoma between different pathogenic mutations and between different phenotypes.

Results: We collected information regarding cancer history in 54 patients with c9orf72 expansion or pathogenic mutations of GRN, MAPT and SQSTM1. 29 subjects had c9orf72 expansion, 4 had MAPT mutations, 20 had GRN mutations and 1 had a SQSTM1 mutation. All the 5 patients with melanoma belong to two unrelated families. Four of them have the diagnosis of ALS and one is an assymptomatic carrier.

Melanoma is significantly higher in c9orf72 expansion carriers ($p = 0.05$). In our sample, melanoma occurred only in ALS patients, but this did not reach statistical significance ($p = 0.155$).

Conclusion: Our study suggests a link between c9orf72 expansion and melanoma. These findings may open a new way to approach and understand ALS and frontotemporal pathophysiology. It also suggests that ALS or FTLD patients with personal or family history of melanoma may be at increased probability of having a c9orf72 expansion, and genetic testing should be considered.

Disclosure: Nothing to disclose

EPO3053

Evaluation of non motor signs in patients with Amyotrophic Lateral Sclerosis

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Background and aims: Amyotrophic Lateral Sclerosis (ALS) is a rare neurological condition caused by motor neuron degeneration.Classically, this disease encompasses pure motor signs. Recently, we have seen the emergence of the concept of "ALS-plus" defined by the coexistence of classic motor clinical signs of ALS and atypical neurological signs. Our study aimed to evaluate the frequency of non motor signs (NMS) in patients with ALS and to propose a diagnostic and therapeutic approach.

Methods: A retrospective study was performed, including ALS follow-up patients in the department of Neurology, Razi Hospital between 2002 to 2017. Evaluation focused on the clinical features of motor and NMS in patients with ALS and on results of paraclinical investigations: electroneuromyography (ENMG), electrophysiological study of the autonomic nervous system (ANS) and saccadic eye records.

Results: We included 140 patients. Mean age at diagnosis was 53.8 years. Sex ratio was 1.74. NMS were identified in 63 patients (45%): 19 patients (14.1%) had cognitive impairment, 4 patients (3%) had oculomotor disorders,12 patients (8.5%) had extrapyramidal signs, 32 patients (22.9%) had sensory disturbances and 56 patients (40%) had dysautonomic signs. A statistically significant correlation were present between bulbar onset and NMS (p=0.008). However, there was no significant correlation between age, duration of evolution or use of Riluzole and presence of NMS.

Conclusion: Thi study confirms the high frequency of atypical signs in patients with ALS. An early diagnosis of these manifestations leads to propose an adapted therapeutic management and an improvement of patients' quality of life.

Disclosure: Nothing to disclose

EPO3054

Comprehensive genetic characterisation of an Argentinian cohort with Amyotrophic Lateral Sclerosis

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Background and aims: Recently, the C9orf72 expansion was detected in 2% of sporadic and 1of 3 families in a series of ALS cases from Argentina, but other ALS-causing genes remain unexplored. We aim to characterise a large Argentinian ALS cohort.

Methods: 26 Argentinian patients with a clinical diagnosis of ALS were scrutinised for disease-causing variation by fragment analysis and targeted next-generation sequencing (NGS).

Results: 13 patients harboured 14 potentially pathogenic alterations in the genes SOD1, TARDBP, FUS, UBQLN2, VCP, CHMP2B, SETX, ATXN2 and C9orf72. 8 out of 12 could be confirmed by Sanger, and after genetic analysis, one variant in FUS and one variant on SETX were considered non-pathogenic. There were 5 reported missense mutations: p.G86S and p.D84G in SOD1, p.R155H in VCP, p.N378D in TARDBP, p.497S in UBQLN and 2 C9orf72 expansions. There was one novel alteration in CHMP2B (p.R32Q) in a subject with a family history of ALS, and presented conflicting prediction scores. Segregation could not be studied. Three intermediate ATXN2 repeats were associated to variants in TARDBP, UBQLN and CHMP2B. The total pathogenic mutation rate was of 27%, which accounts for 63% among familial and 12% of sporadic subjects.

Conclusion: Argentinian populations have a similar genetic landscape for ALS as Europeans. NGS is a cost effective screening methods of genetic variation but the gold standard for confirmation is still Sanger sequencing. The next step of this work is to enlarge our cohort and perform ancestry analysis.

Disclosure: Nothing to disclose

EPO3055

A longitudinal Motor Unit Number Index (MUNIX) Estimation study in Frontotemporal Dementia (FTD)

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Background and aims: Motor Unit Number index (MUNIX) is a non-invasive method that that requires minimal electrical stimulation. The technique involves utilizing the surface-recorded compound muscle action potential (CMAP) and electromyographic (EMG) interference pattern to compute the motor unit number index (MUNIX). This is the first ever study applied MUNIX in FTD. The aim was to identify the presence of any neurophysiologic evidence of lower motor neuron system dysfunction across FTD subtypes by applying MUNIX longitudinally to study consecutive patients with FTD. Clinical parameters and MUNIX findings were also compared across FTD subgroups to explore patterns of lower motor neuron system dysfunction in FTD phenotypes.

Methods: We performed longitudinal MUNIX measurements in 6 muscles in a cohort of 39 FTD (22 bvFTD, 9 nfvPPA, 6 FTD-MND and 2 svPPA) patients, 3-monthly, over 21 months period. The right side was chosen for testing and all participants had no clinical evidence of LMN involvement (muscle weakness, wasting of fasiculations).

Results: Of 39 enrolled patients; results varied in different FTD subtypes. All nfvPPA and svPPA: there was no decline in MUNIX values over study period. MUNIX values were below normal at test1 and declined over time in FTD-MND (as expected). MUNIX values were below normal in 3/22 (14%) of bvFTD patients. MUNIX decline in bvFTD was seen in all muscles without concomitant clinical features of LMN involvement (weakness, fasciculations or wasting).

Conclusion: Lower MUNIX values are present in bvFTD patients suggesting lower motor neuron dysfunction without clinical evidence of ALS in some instances.

Keywords: MUNIX, FTD, Longitudinal study.

Disclosure: Nothing to disclose

Movement disorders 4

EPO3056

Alpha-synucleinopathy manifesting as familial atypical parkinsonism with the presence of rare variants of FBXO7 (PARK15) genes and VPS35 (PARK17)

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Background and aims: Three large pedigrees with familial occurence of atypical parkinsonism were found in a small, isolated region of south-eastern Moravia, Czech Republic; our patient belongs to one of these pedigrees.
Methods: Beside the clinical observation and video documentation, a detailed molecular-genetic analysis to confirm or exclude the presence of PARK mutations was done; finally the autopsy was performed, which focused on the pathological changes in the brain.
Results: The patient suffered from an atypical parkinsonism with the phenopetype of progressive supranuclear palsy-parkinsonism. The molecular-genetic analysis revealed the presence of rare variants of genes FBXO7 (PARK 15) and VPS35 (PARK 17). The autopsy finding was the alpha-synucleinopathy (diffuse presence of Lewy bodies and Lewy neurites , Braak stage VI) with some t-inclusions (threads, pretangles) in hippocampus and both occipital lobes.
Conclusion: In our patients, we have documented the joint presence of rare variants of FBXO7 and VPS35 genes. The pathological substrate of this unique and yet unknown familial parkinsonism is diffuse alpha-synucleinopathy.
Disclosure: Supported by AZV 15-32715A (Czech Republic)

EPO3057

Diffusion tensor imaging of olfactory tract in Parkinson's disease

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Background and aims: Olfactory dysfunction is recognized as one of the earliest indicators of developing Parkinson's disease (PD) and one of the major nonmotor symptoms with a significant impact on quality of life. In the present study, we investigated the possible relationships among olfactory impairment and alterations in diffusion tensor imaging (DTI) of olfactory tracts, comparing a cohort of PD patients and a matched control group.
Methods: Olfactory function of each subject was assessed using the Italian Olfactory Identification Test. Motor disability was assessed in all patients using Unified Parkinson's Disease Rating Scale-III part (UPDRS-III) and Hoehn and Yahr rating scale (H&Y). Imaging was performed on a 3T Philips Achieva MR scanner. MRI pre-processing was performed by DTIPrep, DTI reconstruction and fiber tracking by DiffusionToolkit, tractography analyses using TrackVis. The following parameters were used for groupwise comparison: fractional anisotropy (FA), mean diffusivity (MD), tract volume and length.
Results: 17 patients with PD (mean age 64.9 ± 7.6 years, UPDRS III 24.4 ± 11.7, H&Y stage 1.9 ± 0.5) and 9 controls (mean age 60.7 ± 14.2 years) were recruited. Olfactory identification function of all PD patients was decreased. The region of interest analysis of the olfactory tract showed significant FA signal and volume decreases of the PD group when compared with the control group ($P < 0.05$). Significant correlations were found between the MD values and the H&Y stage ($r = 0.60$, $P < 0.01$).
Conclusion: DTI analyses of olfactory structures may be viable as a means of establishing cohorts of subjects with probable pre-clinical PD.
Disclosure: Nothing to disclose

EPO3058

Dopaminergic adverse-events in COMT-naïve patients starting adjunctive therapy with opicapone: the BIPARK-I double-blind experience

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Background and aims: Assess the occurence of dopaminergic adverse-events (AEs) in levodopa-treated COMT-naïve Parkinson's Disease (PD) patients when starting opicapone (OPC) 50mg or entacapone (ENT).

Methods: Double-blind, 14 to 15-week, placebo- and active-controlled study. In the emergence of dopaminergic-AEs during the first 3-weeks, investigators could titrate the levodopa daily-dose. Dopaminergic-AEs were defined as new or worsening post-baseline treatment. This post-hoc analysis investigated the dopaminergic-AEs occurence, namely, dyskinesia, nausea, hallucinations (including delusion, illusion and disturbance-in-attention), vomiting and orthostatic hypotension.

Results: 359 patients were randomized to placebo (PLC, n=121), OPC-50mg (n=116) or ENT (n=122). Cumulatively, patients taking OPC-50mg reported more dopaminergic-AEs (22%) compared to ENT (16%) and PLC (8%). Subjects with dopaminergic-AEs took levodopa≥700mg/day (on average). Cumulatively, by the end of double-blind, cases of dyskinesia, nausea, hallucination, vomiting and orthostatic hypotension were reported, respectively, by 5%, 1%, 2%, 1% and 0% under PLC; 10%, 11%, 1%, 0% and 2% under ENT; and 17%, 3%, 8%, 1% and 1% under OPC-50mg. However, despite no levodopa-adjustment during last 3-months, the actual (by-day) frequency was 2%, 1%, 0%, 0% and 0% under PLC; 3%, 1%, 0%, 0% and 1% under ENT; and 4%, 0%, 0%, 0% and 0% under OPC-50mg, respectively. Under OPC-50mg, dyskinesia presented an earlier onset than hallucinations. Dyskinesia appear to have a later onset under ENT versus OPC-50mg.

Conclusion: There was an apparent treatment-relationship for dopaminergic-AEs with OPC presenting the highest incidence. These observations support an enhanced dopaminergic efficacy of OPC and whilst dyskinesia could be managed by an early follow-up, hallucinations may require a later-stage follow-up.

Disclosure: Nothing to disclose

EPO3060

Are the MDS-UPDRS-based composite scores clinically applicable?

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Background and aims: In the present study we evaluated the feasibility of various composite scores based on the Movement Disorder Society-sponsored Unified Parkinson's Disease Rating Scale (MDS-UPDRS) as potential clinical outcome measures and subsequently determined their minimal clinically important difference threshold values.

Methods: 1113 paired investigations of 452 patients were reviewed implementing three different techniques simultaneously.

Results: Based on the ordinal regression modeling, the MDS-UPDRS II+III, MDS-UPDRS I+II+III, and the total score of MDS-UPDRS are clinically applicable outcome measures. Any improvement greater than 4.9 points or any worsening more than 4.2 points on MDS-UPDRS II+III represent a minimal, yet clinically meaningful change. In reference to MDS-UPDRS I+II+III, the smallest changes considered clinically relevant were 6.7 and 5.2 points for improvement and deterioration, respectively. The thresholds for the total score of MDS-UPDRS were 7.1 points for improvement and 6.3 points for worsening.

Conclusion: Although the developers did not recommend the usage of composite scores, numerous PD-related studies utilize MDS-UPDRS-based composite scores as their outcome measure. The justification for using each Part score independently is based on the clinimetric properties of the scale. However, in the clinical practice and experimental studies, there may be important reasons to combine the outcomes. Utilizing composite scores may generally provide a broader assessment of PD; however, the combination of the domains may weaken the specificity. Employing ordinal regression modeling, we demonstrated that these composite scores including the total score are clinically applicable and responsive to changes.

EPO3061

A shoe insole delivering vibratory noise to improve freezing in Parkinson's disease

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Background and aims: The freezing of gait (FOG) is one of the most debilitating symptoms in Parkinson's disease (PD). It is one of the symptoms that does not show a significant improvement with the current treatment. Here, we aim to test the efficacy of a non-invasive treatment, an insole called 'Path Feel', as a device that can improve functional walking ability and FOG via haptic feedback in patients with PD.

Methods: The patients were assessed with the following clinical scales: Unified Parkinson's Disease Rating Scale–part III, Gait and Balance scale, Gait and Falls questionnaire, Activities-Specific Balance Confidence Questionnaire, Fear of Falling Avoidance-Behaviour Questionnaire. Pre-assessment: complation of a diary related to falls and episodes of FOG the week before the first session as well as the week before the second session. Clinical session 1: baseline in 3 conditions: a) OFF medications, b) OFF medications with the insoles, c) ON medications with the insoles. Clinical session 2: after a week of wearing the insoles in 3 conditions: a) OFF medications with the insoles, b) ON medications with the insoles, c) ON medications without the insoles. Self-reporting: completion of the questionnaires after a week without wearing insoles.

Results: The Path Feel insoles appear to be well received by the first patient. The improvement of several scores over the 3 session implies that Path Feel did improve the FOG. Interestingly, there was a coherent improvement of all scores during the 3rd week of the study which was the week following the one with the insoles.

Conclusion: This result suggests that the benefit of the vibratory stimulation on the FOG.

Disclosure: Brain Appeal Charity

EPO3062

Persistence of limb dystonia and myoclonus during sleep in Corticobasal Syndrome: report of three clinical cases.

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Background and aims: Thus far, few studies focused on sleep in Corticobasal Syndrome (CBS), documenting REM sleep behaviour disorder and periodic limb movements. No study evaluated the possible sleep modulation of the motor abnormalities as dystonia or myoclonus in these patients.

Methods: Three patients with clinical diagnosis of CBS underwent a nocturnal polysomnography through an extensive EMG montage. All cases presented with asymmetric parkinsonism and limb dystonia±myoclonus.

Results: All patients showed a severe impairment of sleep architecture and efficiency.

In case 1, PSG revealed the persistence of myoclonic jerks and tonic spasms through all sleep stages, sometimes recurring in a periodic fashion (every 20 seconds). Furthermore, prolonged painful contractions of the left arm, arising both during wakefulness and sleep, were observed. Regarding case 2, the polysomnographic finding of a tonic activation on distal muscles of the left arm, during NREM sleep, was associated with further periodic phasic increasing of muscular tone. PLMi was increased (35.5/h).

Finally in case 3, PSG disclosed in all sleep stages the persistence of myoclonic jerks and tonic spasms, especially involving the right arm, even if with low voltage amplitude when compared with those recorded during wakefulness.

Conclusion: We documented the persistence during all sleep stages of dystonia and/or myoclonus in patients with CBS. Modulation of central nervous system connectivity occurring during sleep usually leads to disappearance of almost all the abnormal movement associated with basal ganglia dysfunction. In our patients, instead, the persistence of dystonic posture/myoclonus could indicate a cortical generator.

Disclosure: Nothing to disclose

EPO3063

Deletion in the progranulin gene in a patient with classic clinical features of Parkinson's disease

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Background and aims: Mutations in the progranulin gene (GRN) are known causes of familial forms of frontotemporal dementia with autosomal dominant inheritance. Carriers frequently develop parkinsonism, usually with a partial or absent levodopa response. However, parkinsonism at onset is less common and rest tremor is usually absent.

Methods: Case report.

Results: A 51-year-old male presented with right hand rest tremor, mild depression and apathy. He had a family history of dementia with 6 affected relatives over 3 generations. Most notably, the patient's brother had been diagnosed with Alzheimer's disease at the age of 49. On examination, he had pill-rolling rest tremor on the right and re-emergent tremor. He had mild bradykinesia and rigidity, more on the right. Formal neuropsychometry was normal. The patient had a normal brain magnetic resonance imaging scan. 123I-Ioflupane Single-photon emission computed tomography demonstrated reduced uptake, particularly in the left putamen. Motor symptoms responded well to low-dose pramipexole. Over the next two years, his apathy gradually worsened, he developed binge-eating behaviour leading to considerable weight gain and sleep apnoea. Mutations in C9ORF72, MAPT, TARDBP, FUS, APP, PSEN1, PSEN2 were excluded. Both he and his brother were found to carry a novel 64-bp deletion preceded by a single nucleotide change in the GRN gene, predicted to result in p.Gln401LeufsTer50.

Conclusion: We report a patient presenting with classic features of Parkinson's disease who was eventually found to have a GRN mutation. Notable family history should raise suspicion of a genetic cause even in the case of a seemingly benign presentation.

Disclosure: Nothing to disclose

EPO3064

Incidence of mild cognitive impairment and dementia in Parkinson's disease

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Background and aims: Mild cognitive impairment (MCI) is a common feature of Parkinson's disease (PD) even in the early stages of the disease and represents an important risk factor for the development of PD Dementia (PDD). Aim of our study was to evaluate incidence of MCI and the rate of its progression to PDD.

Methods: PD patients fulfilling the Brain Bank criteria who underwent at least two comprehensive neuropsychological evaluations (baseline and follow-up) within 48 months were enrolled in the study. Diagnosis of PD-MCI and PDD was made according to MDS criteria. Person-time incidence rate of PD-MCI and PDD has been estimated.

Results: 139 non-demented PD patients (men 86, mean age 65.9±9.3, mean disease duration 4.0 ±0.4 years, mean follow-up 24.9±10.3 months) were enrolled in the study. At baseline evaluation, 77 (55.4%) were classified as PD-normal cognition (NC) while 62 as PD-MCI. At follow-up among the 77 PD-NC at baseline, 27 developed MCI and 4 PDD. The incidence rate of MCI was 168,2/1000 person-years at risk (pyar) (95%CI 113.5-242.1). Considering the 62 patients with PD-MCI at the baseline, at follow-up 17 developed dementia (PDD). Incidence rate of PDD among patients with MCI at baseline was of 133.0/1000 pyar (95%CI 79.9-208.3) while among PD patients with NC at baseline was 24.9/1000 pyar giving a RR of 5.31 (95%CI 2.00-14.0; p-value 0.0004).

Conclusion: Our study underlined a high incidence rate of MCI in PD patients. Presence of MCI highly increased the risk of dementia in patients with PD.

Disclosure: Nothing to disclose

EPO3065

Dual-site transcranial magnetic stimulation for the treatment of Parkinson's Disease

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Background and aims: Abnormal oscillatory neuronal activity in the subthalamic nucleus (STN) plays an important role in the pathophysiology of motor symptoms in Parkinson disease (PD). Anatomical studies showed that the primary motor (M1) and dorsal premotor cortex (PMd) project directly to different neuronal populations within the STN ("hyperdirect pathway"). We hypothesized that PD motor symptoms can be ameliorated with transcranial magnetic stimulation (TMS) applied to M1 and PMd with the goal to phaselock and desynchronize oscillating STN neurons via the hyperdirect pathway and through induction of long-term depression-like effects comparable to coordinated-reset DBS.

Methods: Asynchronous repetitive TMS to both a premotor area located at 32 mm anterior of M1 and M1 ("associative dual-site rTMS", "ADS-rTMS") was employed at 1 Hz with in 20 PD patients treated in a blinded, placebo-controlled cross-over design using two D-shaped TMS coils. Clinical outcomes were rated based on video-analysis of MDS-UPDRS-III with two certified raters blinded to treatment modality and additional metrics (tapping, tremor analysis).

Results: We found no significant improvement in the MDS-UPDRS-III or secondary motor outcome parameters (finger tapping performance, spectral power of resting or action tremor activity). Variation of the secondary stimulation site outside M1 (to either 50 mm anterior to M1 or to supplementary motor area) did not induce beneficial effects either.

Conclusion: A single session of ADS-rTMS did not produce a clinically meaningful beneficial effect on Parkinsonian motor symptoms. Successful treatment for PD by non-invasive brain stimulation targeting subcortical nuclei may require more detailed physiological information about the individual brain state and stimulation-induced effects.

Disclosure: The project was funded by the CortExplorer program (P1140048) of the Gemeinnützige HERTIE-Stiftung, Grüneburgweg 105, 60323 Frankfurt, Germany.

EPO3066

Defining the bending angle of PD patients suffering from camptocormia

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Background and aims: Camptocormia is a non-fixed forward bending of the trunk which resolves when lying down. Surprisingly there is no agreement how to measure the bending angle. The purpose of this study is to provide the scientific background for a consensus decision.

Methods: Photos of 42 patients with the subjective complaint of forward bending and PD were taken with a lateral view. Three methods of angle measurement were applied by two independent raters: The perpendicular method (PM) measuring the angle between a line connecting spinous process C7 and L5 and a perpendicular line through L5. The malleolus method (MM) assessing the angle between the same C7/L5 line and a line connecting L5 and the lateral malleolus. The fulcrum method (FM) is assessing a line between the fulcrum of the camptocormia and a perpendicular line.

Results: The measured angles differed between the three methods between 33° (PM), 47° (MM) and 55° (FM). The difference of the angle measured between the raters was 10.1° (FM), 2.4° (MM) and 1.7° (PM).

Conclusion: The three methods differ in the measured angles and the inter-rater reliability for the same patient group. FM lacks a precise definition of the fulcrum leading to a low interrater reliability. PM and MM showed a comparable interrater reliability. While MM is orientated in the individual appearance of the forward bending including the hip flexion, PM showed lower angle degrees because of disregarding this aspect. We propose MM as a suitable method to determine the forward bending angle in camptocormia.

Disclosure: Nothing to disclose

EPO3117

Urinary Symptoms and associated clinical features in Parkinson's Disease

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Background and aims: Lower urinary tract symptoms (LUTS) are highly prevalent in patients with idiopathic Parkinson's disease (IPD). Aim of the study was to analyze the prevalence of LUTS and the possible association with patients' age, disease duration, severity and non -motors symptoms.

Methods: 30 IPD patients, 21 men and 9 women without cognitive impairment (MOCA >24) and under 80 years old were enrolled. All patients underwent the unified Parkinson's disease rating scale (UPDRS) motor section part III and Hoehn-Yahr (H&Y) scale, Montreal Cognitive Assessment (MOCA), Hamilton Anxiety Scale (HAM-A), Hamilton Depression Scale (HAM-D), 3- day voiding diary, uroflowmetry and a standardized questionnaire on incontinence (Incontinence-QoL).

Results: All patients investigated complained of overactive bladder symptoms. Urinary incontinence was significantly associated with higher H&Y stages ($p < 0.005$) and frequency of nocturia with higher UPDRS scores ($p < 0.003$). Old age, longer disease duration and higher H&Y stage were significantly related with reduction in HAM-A scores (mean$\pm$SD: 16.3$\pm$5.8; $p < 0.002$); and also post- void residual volume was related with an increase in HAM-D scores ($p < 0.005$). The I-QoL scores (mean$\pm$ SD: 62.4$\pm$26.2) were significantly associated with the MMSE scores (mean$\pm$SD: 2.4$\pm$0.7; $p < 0.01$).

Conclusion: To our knowledge, this is the first study showing a positive correlation between urinary, neuropsychiatric symptoms and QoL.
Our findings, in line with previous studies, suggest that the presence of LUTS in PD patients are strictly related to age, disease duration and the severity of motor impairment.

Disclosure: Nothing to disclose

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EPO3067

Lymphocyte count and Body Mass Index as biomarkers of treatment response in a Multiple Sclerosis Dimethyl-Fumarate-treated cohort

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Background and aims: In dimethyl-fumarate (DMF)-treated relapsing MS (RMS) patients, few data are available about biomarkers of treatment response. We aimed to assess the predictive value of lymphocyte count (LC) and BMI for treatment response in a real life setting of DMF treated patients.

Methods: We collected clinical, demographic and anthropometric data at the beginning (T0) of DMF. LC were assessed at T0 and after 3(T3) and 6(T6) and 12 (T12) months. Relapses within T6 and T12 were considered to evaluate clinical activity; Gadolinium enhancing (Gd+) and new T2 lesions, defined MRI activity at T6 and T12. To correlate LC and BMI with clinical and MRI response, Pearson and Spearman tests were performed. We evaluated using logistic regression models, whether BMI or LC can predict treatment response.

Results: Our cohort of 165 DMF-treated patients was followed up for 15±7 months. The mean BMI at baseline was 24.19±4.48. We observed an inverse correlation between BMI and relapses within T6 (r=-0.31, p=0.001) and T12 (r=-0.32, p=0.019). We also found an inverse correlation between BMI and MRI activity at T12 (r=-0.32 p=0.012). At the multivariate models, predictive factors for GD+ lesions at T12 resulted LC at T3 (p=0.037, OR=1.084, CI=0.997-1) and baseline BMI (p=0.033, OR=0.887, CI=1.032-2.131). Predictive factors for new T2 lesions at T12 were LC at T3 (p=0.005, OR=1.010 CI=0.99-1) and baseline BMI (p=0.026, OR=0.997, CI=0.98-1).

Conclusion: BMI and LC during DMF can be considered early biomarkers of treatment response.

Disclosure: Dr. Paolicelli received honoraria for consultancy and/or speaking from Biogen Idec, Merck-Serono, Almirall, Sanofi-Aventis, TEVA, Novartis and Genzyme. Dr. Manni, Dr. Iaffaldano A, Dr. D'Onghia and Dr. Messina have declared that no competing interests exist. Dr. Iaffaldano P. has served on scientific advisory boards for Biogen Idec and Bayer, and has received funding for travel and/or speaker honoraria from Genzyme, Sanofi-Aventis, Biogen Idec, Teva and Novartis. Prof. Trojano received honoraria for consultancy or speaking from Biogen, SanofiAventis, Merck Serono, Novartis, Genzyme, TEVA, and Bayer-Schering and research grants from Merck Serono, Biogen, and Novartis.

EPO3069

Imaging correlates of EDSS in Multiple Sclerosis

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Background and aims: The Expanded Disability Status Scale(EDSS) is the most widely used neurological disability scale in Multiple Sclerosis(MS), mostly assessing functional systems related to motricity. Its correlation with MRI parameters is still poorly understood.

Objective: To identify which brain MRI volumetric parameters correlate with neurological incapacity as quantified by the EDSS scale.

Methods: 60 consecutive MS patients and 60 healthy controls(HC) were enrolled, matched by sex and age. Neurological impairment in MS patients was determined by the EDSS. All participants underwent 3Tesla-MRI. Volumetric analysis was performed using FreeSurfer software, and the following volumes were obtained:T1 and T2 lesions; total, subcortical and cortical grey matter; white matter; brainstem; cerebellum; corpus callosum; thalamus, pallidum, caudate and putamen.

Results: The volume of all brain structures analysed was lower for MS patients when compared to HC(p<0.05). There was positive correlation between the EDSS value and the lesional volume in T2(r=0.506 p <0.01) and T1(r=0.438 p=0.001), and negative correlation with brainstem (r=-0.398 p=0.04), cerebellar (r=-0.298 p=0.024), pallidum (r=-0.331 p=0.012) and putaminal (r=-0.315 p=0.017) volumes. Overall grey matter and white matter volumes did not correlate with EDSS value. In linear regression analysis, the lesional volume in T2 was the only variable with predictive value for EDSS (r2=0,302 p<0.001).

Conclusion: Neurological disability measured by EDSS correlated mainly with the volume of white matter lesions and brain structures involved in motor control circuits, possibly reflecting the fact that the scale is dominated by gait function.

Disclosure: Nothing to disclose

EPO3070

Permantent lymphopenia and risk of PML in MS patients in real word

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Background and aims: Dimethylfumarate (DMF) is an oral drug for the treatment of RRMS. About6%of patients on DMFhad an absolute lymphocyte count equal to or less than 500/mL in trials. Progressive multifocal leucoencephalopaty (PML)cases have been reported in patients on DMF with moderate and permanent lymphopenia. It seems that durable moderate lymphopenia is a risk factor of PML in patients treated with DMF
Our objetive is to analyse the characteristic of the patients with lymphopenia in a real world MS cohort treated with DMF.

Methods: Retrospective observational study including patients with RRMS on DMF and analyzethe clinical features of those patients, who have presented lymphopenia during at least3months of treatment.

Results: 188patients were studied. 57(30,31%)presented lymphopenia for more than three months.42 (73,7%)were women. The average age was 44,05(23-70), and 17were older than 50 years. The mean time from the start of treatment to the onset of lymphopenia was 8.73months(1-26). The grades of significant lymphopenia : Grade2:20 patients (35,1%); Grade3:24 patients (42,1%); Grade4: 1(1,8%). The rate of lymphocites no recovery was 82,50%.Because of safety reasons, DMF was withdrawn in 33 patients. Of the patients who recovered from lymphopenia, the average recovery time was 10,10months (2-27) after withdrawal.

Conclusion: In the real world analysis ,one third of patients presented lymphopenia and from these patients more than a half had to stop the drug for risk of PML. Moreover, The recovery of the number of lymphocytes was very slow, and must be taken into account for the choice of the next disease modifying drug.

Disclosure: Nothing to disclose

EPO3071

Application of tRNS to improve Multiple Sclerosis Fatigue: a sham-controlled study

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Background and aims: Fatigue is one of the most common, early, and disabling symptom in Multiple Sclerosis (MS). tDCS on Dorso-Lateral Prefrontal Cortex seems to give positive results on MS fatigue. Recently, a new stimulation protocol, transcranial Random Noise Stimulation (tRNS), showed powerful facilitatory effects on motor cortex in healthy subjects and ameliorated pain in MS patients. Here we aimed to explore effects of motor cortex tRNS in MS fatigue.

Methods: 13 MS fatigued patients were enrolled in a blind, sham controlled tRNS study. 7 patients received 1.5 mA, 101-640 Hz tRNS stimulation and 6 patient received sham stimulation, both stimulations applied daily over M1 for 15 minutes, for two consecutive weeks. Outcome measures were Modified Fatigue Impact Scale (MFIS) for fatigue, BICAMS for cognitive impact, Purdue Pegboard for manual dexterity, Timed 25 Foot Walking Test (T25FWT) for fatigability, MSQoL-54 for quality of life.

Results: ANOVA showed statistically significant improvement in MFIS physical subscale in real stimulation group (Real-p=0.004, Sham-p=0.22). SDMT scores improved only in tRNS subjects (p=0.01). MSQoL-54 scores showed a significative improvement only in tRNS patient (REAL-p=0.02, Sham-p=0.5) Patient Global Impression of Perceived Fatigue was significatively reduced in tRNS group (p=0,005).

Table 1 Sample characteristics

	tRNS	SHAM	p-value
Mean Age ± SD	36.7 ± 9.4	47.3 ± 5.3	0.03
Mean age at onset ± SD	24.7 ± 6	34.5 ± 7.5	0.02
Mean age at diagnosis ± SD	29-3 ± 6-3	37.3 ± 5.5	0.03
Mean EDSS ± SD	2-0 ± 1-1	3.1 ± 1.5	0.16
Mean MSSS ± SD	3 ± 3	3.6 ± 2.9)	0.70
Sex (M/F)	2/5	1/5	0.61

Table 1. Demograpnid and clinical features of the real and sham groups

Conclusion: tRNS on primary motor cortex can decrease MS fatigue. If further studies on larger samples validated and strengthened the results obtained so far, the development of stimulation device suitable for self-managed home based treatment should be strongly pursued to optimize management of such disabling symptom in MS.

Disclosure: Nothing to disclose

EPO3072

Immunomodulatory therapy reduces elevated nitric oxide levels in multiple sclerosis patients

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Background and aims: Recent research indicates that apart from reactive oxygen species, reactive nitrogen species, in particular the free radical nitric oxide (NOx) may be a driving factor in multiple sclerosis (MS) pathology. There are reports investigating NOx in cerebrospinal fluid, but the role of serum NOx (sNOx) in MS remains largely unclear. Here, we aimed to investigate sNOx in MS patients compared to healthy donors (HD) and assess its relation to clinical data.

Methods: 214 samples from 29 clinically isolated syndrome (CIS), 109 MS patients and 79 HD were analysed. Among CIS/MS patients 86 (62.3%) received immunomodulatory therapy (interferon-beta n=53, glatiramer acetate n=13, natalizumab n=20). sNOx concentration was quantified spectrophotometrically using the Active Motif® Nitric Oxide Quantitation Kit.

Results: Increased sNOx levels were found in untreated (median 9.1 IQR 7.3-14.2 μM) (p<0.01) compared to treated MS patients (median 6.6 IQR 4.9-10.3 μM). In CIS/MS we found higher sNOx in female (median 8.9 IQR 6.1-13.4 μM) compared to male (median 6.6 IQR 4.9-9.1 μM) patients (p<0.05). sNOx was unrelated to age, the Expanded Disability Status Scale score, disease duration and age at disease onset.

Conclusion: Increased sNOx levels are present in untreated MS patients, which are reduced to levels of HD under immunomodulatory therapy. Female MS patients seem to be more affected by an imbalanced sNOx status. Future studies are warranted to investigate if serum NOX may serve as a marker to monitor disease activity and treatment efficacy in MS.

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EPO3073

Potential effects of dimethyl fumarate on central cholinergic transmission explored by short latency afferent inhibition in multiple sclerosis

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Background and aims: Dimethylfumarate (DMF) is an oral agent approved for the treatment of relapsing-remitting multiple sclerosis (RRMS). DMF is able to activate the peripheral and centralnuclear factor erythroid-2-related factor (NRF2) pathway and stimulate nicotinic acid HCA2/GPR109A receptors. These pathways are also involved in acetylcholine (Ach) transmission, as shown in vitro. Ach is increasingly recognized to play a role in immunomodulation and neuroprotection.

Aim of this study is to explore the potential effects of DMF on central cholinergic transmission measured by short latency afferent inhibition (SAI) in MS patients.

Methods: In 20 RRMS naïve patients, who started DMF according to clinical practice, we performed SAI at baseline and 6 months after.

Two control groups were provided: I. 20 RRMS naïve patients who started INF-beta (INFg) according to clinical practice; II. 20 healthy subjects (HCg). Disability progression was investigated at baseline and 6 months after by EDSS. Side effects (SE) were also collected.

Results: SAI curves were not different at baseline comparing DMF and INFg at baseline and HSg.

SAI significantly improved after 6 months in DMF group (mean SAI at 20 and 24 ISI pre to post p=0.010) while there was no significant effect on SAI in INFg.

EDSS was unchanged comparing baseline and 6 months values; no severe SE were reported

Conclusion: Our study showed that DMF is able to improve SAI in MS patients, providing in vivo evidence of its influence on synaptic transmission. The facilitating action on the central cholinergic system may represent an additional mechanism of action, with potential implications for neuroprotection.

Disclosure: Nothing to disclose

EPO3074

Quantitative EEG differentiate Multiple Sclerosis with and without Cognitive Impairment from healthy controls at the beginning of the disease: preliminary data

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Background and aims: The present study aims to asses possible qEEG differences between newly diagnosed Multiple Sclerosis (MS) patients with or without Cognitive Impairment (CI).

Methods: We enrolled 13 patiens (18-5 years old) treated with first-line drugs for <6 months, and 16 healthy controls. All subjects underwent neuropsychological assessment including BICAMS and BDI. EEG recordings were performed during a cognitive task (computerised "SDMT" subtest of BICAMS) and at rest (5 minutes before and after task). Based on neuropsychological assessment patients were diagnosed as with -MSCI group- or without -MS group- cognitive impairment: only data from MSCI patients matched for sex, age (±5 years) and education to both an MS patient and a healthy control were analysed. Power spectrum analysis (theta, alpha, beta bands and sub-bands) were performed (EEGlab extension for MatLab). Data were log-transformed and analysed through repeated measures ANOVA.

Results: A significant interaction group (MSCI, MS, control) x condition (rest, task) x band (alpha, beta, theta) was observed. Post-hoc analyses showed significant differences between MSCI and both MS and controls in all EEG bands at rest (p<.05), whereas MS patients significantly differed from controls only in alpha2 and beta bands (p<.05). In task condition MSCI significantly differed from controls in alpha and beta bands, whereas MS in theta band (p<.05).
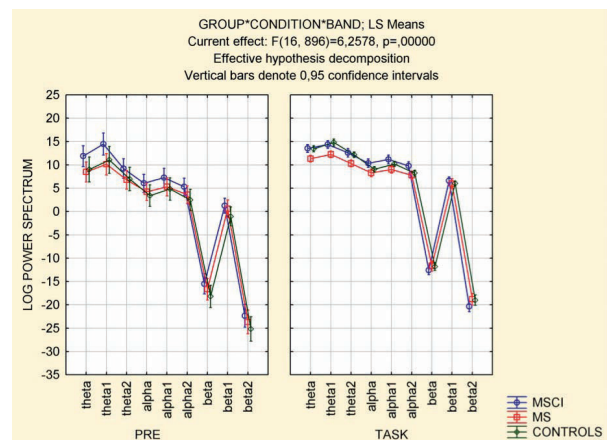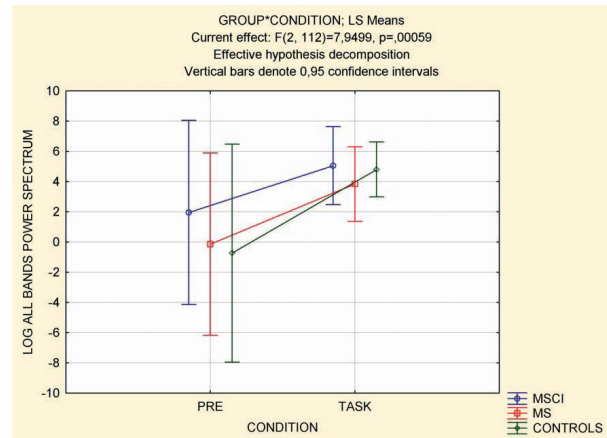
Conclusion: If confirmed in larger series, our results seem to support the hypothesis that qEEG differences exist among MSCI, MS and healthy controls, opening to a new possible neurophysiological hallmark of cognitive impairment in MS patients.

Disclosure: Nothing to disclose

EPO3075

Defective GABAergic transmission is associated with alexithymia in Multiple Sclerosis

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Background and aims: Alexithymia is a multicomponent personality construct characterised by difficulty in identifying feelings or describing them, and an externally oriented thinking. It could affect between 10 and 53% of patients with Multiple Sclerosis (MS). Defective GABAergic transmission and interhemispheric transfer were recently described in the context of alexithymia, but no studies were performed in MS.

Methods: 22 MS patients were classified as alexithymic (n=10) and non-alexithymic (n=12) according to the Toronto Alexithymia Scale score (TAS). Transcranial magnetic stimulation (TMS) was employed to record the interhemispheric inhibition and cortical silent period (CSP). Socio-demographic, clinical and neuropsychological data were obtained. Mann-Whitney and Fisher's exact tests were used for group comparison. Correlation analysis between TAS scores and TMS measures were performed using the Spearman rank correlation coefficient.

Results: In the absence of group difference with regards to clinical, socio-demographic and neuropsychological data, alexithymic patients had significantly shorter CSP duration (mean: 84.34±49.73, median: 91.50, vs. mean: 159.33±76.96, median: 148.50, respectively; p=0.03) than their non-alexithymic counterparts. In addition, TAS scores were significantly inversely correlated with CSP duration (r=-0.59; p=0.004).

Conclusion: This is the first study to address the neurophysiological underpinning of alexithymia in MS patients. In this population, alexithymia might be the result of a defective GABAergic transmission. Further research is needed to confirm the current results.

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EPO3076

Vaccines and Optic Neuritis: a systematic review

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Background and aims: Vaccinations are often the most effective tool against some diseases known to mankind. Case reports of optic neuritis (ON) following vaccination can lead to distrust in the safety of vaccines, therefore it is important to gather existing knowledge on vaccines and ON in order not to confuse temporal and causal relations.

Methods: This study is a literature review on the role of vaccines regarding the risk of developing ON.

Results: A systematic literature review on the database PubMed.

Conclusion: The summarised results of the studies did not raise sufficient evidence to back up a positive association between ON and vaccination against HBV, HAV, HPV, MMR, influenza, variola, varicella, diphtheria, tetanus, pertussis, anthrax, meningococcal, pneumococcal or typhoid. However, since the identified studies of vaccines and ON were limited, a complete exclusion of correlation cannot be made.

Disclosure: Nothing to disclose

Muscle and neuromuscular junction disease 2

EPO3077

Non-invasive evaluation of sudomotor function in patients with Myasthenia Gravis

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Background and aims: Myasthenia Gravis (MG) is an autoimmune disease resulting in most cases from autoantibodies against the acetylcholine receptor (anti-AchR) at the neuromuscular junction. Dysautonomia is not a commonly recognised feature of this disorder although it has been described in several case reports. Electrochemical Skin Conductance (ESC), assessed by Sudoscan®, is a non-invasive method that allows evaluation of sweat gland function. Since sweat glands are innervated by sudomotor, post-ganglionic, cholinergic sympathetic C-fibers, we believe that ESC could be a reliable method for assessing hypothetical autonomic dysfunction in MG patients.
Methods: ESC measurements were prospectively assessed in patients with generalised MG followed at a Neuromuscular Disease Outpatient Clinic and in healthy controls. Patients with Diabetes Mellitus, anticholinergic medication, or electrophysiological findings of peripheral neuropathy were excluded. Data regarding demographic and disease features were collected. For statistic analysis we performed chi-square or Mann-Whitney U-tests for comparison between both groups.
Results: We included 24 patients, mean age of 46.4 ± 10.6 years, female predominance (75%) and mean BMI of 26.5 ± 5.1. Average disease duration was 12.5 ± 8.9 years. Most patients had known serum positivity for anti-AchR (65%). Controls (n=37) were younger (39.6 ± 11.6; p=0,02) with no differences in other baseline characteristics. We found no difference in feet (76.8 ± 7.9 vs 79.7 ± 5.1; p=0,126) and hand (70.7 ± 14.6 vs 70.0 ± 11.9; p=0,83) ESC measurements between both groups. Sudomotor function in MG patients was within the normal range.
Conclusion: Sudomotor function was similar between MG patients and healthy controls.
We found no evidence of autonomic dysfunction in patients with generalised MG as assessed by ESC.
Disclosure: Nothing to disclose

EPO3078

Whole-exome sequencing identifies double trouble in a patient with neuropathic and myopathic symptoms

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Background and aims: We present a 39-year-old male patient with progressive proximal weakness, atrophy of thighs, gluteal and parts of the shoulder musculature. By contrast there was hypertrophy of calf deltoid and trapezius muscles. Additional clinical signs included winged scapula, hollow back, Trendelenburg gait, positive Gower sign, funnel chest, decreased muscle reflexes and gynecomastia. Family history was positive as his father showed similar myopathic symptoms, while mother and sister reported unspecific gait disturbance.
Additional pathological findings: While EMG showed myopathic pattern, nerve conduction study was compatible with axonal polyneuropathy. CK and myoglobin were elevated. On MRI thigh musculature showed significant atrophy with volume loss and fatty degeneration.
Methods: To unravel the genetic cause of his disease we performed a next-generation-sequencing (NGS).
Results: NGS detected two (so far unreported) missense mutations in different genes in the index patient: 1., heterozygous mutation within RYR1 (c.1160T>C p. Leu387Pro) compatible with autosomal dominant myopathy (OMIM #180901), and 2., heterozygous mutation within MORC2 (c.311C>T p.Ala104Val) compatible with autosomal dominant axonal polyneuropathy CMT2Z (OMIM #616688) While the father was found to carry the mutation in the RYR1 gene, mother and sister are carriers of the mutation in the MORC2 gene. Thus, the genetic findings are in accordance with the clinical manifestations of the index patient and the affected family members.
Conclusion: Along with comprehensive clinical investigations NGS may help to establish the genetic diagnosis of neuromuscular diseases with even complex clinical constellations.
Disclosure: Nothing to disclose

EPO3079

Progressive respiratory failure: an unusual case of polymyositis

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Background and aims: Polymyositis (PM) is an inflammatory myopathy characterized by progressive weakness, predominantly proximal. Main histological features are fiber size variability, scattered necrotic and regenerating fibers and perivascular and endomysial cellular infiltrates.

Methods: We present a patient, 44 years old, who suffered from breathing shortness. He came to our observation because of elevated CK levels (950 UI), diurnal drowsiness and severe dyspnea. At neurological examination, he had a mild waddling gait and proximal weakness. We performed electromyography (EMG), muscular magnetic resonance (MRI) of diaphragm and upper limbs, muscle biopsy (MB), and pneumological evaluation with spirometry, nocturnal saturimetry and polysomnography.

Results: EMG displayed a myopathic pattern. Muscle MRI pointed out edema of the upper limbs and diaphragmatic muscles; specific sequences showed a severe reduction of the diaphragmatic excursion.Pneumological evaluation evidenced a severe restrictive syndrome, hypercapnia, nocturnal desaturation, high Apnea Hypopnea Index (49.5). MB revealed fiber size variability, scattered necrotic regenerating fibers with perivascular and endomysial cellular infiltrates (inflammatory myopathy). He started Prednisone 75 mg/die and Azathioprine 100 mg/die. 3 months after the patient showed clinical improvement, confirmed by muscle MRI that pointed out a drammatic reduction of the edema, even at the diaphragm.

Conclusion: Hypercapnic respiratory failure due to respiratory muscle involvement as PM presentation is a very rare event and it is described in less than 10% of patients with inflammatory myopathies. In our patient, progressive hypercapnic respiratory failure led to suspect PM that improved after therapy as confirmed by muscle and diaphragmatic MRI, useful tool either for diagnosis or for follow up.

Disclosure: Nothing to disclose

EPO3080

Comparison of thymomatous and non-thymomatous myasthenia gravis on outcome after thymectomy

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Background and aims: To describe the clinical profile and differentiate the clinical features of thymomatous (MGT) and non-thymomatous myasthenia gravis (NTMG) who underwent thymectomy and clinical outcome in a cohort of patients at the Virgen de la Arrixaca University Hospital.

Methods: Demographic information, clinical staging data, surgical and treatment details and patient follow-up data were obtained with a retrospective review of thymectomies performed between 2006-2016.Using the Myastenia Gravis Foundation of America (MGFA) post-intervention status classification, Complete Stable Remission, Pharmacologic Remission and Minimal Manifestatios and Improved were defined as Good Clinical Outcome (GCO) and Unchanged, Worse, Exacerbation or Died of MG as Poor Clinical Outcome (PCO).

Results: In 43 consecutive thymectomies for MG, 11 (25.6%) had pathologic diagnosis of thymoma. Non-thymomatous cases were hyperplasia thymic 21 (48,8%), thymic rests 9 (20,9%) and other findings 2 (4,7%). On univariate analysis, age at diagnosis (MGT 53±20 years vs MGNT 33±24 years), men (54,5% vs 18,8%), findings in mediastinal imaging (100% vs 58,1%), thoracotomy (36,4% vs 9,4%) and time to surgery were statistically significant between two groups. There no was difference at distribution of patients using MGFA Clinical Classification, serological tests or treatment before or a year after thymectomy. MGT was associated with poor clinical outcome a year after surgical intervention (PCO 46,2% vs GCO 16,7% OR 4.286; 95% CI, 1.928-19.796).

Conclusion: The not immediate benefit of thymectomy may be relationated with thymus role in pathogenesis of MG.

Disclosure: Nothing to disclose

EPO3081

Collagen VI encoding genes mutations-phenotypic variability in a cohort of Portuguese patients

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Background and aims: Bethlem myopathy and Ulrich Congenital Muscle Dystrophy are two classical phenotypes associated with mutations of collagen VI encoding genes (COL6A1, COL6A2 and COL6A3). However, a wide range of clinical presentation has been identified.

Methods: Review of clinical cases.

Results: Case 1. A 50-year-old male presented slowly progressive muscle weakness, beginning in childhood. Neurological exam revealed proximal limb muscle weakness (grade 4), contractures of fingers flexors muscles and shortening of the Achilles tendons. His 28-year-old daughter and 19 year-old niece had an analogous but less severe clinical presentation. A heterozygous mutation was found in COL6A1 gene in the three patients.

Case 2. A 29-year-old female presented with muscle weakness in childhood, slowly progressing towards a limb-girdle pattern of muscle weakness (grade 3) and distal muscle contractures. A heterozygous mutation in COL6A1 gene was identified. The same mutation was also identified in her mother.

Case 3. A 55-year-old male presented with muscle weakness begging in childhood, slowly progressive, with proximal lower limb muscle weakness (grade 4), lumbar hyperlordosis and distal muscles contractures. A homozygous mutation in COL6A2 was identified. His consanguineous parents were heterozygous for the same mutation.

Case 4. A 32-year-old male presented in childhood with delayed motor milestones and slowly progressive muscle weakness. Neurological examination identified a proximal muscle weakness (grade 4-), keloid scars and distal contractures. A heterozygous pathogenic mutation in COL6A2 was identified in molecular studies.

Conclusion: The clinical cases presented confirm the significant phenotypic variability in patients with collagen encoding genes mutations.

Disclosure: Nothing to disclose

EPO3082

Polysomnography in patients with Myasthenia Gravis (MG)

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Background and aims: MG is a rare neuromuscular junction autoimmune disorder with a skeletal muscle weakness leading to respiratory failure in 30% cases that is often overlooked and more often revealed while asleep.

Methods: We examined 19 MG patients (18 with generalized MG) without breathing disorder related complaints, 4 men and 15 women, the age was 57 (34;67), min/max 22/85 years old. The research was performed, using polysomnograf Polymate YH-1000C (BMC, China).

Results: We revealed changes in nocturnal saturation in MG patients. Me AHI 5.3 (2.0;12.7), min/max 0.3/22.9; Me ODI 6.1 (3.8;9.4), min/max 1.3/15.7, that indicates increasing of these indexes in comparison with normal indexes. SpO2 min 81%(75;86) min/max 31/90. SpO2 mean 95% (94;96) min/max 93/97–was at the lower level of standard values. Increasing AHI was revealed in 10 patients (52,6%), from them with moderate increase in 4 patients (40%). Increasing ODI–in 14 patients (73.7%), with moderate increase–in 1 patient (7%). Decrease SpO2 mean was revealed in 5 MG patients (26%). Among patients with bulbar dysfunction (12 patients-63%) increase AHI was revealed in most cases–7 patients (58%), with moderate increase–in 4 patients (57%); increase ODI in 4 patients (33%), with moderate increase–in 1 patient (25%); decrease SpO2 mean in 4 MG patients (33%).

Conclusion: When carrying out polysomnagraphy in MG patients without breathing disorder increasing AHI and ODI, while decreasing SpO2 mean was revealed more than at each 2nd patient, that indicates predisposition of MG patients to development respiratory impairment while asleep. More often such changes occur among patients with bulbar dysfunction.

Disclosure: Nothing to disclose

EPO3083

Serum PDGF-BB as a biomarker for the follow-up of late-onset Pompe patients

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Background and aims: Enzymatic replacement therapy stabilizes late onset Pompe disease (LOPD) progression, however is not clear whether earlier treatment could produce better outcome. Decision on starting treatment is based in the presence of muscle weakness, although irreversible fatty infiltration could already be present leading to disability. There are still not validated biomarkers related with the progression of the disease guiding to the start of treatment. We analysed serum concentration of several profibrotic growth factors (GF) in 37 LOPD patients and correlated results with different clinical variables.

Methods: We studied all patients with several motor function tests, spirometry and quantitative muscle MRI (qMRI). GF serum concentrations were analysed using ELISA in blood samples of patients and compared to 48 healthy controls using Mann-Whitney U test. We used Spearman test and ROC curves to study correlation between serum concentration and clinical parameters. Statistical significance was set at $p < 0.05$.

Results: We observed significant differences in serum concentration of TGF-beta, PDGF-BB, PDGF-AA and CTGF between patients and controls. PDGF-BB concentration was significantly lower in symptomatic compared to asymptomatic LOPD patients. PDGF-BB was also lower in patients with more than 20% thigh fatty infiltration analysed using qMRI. ROC curves also supported a good correlation between serum PDGF-BB concentration and the presence of symptoms. We did not found significant correlation between serum concentrations and results of muscle function tests.

Conclusion: PDGF-BB serum concentration is a good biomarker candidates that could be useful in order to identify suitable LOPD patients to be treated earlier in their disease's progression.

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EPO3084

Pain in patients with Myotonic Dystrophy 1- is there a neuropathic component?

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Background and aims: Myotonic Dystrophy 1 (DM1) is an inherited multisystem disorder caused by a CTG trinucleotide repeat expansion in the Myotonic dystrophy protein kinase gene on chromosome 19. In addition to muscular dystrophy and myotony, some patients develop polyneuropathy. Little is known whether DM1 patients experience pain. We have followed a large group of DM1 patients, and noted that extensive pain was quite common in this group. The occurrence of pain in DM1 and whether a neuropathic component is present, was studied.

Methods: A thorough assessment of pain (localisatien and intensity), psychiatric issues and CTG expansion size, were investigated in 50 DM1 patients. In a subgroup of 20 patients; nerve conduction, quantitative sensory testing and skin biopsy for quantification of intraepidermal nerve fibers were performed. These patients underwent a neurological examination focused on sensory findings, mechanical allodynia or hyperalgesia.

Results: The participants report a large number of pain locations and a high pain intensity with a clear gender difference (more common in women). Preliminary analysis from the subgroup comfirm that neuropathy can be the cause of the reported pain in some of the participants. Exact occurence of neuropathy, and how this relate to the reported and other features of DM1, will be presented.

Conclusion: Pain in DM1 is prevalent. The presence of peripheral neuropathy could be relevant to understand pain in DM1, but more studies are needed to explain the high levels of pain reported.

Disclosure: Nothing to disclose

EPO3086

Mitochondrial multi-organ disorder syndrome score generated from definite mitochondrial disorders

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Background and aims: Mitochondrial disorders(MIDs) frequently present as mitochondrial multi-organ disorder syndrome(MIMODS) already at onset or evolve into MIMODS during the course. This study aimed to find which are the organs/tissues most frequently affected in MIMODS, which are the most frequent abnormalities within an affected organ, if there are typical MIMODS patterns, and to generate a MIMODS-score to assess the diagnostic probability for a MID.

Methods: Retrospective evaluation of clinical, biochemical, and genetic investigations of adult, definite MIDs.

Results: Included were 36 definite MID patients, 19 males, 17 females, aged 29-82y. The diagnosis was based on genetic testing (n=21), on biochemical investigations (n=17), or on both (n=2). The number of organs most frequently affected was four ranging from 1-9. MIMODS was diagnosed in 97% of patients. The organs most frequently affected were the muscle (97%), central nervous system (CNS) (72%), endocrine glands (69%), heart (58%), intestines (55%), and peripheral nerves (50%). The most frequent CNS abnormalities were leucencephalopathy, prolonged visually-evoked potentials and atrophy. The most frequent endocrine abnormalities included thyroid dysfunction, short stature, and diabetes. The most frequent cardiac abnormalities included arrhythmias, systolic dysfunction, and hypertrophic cardiomyopathy. The most frequent MIMODS patterns were encephalomyopathy, encephalo-myo-endocrinopathy, and encepalo-myo-endocrino-cardiopathy. The mean±2SD MIMODS score was 35.97±27.6 (range: 11-71). A MIMODS score >10 was regarded as indicative of a MID.

Conclusion: Adult MIDs manifest as MIMODS in the vast majority of the cases. Organs most frequently affected in MIMODS are the muscle, CNS, endocrine glands, and heart. A MIMODS score >10 suggests a MID.

Disclosure: Nothing to disclose

Neurogenetics 2

EPO3087

Frequency of huntingtin gene intermediate alleles in neurodegenerative diseases

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Background and aims: Even when carriers of Intermediate Alleles (IAs) do not develop HD there are some reported associations between IAs and HD symptoms. The role of IAs in other neurodegenerative disorders has not been fully assessed. Here we searched IAs in different neurodegenerative diseases.

Methods: First we screened expansions of the huntingtin gene in a pool of samples from patients previously diagnosed with AD (n=1053), PD (n=562) and FTD (n=225). We also screened a pool of 342 healthy controls recruited through the Health Community Service (elderly subjects who agreed to participate). Genotyping was performed by means of DNA fragment analysis. Then we computed the relative frequency of IAs in each group and compared frequencies between groups.

Results: We found 3 cases with expansions within the pathological range. These three cases were previously diagnosed with AD. The relative frequency of IAs for each group: 6% (63/1053) in AD, 5.3% in FTD (12/225), 3.3% in PD (19/562) and 2.9% in controls (10/342). The genotype frequency of IA was significantly more frequent among AD patients vs controls (p.=0.027, Yate correction; Odds ratio=2.11). In the FTD cohort, the genotype frequency raised 5.3% but was not significantly different from controls (p=0.16).

Conclusion: The frequency of IAs is higher in AD than in other neurodegenerative diseases and controls. IAs may play a role in the pathogenesis of neurodegenerative diseases, particularly in those presenting with cognitive impairment. More studies are needed to replicate these findings.

Disclosure: Nothing to disclose

EPO3088

"If you hear hooves behind you, don't expect to see a zebra": diagnosis of spinal muscular atrophy type III by whole-exome sequencing

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Background and aims: Spinal Muscular Atrophy (SMA) is an autosomal recessive disease, causing severe progressive muscle weakness due to loss of motor neurons in the spinal cord and the brainstem. Motor neuron degeneration is caused by homozygous absence of SMN1, encoding the "survival of motor neuron" (SMN) protein. The highly homologous SMN2 gene, which differs at only a single position within the coding sequence, can modify SMA disease severity due to its capability of driving low levels of SMN protein expression.

Methods: We developed a computational method for determining SMA (carrier) status in whole-exome sequencing (WES) data, based on statistical analysis of relative read coverage profiles at the nearly identical SMN1 and SMN2 loci.

Results: We identified two siblings, a young boy (10y) and his sister (6y), born to consanguineous Syrian parents, with progressive proximal muscle weakness (with mild elevation of serum creatine kinase levels, ~600U/L) and gait disturbance. WES variant analysis did not yield pathogenic variants in any known myopathy or neuropathy gene. Surprisingly, however, missing read coverage at SMN1 exon 7 was highly indicative for homozygous loss of SMN1. In both patients, multiplex ligation dependent probe amplification (MLPA) confirmed loss of SMN1 and detected four SMN2 copies. Thus, genetic findings were compatible with the diagnosis of juvenile SMA type III (OMIM # 253400).

Conclusion: This case reports underlines the importance of read-depth analyses in clinical WES, also of inherently difficult chromosomal regions (such as the SMN locus), which are commonly excluded from routine analysis.

Disclosure: Nothing to disclose

EPO3089

Jewish MJD patients of Yemenite descent share a recent common ancestor

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Background and aims: Jews arrived to Yemen mostly in the 2nd century, maintaining close communal structures. In 1994, one kindred from Yemen was described as the first Jewish family with Machado-Joseph disease (MJD), a dominant ataxia caused by the expansion of a (CAG)n in ATXN3. MJD is spread worldwide due to an ancient mutation of Asian origin (Joseph lineage). A second de novo expansion arose in a distinct haplotype (Machado lineage); other independent origins are still under study.

Methods: We genotyped 46 MJD patients and relatives, from 6 Israeli Yemenite families, and 100 normal chromosomes, for 28 SNPs spreading 15kb around the (CAG)n, and 8 STRs and one indel in the flanking region. Haplotypes were inferred by segregation; in controls, we used PHASEv2.2 whenever needed.

Results: All Yemenite MJD families shared extended haplotypes, showing no mutation or recombination after a common origin. They differ in 2 SNPs (rs12895357, rs12588287) from the Joseph lineage. Considering the short distances to the (CAG)n (1bp and 396bp, respectively), recombination is unlikely to explain this haplotype. To test for a new mutational origin in this population, we searched for the presence of this Joseph-derived haplotype in Yemenite Jewish controls; the finding of a normal (CAG)32 allele sharing the SNP background with MJD Yemenite patients did not rule out this hypothesis.

Conclusion: Our results pointed to a recent origin/introduction of MJD in the Yemenite population, based on lack of diversity found. To clarify the possibility of third mutational origin for this Joseph-derived lineage, a comparison with MJD haplotypes worldwide is required.

Disclosure: Nothing to disclose

EPO3090

Combined frontotemporal dementia due to C9Orf72 expansion and neurodegeneration with brain iron accumulation in the context of hypoceruloplasminemia

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Background and aims: C9Orf72 expansion is the most common mutation in frontotemporal lobar degeneration and amyotrophic lateral sclerosis. Though rare, co-occurrence of second mutations (ATXN2, TDP43, FUS...), influence disease presentation and progression.

Methods: Case report.

Results: 60-year-old male with six-years history of limb and facio-oromandibular movement disorder. He also referred liquid dysphagia in the previous three years, and subtle memory impairment. He had an older sister with symptoms consistent with primary progressive aphasia.

Neurological examination revealed limb and facial chorea, facial and orolingual dystonia, fragmented ocular pursuit, vertical gaze paralysis, dystonic dysarthria and bradylalia, hypomimia and mild limb rigidity. MMSE 30/30.

MRI showed frontotemporal atrophy plus iron deposition in striatum and substantia nigra. Blood tests revealed low serum copper (39) and ceruloplasmin (11.5), normal iron, ferritin and urine copper, and no achantocytosis. Analysis of IT15 and FTL genes showed no alterations.

The patient had 2 missense mutations in CP gene (exon5:c.G929A:p.R310H; and exon16:c.G2684C:p.G895A). These mutations have ExAC frequency <0.001 and Polyphen2 score of 0.8 and 1. During the next two years he developed cognitive and behavioural impairment, worsening of dystonia and dysphagia. He died at 63. Neuropathology showed TDP-43 pathology type B, with p62+ inclusions in cerebellum, and intraneuronal and glial iron deposition in lenticular, hypothalamic nuclei, and substantia nigra. Subsequent C9Orf72 analyses revealed a hexanucleotide expansion.

Conclusion: Extrapiramidal movement disorders have been reported in some patients with C9Orf72 expansion but this is the first case of a co-occurrence of a second mutation explaining this particular phenotype.

Disclosure: Nothing to disclose

EPO3092

Phenotype of three pathogenic variants of CACNA1A gene in Slovak families with episodic ataxia type-2

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Background and aims: Episodic ataxias (EAs) are rare autosomal dominant neurological disorders characterized by recurrent relapses of ataxia lasting minutes to hours. The most common subtype is EA type-2 (EA2) caused by pathogenic variants of calcium voltage-gated channel subunit alpha1 A gene (CACNA1A) on chromosome 19p13.
Methods: We examined three Slovak three-generation families with episodic ataxia. Complex differential diagnosis in each family was performed. Genomic DNA of the family members was extracted from peripheral blood and amplified by polymerase chain reaction. CACNA1A variants were screened by Sanger sequencing.
Results: Genetic analysis with direct sequencing revealed two novel heterozygous variants of CACNA1A-c.5264 G>A (p.Glu1755Gly) and c.889 G>A (p.Gly297Arg) located in highly conserved parts of the gene. Pathogenetic variant c.3832 C>T (p.Arg1278Ter) detected in third family has been already described in few families with epilepsy. We described and compared episodic and interictal signs of 10 affected family members. Acetazolamide was effective in each variant.
Conclusion: We described phenotype of three pathogenetic variants of CACNA1A gene in Slovak families with episodic ataxia type-2. We identified two novel missense variants of the gene.
Disclosure: Nothing to disclose

EPO3093

Clinical exome sequencing in dementias: a preliminary study

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Background and aims: Dementias are clinically and a genetically heterogeneous group of neurodegenerative disorders. Often, dementias with genetic etiology are clinically indistinguishable from non-genetic ones. The aim of this retrospective study was to evaluate the yield of clinical exome sequencing in dementias, potentially associated with monogenic genetic predisposition.
Methods: For this purpose 20 consecutive patients younger than 65 years were studied in the period from January 2014 to December 2017; 13 with the diagnosis of Frontotemporal dementia (FTD), 4 with early-onset Alzheimer disease (EOAD) and 3 with unspecified dementia. In addition to clinical exome sequencing including 32 dementia and 85 neurodegenerative diseases associated genes, C9orf72 (G4C2)4 hexanucleotide expansion was tested in all patients.
Results: We found genetic etiology in 6 patients: 2 mutations in the PSEN1 gene (p.Pro264Ser and p.Phe105Cys) in the EOAD patients, C9orf72 expansion and MAPT (c.1920+16C>T), mutation in the FTD group of patients as well as MAPT (c.1920+16C>T) mutation and likely pathogenic mutation in the TYROBP mutation (p.Asp32Asn) in patients with unspecified diagnosis.
Conclusion: Our preliminary results imply significant diagnostic yield in identifying rare genetic causes of dementia, combining comprehensive clinical exome sequencing and targeted C9orf72 expansion testing.
Disclosure: Nothing to disclose

EPO3094

The C9ORF72 repeat expansion in Greek patients with neurodegenerative disorders

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Background and aims: The C9ORF72 hexanucleotide repeat expansion, an established cause of frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS), has also been identified in patients with other neurodegenerative disorders. Recent studies from the Neurogenetics Unit, Eginition Hospital have individually investigated the frequency of the C9ORF72-expansion in cohorts of Greek patients with ALS, FTD, and Huntington disease (HD)-like syndromes. The aim of the present report is to update and expand data on the frequency of the expansion in a broader spectrum of neurodegenerative disorders.

Methods: Using molecular biological techniques, including repeat-primed PCR, genetic testing for the C9ORF72 repeat expansion was performed in 549 patients with neurodegenerative disorders (331 ALS, 65 FTD, 44 HD-like, 55 Alzheimer's disease (AD) and 54 with other dementia syndromes) and 321 healthy controls.

Results: In total, 33 patients with ALS (10.0%, 33/331), 14 with positive family history (56.0%, 14/25) and 19 sporadic (6.2%, 19/306), 6 patients with FTD (9.2%, 6/65), 5 with positive family history (27.7%, 5/18) and 1 sporadic (2.1% 1/47), 2 patients with HD-like syndromes (4.5%, 2/44) and 1 patient with AD (1.8%, 1/55) were expansion-positive. Patients with other dementia syndromes and healthy controls tested negative for the expansion.

Conclusion: The frequency of the C9ORF72 repeat expansion in Greek patients with neurodegenerative disorders is high, in line with other European populations. In fact, the frequency of the expansion in Greek familial ALS remains among the highest in Europe. The expansion is also the most common genetic cause of HD-like syndromes in Greece.

Disclosure: Nothing to disclose

EPO3095

Higher relative proportion of Leber's Hereditary Optic Neuropathy in premenarchal and postmenopausal women supports a protective role of estrogens

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Background and aims: Leber's Hereditary Optic Neuropathy (LHON) is caused by mitochondrial DNA mutations, whose overall penetrance is markedly higher in males than females. Accordingly, a protective role of estrogens has been suggested. Here we investigated whether women's reproductive age (menarche, childbearing age, menopause) influences onset of disease.

Methods: Out of 418 LHON patients in our database, 277 were analysed regarding gender, age at onset and genetic mutation; 226 (81.6%) patients were male and 51 (18.4%) female. The distribution of age at onset was analyzed by gender and across three age categories which reflect the three reproductive life stages of women: pre-menarche ($\leq$12 years), childbearing age (13-49 years) and menopause ($\geq$50 years). Mann-Whitney-U –Test was used for statistical analysis of non-parametric samples. A survival analysis with log-rank test was performed.

Results: The mean age at onset was significantly later (p<0.001) in female than male patients (37.4 vs. 26.0 years). Remarkably, the proportion of early and late-onset disease was higher in women than in men (15.6% vs. 8.8% and 29.4% vs. 8.8%), while the proportion was lower between 13 and 49 years (54.9% vs. 82.3%). There was no significant difference between groups regarding the causal mutation.

Conclusion: The higher mean age at onset and the higher proportion of females in early and late-onset age groups suggest a preponderance of protective factors or a relative absence of damaging factors in female LHON mutation carriers during childbearing age. These results support a protective effect of estrogens in female LHON patients.

Disclosure: Nothing to disclose

EPO3096

The strange case of vanishing memory after a fall

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Background and aims: Vanishing white matter disease (VWMD) is an inherited leukoencephalopathy caused by a mutation in the EIF2B gene. The disease has a wide phenotypic variation and clinical manifestations usually begin in childhood. We present a case of an adult onset form of the disease.

Results: A 23-year-old male was admitted to our hospital due to a severe traumatic brain injury after a fall. After motor recovery, the patient started complaining of memory loss. Physical examination was unremarkable. Neuropsychological tests revealed a multiple domain cognitive impairment. Brain MRI showed a diffuse white matter lesion. Additional investigation was normal except for the presence of oligoclonal bands in CSF. Main brain inflammatory and genetic disorders with white matter involvement were excluded and no diagnosis was assumed. The patient seemed to have no disease progression for many years. 20 years later he was revaluated due to further deterioration: pyramidal and cerebellar signs were identified, neuropsychological tests revealed a severe cognitive decline and brain MRI showed symmetrical and diffuse white matter lesions. After discussion with a geneticist, the clinical diagnosis of VWMD was warranted and a mutation in the EIF2B gene was identified. Familial genetic counselling was performed.

Conclusion: Although VWMD typically occurs in children this disease should be considered in the differential diagnosis of leukodystrophies in adults. Homozygous mutation of EIF2B5 gene as found in this case is frequently associated with late onset and slow progression. Subjects with this disorder are particularly vulnerable to stressors such as head trauma which may trigger the first symptoms.

Disclosure: Nothing to disclose

EPO3097

Coexisting CACNA1A pathogenic variant and MJD expansion in a single family

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Background and aims: Despite the identification of an increasing number of genes causing dominant spinocerebellar ataxias (SCAs), a significant proportion of cases are still left without a diagnosis. MJD/SCA3 is the most prevalent SCA worldwide. CACNA1A ataxia-causing sequence variants are typically associated with episodic ataxia type 2 and familial hemiplegic migraine, but may also cause a slowly progressive form of cerebellar ataxia.

Methods: Case report of a family with both CACNA1A-associated ataxia and MJD/SCA3.

Results: Two siblings, an 78-year-old man (patient #1) and a 90-year-old woman (patient #2), presented with a slowly progressive cerebellar syndrome, consisting of dysarthria, limb and gait ataxia, starting in their 20s. Family history suggested an autosomal dominant inheritance. Brain MRI showed global cerebellar atrophy. Genetic testing for SCA2, MJD, SCA6, SCA7, SCA10, SCA12, SCA14 and DRPLA was negative.

Patient #3 (son of patient #1) presented at age 26 years with nystagmus, dysarthria, pyramidal signs in the lower limbs and spastic-ataxic gait. His parents were consanguineous. His mother died at age 30 and was said to have had a wide-based gait. Brain MRI depicted mild cerebellar atrophy. A test requested by another neurologist showed an expansion for MJD/SCA3. A NGS panel for AD ataxias subsequently confirmed both patient #1 and #2 (but not patient #3) carried a pathogenic variant in CACNA1A, c.1748G>A (p. Arg583Gln).

Conclusion: Albeit rare, multiple gene mutations responsible for a dominantly-inherited cerebellar ataxia phenotype may coexist in a single family. We highlight the role of NGS in achieving a definite diagnosis in such cases.

Disclosure: Nothing to disclose

Neuro-ophthalmology/neuro-otology

EPO3098

Ocular Vestibular Evoked Myogenic Potentials (oVEMPs): the mid-lateral recording position produces worse responses than the midline position in elderly patients

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Background and aims: oVEMPs are a non-invasive method of evaluating mainly utriculo-ocular pathway function. Initial studies have shown that the optimum recording position is at the midpoint of the inferior orbital ridge, although more recent studies have shown that a more lateral position (between midpoint and lateral canthus) produces larger amplitude responses. However, the latter studies have been done in young individuals (less than 60 years of age).

The aim of this study is to map the oVEMP response and compare between young and elderly individuals.

Methods: Two groups of healthy volunteers (10 each) with no relevant neurotological history were examined: young and elderly (age range 14-50 years and 60-80 years respectively). Stimulation was performed using 500 Hz tone air-conducted auditory stimulation at 120 dB pSPL intensity monaurally with contralateral masking noise. Surface recording was performed from the tonically active inferior oblique muscle with active recording electrodes at five locations along the inferior orbital ridge (medial and lateral canthus, midline and midway between midline and each canthus).

Results: In both groups, the midline recording location for oVEMPs produced optimum and comparable responses with respect to measuring the preceding baseline-to-negative peak amplitude. Significantly smaller amplitudes were recorded from the midlateral position in the elderly, when measuring the negative peak-to-following positive peak, compared to young subjects.

Conclusion: The recent discovery of possible use of the midlateral location is worse in the elderly when measuring offset amplitude. It also demonstrates that optimum recording positions, especially when determined in a young population, do not necessarily apply to all ages.

Disclosure: Nothing to disclose

EPO3099

Features of diagnosis of visual field defects by method of threshold perimetry in Parkinson's disease patients with motor fluctuation

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Background and aims: Visual dysfunction in Parkinson's disease (PD) includes reduced color discrimination, contrast sensitivity, motion perception, etc. The basis of these disorders is retinal dopaminergic system (RDS) insufficiency, which leads to functional and structural retinal disorders. It is well known that glaucomatous-like visual field (VF) defects also often occur in PDpatients. To resolve the disputable question whether these defects are caused by functional or structural changes in the retina, we investigated the VF in different periods of levodopa action.

Aim: To estimate the variability of VF defects in PD patients over "on-off"-periods.

Methods: 24 non-glaucoma PD patients aged 46 to 65 years were examined. Perimetry included 24-2 and 60-4-SITA algorithms for detection of VF defects and determination of sensitivity thresholds in the central and peripheral parts of the retina.

Results: Most often the defect was located in the upper and/or nasal segments (n=18) mainly in the peripheral parts of the retina. In comparison with the on-period the decrease in the generalized photosensitivity within the off-period was more typical for peripheral VF. Within the on-period, we also observed a significant increase in local photosensitivity in those retinal segments where within the off-period the VF defect was revealed (Figure). Peripherally retinal nerve fiber layer thinning was observed more often when VF defects and generalized photosensitivity were unchangeable within "on-off"-periods.
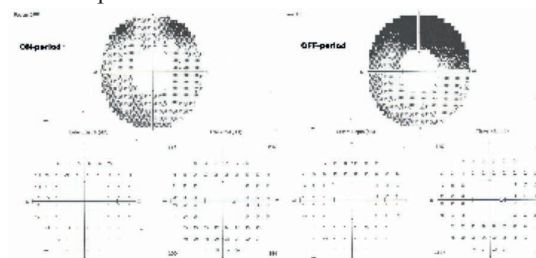
Figure. Variability of the VF defect and generalized photosensitivity in "on-off" periods (Peripheral 60-4 Threshold Test)

Conclusion: Variability of the VF defect and generalized photosensitivity in "on-off"-periods is a distinctive feature of PD patients. Dynamic of sensitivity thresholds reflects changes in functional condition of the retinal cells that is determined by the levodopa level.

Disclosure: Nothing to disclose

EPO3100

Unsteadiness and falls in Kennedy disease: vestibular or somatosensory dysfunction?

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Background and aims: Kennedy disease is an X-linked recessive bulbospinal neuropathy, caused by a CAG expansion in the androgen receptor gene. Falls and unsteadiness in these patients are out of proportion of muscular weakness. Here, we aimed to investigate the cause of this disequilibrum by assessing vestibular, somatosensory, oculomotor and overall balance function.

Methods: Vestibular function was assessed by the video Head Impulse Test and balance was evaluated with static posturography. Sensory nerve function was measured with conventional sural nerve neurography. Finally, saccadic eye movements were quantified by computing the main sequence.

Results: In total, 6 patients were included (age range 40 to 62 yo, CAG repeats 44 to 50). Four patients had normal (0.92±0.08), whereas two patients showed low (0.43±0.11) VOR gains. These two subjects, however, had no corrective saccades, raising the suspicion that the low gain was due to low eye movement velocity without a final retinal error after the completion of the eye movement. Indeed, these two subjects had slow saccades with increased main sequence time constants. Sural SNAPs were markedly low in all patients (2.5±1.5 μV). Posturographic parameters were abnormal in all subjects showing a strong visual dependency as reflected in the computed Romberg quotients.

Conclusion: Our data suggest that postural unsteadiness in Kennedy disease stems mainly from a somatosensory deficit. Vestibular function is spared. Interestingly, some patients exhibit abnormally low velocities in fast eye movements (saccades and high velocity VOR) raising the possibility of an ocular motor neuron degeneration in the brainstem.

Disclosure: Nothing to disclose

EPO3102

The video Head Impulse Test in patients with cerebellar ataxia

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Background and aims: Vestibulo-ocular reflex (VOR) is a reflex that stabilizes the gaze during head motions by compensatory eye movements contrary to the head. The assessment of the VOR by the head impulse test allows to detect paresis of the semicircular canals (peripheral vestibular dysfunction). However, cerebellar impairment can interfere with some dynamic VOR changes during HIT. The aim of the study was to analyze the video Head Impulse Test findings–to assess the VOR and to analyze corrective saccades in patients with cerebellar ataxia and to compare these findings with a group of patients with peripheral vestibulopathy and with healthy controls.

Methods: 45 patients with cerebellar ataxia were examined (11 genetically determined, 34 IDCA), results were compared with 15 patients with peripheral vestibulopathy and 25 healthy persons. Subjects were examined with the video Head Impulse Test, we evaluated gain of VOR and distribution of the corrective saccades. Vestibular reactivity was examined by means of ENG with rotational and caloric testing. Range of impairment in patients with cerebellar ataxia was assessed by SARA.

Results: The video Head Impulse Test, especially the distribution of the corrective saccades helps to distinguish patients with cerebellar impairment from the patients with vestibular impairment and healthy controls. Scattered corrective saccades prevail in patients with cerebellar ataxia (64%), gathered saccades in peripheral vestibulopathy.

Conclusion: The video HIT allows to identify and quantify combined vestibular and cerebellar pathology. VOR gain could serve as a neurophysiological biomarker of the disease and thus help in the diagnostic algorithm.

Disclosure: Nothing to disclose

EPO3103

Paroxysmal positional ocular flutter and square wave oscillations associated with middle cerebellar peduncle demyelination

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Background and aims: Positional ocular flutter (POF) is a rare disorder, with only two cases described in the literature in one patient with degenerative ataxia and one other with Krabbe's disease. However, an underlying focal/strategic lesion has not been identified yet. We present a patient with a right middle cerebellar peduncle demyelinating lesion in association with symptomatic positional ocular flutter, in whom the use of dalfampridine was not effective.

Methods: Review of clinical case.

Results: A 24 year-old woman diagnosed with multiple sclerosis presented with a 3-year history of paroxysmal oscillopsia and nausea when moving to supine position. Brain MRI revealed several demyelinating lesions in the supratentorial region, and one located at the anterior and medial aspect of the right middle cerebellar peduncle. Video-oculography in upright position showed occasional single saccadic pulses and square-wave jerks during fixation. When moving to head hanging position, a ~2 second positional ocular flutter (slow phase velocity 11°/sec) followed by ~30 second square-wave oscillations was consistently precipitated, along with oscillopsia and intense nausea. She was started on dalfampridine, 10mg bid. 180 minutes after first drug intake, positional ocular flutter on head hanging was unchanged. Five days later, dalfampridine–related side effects led to drug discontinuation.

Conclusion: Given POF strictly positional nature, the impairment of the cerebellar saccadic-otolithic network might be one of the underlying mechanisms. Although beneficial in other cerebello-vestibular disorders, dalfampridine does not seem to be effective in POF associated with cerebellar demyelination.

Disclosure: Nothing to disclose

EPO3104

Physiological pituitary hyperplasia: a case report of under-recognised cause of neuroophtalmology disturbances in pregnancy

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Background and aims: Anterior pituitary undergoes physiological enlargement during normal pregnancy as a result of lactotroph hyperplasia. Compression of the optic chiasm by enlarged pituitary gland often results in visual field defect.

Methods: A 28-year-old female in 37th week of pregnancy was admitted to our hospital due to blurred vision and transient visual loss in the right eye. No other symptoms were present. The past medical history was unremarkable.

Results: Examination revealed normal blood pressure and normal urinalysis. Neurologic examination and funduscopic examination were within normal limits. Best visual acuity was 0.9 in the right eye and 1.0 in the left eye. The visual field demonstrated bitemporal hemianopsia. The MRI of the brain with angiography and venography demonstrated physiological pituitary enlargement with pressure on the optic chiasm resulting in bitemporal hemianopsia. Due to the patient's late pregnancy stage, after the diagnostic workup, she was transferred to the Department of Obstetrics and Gynecology in a different hospital for further observation and treatment.
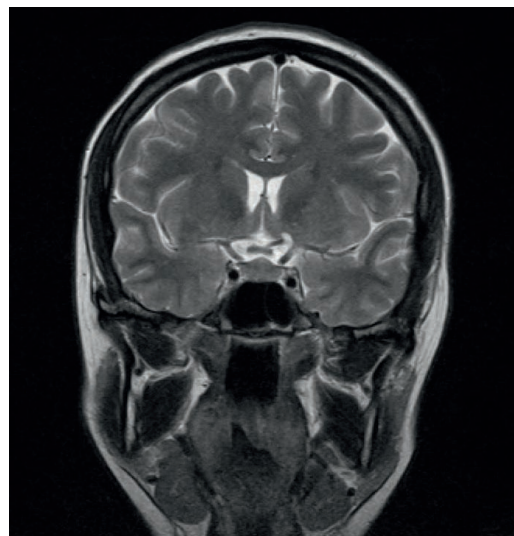
MRI coronal view showing pituitary enlargement during pregnancy
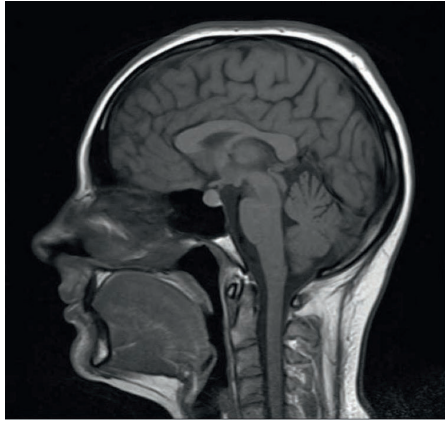
MRI sagittal view showing pituitary enlargement during pregnancy

Conclusion: Beside of much more serious diseases that may occur during pregnancy and cause visual disturbances (e.g., preeclampsia and eclampsia, posterior reversible encephalopathy syndrome, reversible cerebral vasoconstriction syndrome, stroke and venous sinus thrombosis), to avoid unreasonable diagnostic and therapeutic procedures, neurologists and radiologists should be aware also of possible visual disturbances by physiological pituitary enlargement. The field defects raising from this entity have good prognosis, with recovery occurring one week postpartum

Disclosure: Nothing to disclose

EPO3105

Cervical vestibular evoked myogenic potentials in benign paroxysmal positional vertigo

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Background and aims: Benign paroxysmal positional vertigo (BPPV) is the most frequent cause of vertigo. Vestibular evoked myogenic potentials (VEMPs) generated by activation of the vestibulo-collic pathways can be analyzed easily and can make contributions to the understanding of the pathophysiological mechanisms underlying BPPV. The aim of this study was to evaluate cervical VEMPs (cVEMPs) in patients with BPPV.

Methods: Fifty four patients with BPPV were enrolled in the study. There were 19 men and 35 women with ages ranging from 18 to 65 years (mean age, 52.43 ± 10.59 years). 45 age and sex matched healthy volunteers constituted the control group. P13 and n23 latencies and corrected p13-n23 amplitudes of the cVEMPs were taken into consideration.

Results: cVEMPs were recorded from both sides in all healthy subjects and patients. P13 latencies of the BPPV patients were significantly delayed ($p < 0.05$) when compared with the healthy controls. n23 latencies and corrected p13-n23 amplitudes were not significantly affected ($p > 0.05$).

Conclusion: Delayed p 13 latencies in patients with BPPV may suggest that BPPV is caused by damage to the otolith organs.

Disclosure: Nothing to disclose

Sleep disorders

EPO3106

Influence of long-term therapy of RLS on patients' quality of life.

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Background and aims: The aim of this study was to assess which initial features of restless legs syndrome (RLS) have the strongest influence of the quality of life (QoL), what kind of improvement is most strongly correlated with change in patients' quality of life and which aspects of patients quality of life are improved most with succesful therapy of RLS.

Methods: We have analyzed data of an outpatient population of RLS subjects. We have compared their initital clinical data (severity of RLS, insomnia, daytime sleepiness and quality of life measured with EQ-5D) with data available after succesful therapy and follow-up

Results: There were 100 RLS patients participating in the study (15 men; mean age 66.4 years; mean course of the disease 15.1 years). Initially there was significant correlation between severity of insomnia and quality of life. Nevertleness, the change in Qol was significantly positively correlated with improvement in severity of RLS. The domains of QoL which improved significantly were everyday activities, pain and anxiety.

Conclusion: Our results suggest that it is disordered sleep that has the strongest influence on patients' quality of life before therapy. Qol improvement is most strongly correlated with total IRLSS score.

Disclosure: Nothing to disclose

EPO3107

Correlation between EEG spectral power and heart rate variability in patients with obstructive sleep apnea

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Background and aims: Seminal studies suggest that patients with obstructive sleep apnea (OSA) have sleep fragmentation and higher risk of autonomic nervous system (ANS) dysfunction. The aim of this study was to correlate EEG spectral power and heart rate variability in patients with OSA and non-OSA subjects.

Methods: Overnight polysomnography with EEG spectral power analysis was performed in 33 consecutive patients (15 female, mean age 48.67 ± 14.08 years). 14 patients had obstructive sleep apnea syndrome (OSAS) whereas 19 were non-OSAS subjects. They all underwent standardized battery of ANS testing, including blood pressure and heart rate response to Valsalva maneuver, deep breathing test and head up tilt table test. In all study subjects heart rate variability (HRV) was determined.

Results: Negative correlation was found between EEG beta power (F4-01) and LF (rs=-0.560, p=0.013) and in non-OSA subjects. In OSA patients, negative correlation was found between EEG beta power (F4-01) and LF/HR (rs=-0.552, p=0.041) and positive correlation was observed between EEG beta power (F4-01) and HFnu (rs=0.552, p=0.042). HRV parameters did not show significant correlation with EEG alpha power, EEG theta power and EEG delta power in any patient group.

Conclusion: The results of this study suggest that cardiovagal dysfunction might be associated with cortical arousal and sleep fragmentation in OSA patients.

Disclosure: Nothing to disclose

EPO3108

Multiple Sclerosis and Obstructive Sleep Apnea: a systematic review and meta analysis

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Background and aims: Obstructive Sleep Apnea (OSA) has been frequently reported present in patients with multiple sclerosis (pwMS). The aim of this study was to perform a systematic review and meta-analysis of available scientific evidence on the likelihood of OSA in pwMS.

Methods: A systematic review of the literature (PubMed library, Web of Science library) was performed for studies investigating OSA in pwMS for results up to July 2017. We identified 717 studies, of which 7 studies compared frequency of OSA in pwMS to healthy controls (HC). Polysomnography (PSG) as standard and objective diagnostic instrument was performed in 5 studies, while 2 studies used subjective assessment instruments (1 questionnaire and 1 self-report).

Results: PwMS had a significantly higher frequency of OSA compared to HC [421/1101 patients vs. 167/979 controls; odds ratio (OR) 3.28, 95% confidence interval (CI) 2.64–4.07, p=0.00001] if taking into account both subjective and objective (PSG) diagnostic instruments (Figure 1). No significant difference in frequency of OSA between pwMS and HC [61/175 patients vs. 34/111 controls; odds ratio (OR) 1.84, 95% confidence interval (CI) 0.94–3.62, p=0.08] was observed in PSG studies. Subjective assessment tools of OSA risk revealed a significantly higher frequency of OSA in pwMS vs. HC [360/926 patients vs. 133/868 controls; odds ratio (OR) 3.50, 95% confidence interval (CI) 2.79–4.40, p <0.00001].
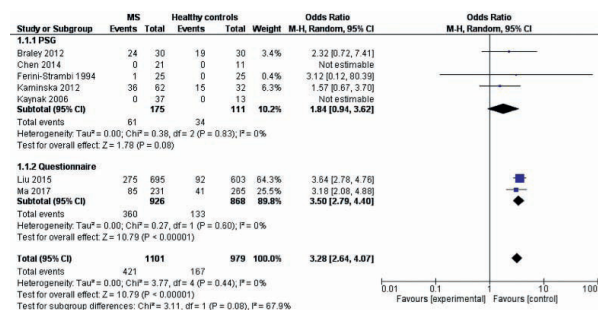
Odds ratios (OR) for OSA in pwMS based on data from each individual study and from the pooled analysis. By ''favors control/favors disease'' it is meant that there is an increased likelihood of OSA; thus these data indicate that the likelihood of having PPH is higher in patients with neurological diseases than in healthy controls.

Conclusion: The likelihood of having OSA in pwMS is higher considering both, subjective and objective (PSG) diagnostic instruments. However, PSG study showed no significant difference in OSA frequency.

Disclosure: Nothing to disclose

EPO3109

The role of polysomnography in predicting respiratory failure in a patient with acute ischemic dorsolateral medullary infarction

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Background and aims: Acute unilateral dorsolateral medullary infarction (UDLMI) may cause acute respiratory failure. We assume that subclinical respiratory disturbances may be detected by polysomnography (PSG) in these patients before the onset of overt respiratory failure. We present a patient with UDLMI in whom PSG was recorded before and after transient respiratory failure.

Methods: A 58-year-old man with acute right-sighted UDLMI and concomitant cerebellar infarction was admitted to our stroke unit. PSG, recorded on the third hospital night, revealed periodic breathing (PB) which occurred mainly in non-rapid eye movement sleep (NREM) and consisted of 3-4 breaths of constant amplitude followed by central apnea with oxygen saturation drop from 95% to 80-90% and an arousal.

Results: PB represented 74% of total recording time, apnea-hypopnea index (AHI) was 163/hour (Image 1). A sudden respiratory failure occurred in the evening. He was intubated and transferred to intensive care unit. PSG was repeated 2.5 months after admission when he was weaned from mechanical ventilation support. PB still occurred in the NREM sleep in a different, crescendo-decresendo, pattern consisting of 10-12 breaths followed by central apnea with mild saturation drop to 89-90%. PB represented 54% of total recording time, AHI was 63/hour (Image 2).
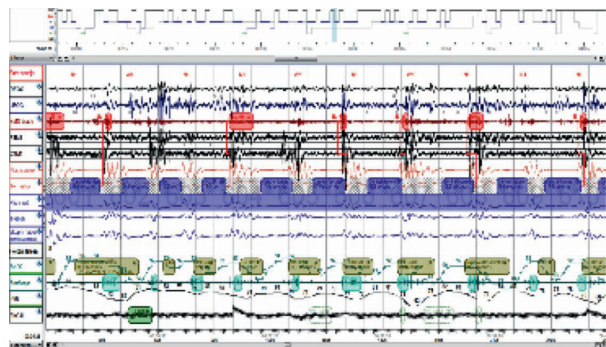
Image 1.
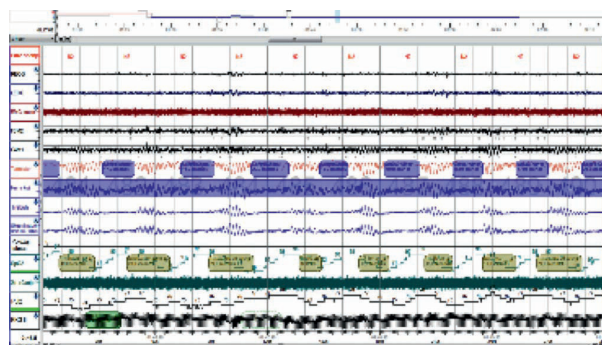
Image 2.

Conclusion: Our case report shows that PSG can detect subclinical breathing disturbances in patients with UDLMI before the onset of overt respiratory failure and after respiratory failure resolution. PSG could therefore be used as a screening tool for detecting patients at risk, for timely introduction of non-invasive ventilation and for long-term clinical monitoring.

Disclosure: Nothing to disclose

EPO3110

Treatment with safinamide in patiens with restless legs syndrome

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Background and aims: Restless legs syndrome (RLS) is a common sensorimotor disorder characterized by an urge to move, and associated with uncomfortable sensations in the legs. Refractory RLS is characterized by unresponsiveness to dopamine agonists (DA) or alpha-2-delta ligands (A2DL) due to inadequate efficacy, augmentation, or adverse effects.

Methods: Safinamide was used in patients with refractory RLS after previous treatment with at least one of the following: DA or A2DL. Restless Legs Syndrome Rating Scale (RLSRS) was used for measuring outcomes. This scale was administered at visit 1 (enrollment) and at visit 3 (3 months after inclusion). Visit 2 was planned 4 weeks after enrollment in order to assess whether the dose of 50 mg once a day of safinamide was effective.

Results: 5 patients were included with a range of ages between 52 and 71 years old. Three of the patients were female and 2 were males. All of them had been previously treated with at least 2 different groups of drugs (DA+clonazepam: 2/5, DA+clonazepam+A2DL: 3/5). In 2 of them DA had been stopped because of adverse events. Range of RLSRS score was between 14 and 28. Mean reduction in RLSRS was 11 points with a greater effect in those patients with a milder disease. Safinamide was well tolerated by all patients.

Conclusion: Safinamide seems to be effective and well tolerated in patients with refractory RLS. Treatment with safinamide could be more effective when used as early treatment. Safinamide is well tolerated when adverse events to DA appear.

Disclosure: Nothing to disclose

EPO3111

Sleep disorders: a key symptom in multiple neurological disorders

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Background and aims: In many neuroimmunological disorders disturbance of sleep and wakefulness play a keyrole. Sleep complaints are often underrepresented in neurological medical history. The aim was to summarise different case reports to emphasise the importance of sleep history in the context of neurological disorders.

Methods: Analysis of case records.

Results: A 69-year-old male reported about strange behaviors during sleep. During these behaviors he fell of the bed twice. He was amnestic for the nocturnal behavior. Sleep was not refreshing. During the day he suffered from involuntary sleep attacks. A few months later he also developed gait instability and ocular motor disturbance as well as chorea like movement disorder. He was diagnosed with Anti-IgLON5 disease. A 33-year-old suffered from excessive daytime sleepiness for more than 1.5 years and from hypnagogic hallucination, sleep paralysis and automatic behavior. Cataplexies were not present. Polysomnography revealed the diagnosis of narcolepsy. He was finally diagnosed with Ma2 Antibody encephalitis associated with germ cell tumor. Insomnia was the first symptom a 51-year-old man suffered from. Insomnia occurred 2 years before muscular symptoms like myalgia, cramps and fasciculations. He was diagnosed with Caspr2 antibody positive Morvans syndrome.

Conclusion: Sleep symptoms play a central role in different neuro immunological disorders. As demonstrated, disturbance of sleep and wakefulness can precede the full blown disorder. Beside parasomnias, disturbance of sleep initiation and maintenance should not be dismissed. Taking a precise sleep history could offer a useful instrument to detect autoantibody mediated neuroimmunological diseases in an early stage of disease.

Disclosure: Nothing to disclose

EPO3112

Atypical clinical and serological presentation of two patients with anti-IgLON5-antibodies-a case series

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Background and aims: The anti-IgLON5-disease is an antibody-related neurodegenerative disorder with a characteristic sleep disorder. Here we report two novel cases of anti-IgLON5-syndrome with atypical clinical and serological presentation.

Methods: Diagnostic workup in case-1 included peripheral nerve conduction, evoked potentials, cerebral/spinal MRI and whole body 18F-FDG-PET as well as HLA-analysis and two nights of video polysomnography (V-PSG). In case-2 cerebral MRI, 123J-FP-CIT, 18F-Fallypride, HLA-analysis, cognitive testing, L-DOPA test and two nights of V-PSG were performed. Laboratory testing of blood and CSF included screening for vasculitis, paraneoplastic, antineuronal, antiganglioside, myositis, and thyroid antibodies in both cases.

Results: Case-1 presented with lower motor neuron syndrome without a sleep disorder. Anti-IgLON5-antibodies were detected in serum and CSF with a predominant IgG4 subtype and lower levels of IgG1. HLA analysis revealed DQB1*05:01, but missed DRB*10:01. Treatment with i.v.immunoglobulins leaded to clinical improvement. Case-2 presented with PSP-symptoms, insomnia and day time sleepiness over 8 years. Anti-IgLON5-antibodies were found only in serum (predominant IgG4). HLA-analysis revealed DRB1*03:14 and DQB1*02:05. Cerbral MRI demonstrated a distinct mesencaphal atrophy,123J-FP-CIT showed an attenuation in the striatum, 18F-Fallypride was negative. V-PSG revealed reduced sleep efficacy, a mild sleep apnea syndrome, but no parasomnia.

Conclusion: We present two novel anti-IgLON5 patients that miss the HLA DRB1*10:01 haplotype and have atypical clinical phenotypes. Case-1 has anti-IgLON5-antibodies in serum and CSF and the lower motor neuron syndrome may represent a novel phenotype in the anti-IgLON5 spectrum responding to immunotherapy. In contrast, the clinical relevance of anti-IgLON5-antibodies only in serum of case-2 needs further investigations.

Disclosure: Nothing to disclose

EPO3113

Clinical presentation of obstructive sleep apnoea without oxygen desaturation

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Background and aims: In a subgroup of obstructive sleep apnoea (OSA) patients, respiratory events are associated with arousals without oxygen desaturation. It is not known if this phenotype has a different clinical presentation.

Methods: We analysed 364 polysomnographies (PSG) with >30min of REM sleep and either RDI≥15 or RDI≥10 and clinical suspicion of OSA. Non-desaturating (ND) phenotype was defined as oxygen desaturation index (ODI) <5 and desaturating (D) as ODI≥5. REM-predominant OSA was defined as RDI-REM/RDI- NREM>2. We analysed a subgroup of 32 ND patients and 31 controls (matched for age, sex, and RDI) with self-reported symptom questionnaires. Comparisons between groups used Mann-Whitney, Chi-squared, or Fisher exact test.

Results: 83 patients were ND. Mean age (57.7 ± 14.0 vs. 46.7 ± 15.7) and BMI (29.0 ± 4.7 vs. 26.7 ± 4.0) were higher in group D. Group ND had more women (47% vs. 31%). RDI was significantly higher in group D (30.5 ± 16.9 vs. 15.9 ± 14.8). 62% D had higher RDI during REM, compared to 47% ND (p=0,016). This difference increased in moderate severity OSA, with 36% REM-predominant OSA in group D and 10% in ND (p=0.002). Symptoms were similar between groups, but more ND patients rated symptoms as frequent or persistent (43% vs. 13%; p=0.01).

Conclusion: The ND phenotype is less common. This group is younger, has lower BMI, and less severe OSA. Events in REM sleep are more frequent in the D group, possibly because of different underlying mechanisms. The ND group had more frequent symptoms, supporting the importance of arousals in OSA physiopathology and the need for complete PSG in selected patients.

Disclosure: Nothing to disclose

EPO3114

Lack of intracortical facilitation to paired-pulse TMS in patients with "idiopathic RBD": a preclinical marker of synucleinopathy?

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Background and aims: Transcranial magnetic stimulation (TMS) provides several measures of motor cortex excitability in vivo, even subclinically. TMS changes, namely a reduced intracortical inhibition and facilitation, have been reported in Parkinson's disease, even in its early stage. REM sleep behavior disorder (RBD) often precedes the onset of synucleinopathies, although very few TMS studies have been carried out so far.

Methods: 60 patients with idiopathic RBD (median age 62.0 years, range 57.0-72.0; median disease duration: 3 years, range 1-4) and six age-matched healthy subjects (median age 62.0 years, range 56.0-65.0) underwent single- and paired-pulse TMS. Resting motor threshold, cortical silent period, latency and amplitude of motor evoked potentials, central motor conduction time, short-latency intracortical inhibition, and intracortical facilitation (ICF) were recorded through a figure-of-eight coil from the right first dorsal interosseus muscle. All participants were right-handed and drug-free. A screening for cognitive status, depressive symptoms, and diurnal sleepiness was also performed.

Results: Neurological examination was normal and no cognitive deficit, depression, or excessive sleepiness were detected in all participants. Compared to controls, patients exhibited a significant loss of ICF (median 0.6, range 0.1-1.1 vs. 1.4, range 1.4-1.8; p<0.05). The other TMS measures did not differ between the groups.

Conclusion: This finding suggests a subclinical electrocortical dysfunction in patients with RBD, raising the possibility that impaired ICF might precede the onset of an overt extrapyramidal syndrome. Such an impairment may result from an excitatory/inhibitory imbalance within intracortical motor circuits. RBD confirms to be a potential determinant of future neurodegeneration also at the TMS level.

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EPO3115

Sleep disorders in children with cerebral palsy

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Background and aims: Children with cerebral palsy (CP) are considered to be a population at risk for sleep disorders (SD). SD can lead to important medical problems that affect the child and family and influence their quality of life. The aim of this study was to asses SD in children with CP.
Methods: The study included 50 children (28 boys) with CP aged 2 to 6 years (mean 5y 2m StDev 11 mo) and 50 healthy children (26 boys) aged 2 to 6 years (mean 4y 10 mo StDev 10 mo). SD were assessed using the Sleep Disturbance Scale for Children.
Results: SD was statistically significantly higher in patients with CP compared with the control group. 18 children (36%) from study group had an abnormal total sleep score, compared to 3 children (6%) in the control group (p<0.05). The most frequent sleep troubles in the study group were: disorders of excessive somnolence (28%), sleep breathing disorders (24%) and difficulties in initiating and maintaining sleep (20%).
Conclusion: SD are more common in children with CP than in the control group; excessive somnolence, sleep breathing disorders and difficulties in initiating and maintaining sleep being the most frequent disturbances. Thus, to avoid the negative impact of SD in CP children, SD screening should be a routine clinical practice for these children. At the same time Sleep Disturbance Scale for Children is an easy method for early identifying and early management of SD and a better outcome can be expected.
Disclosure: Nothing to disclose

EPO3116

Longitudinal assessment of sleep disturbances after traumatic brain injury: a one-year prospective study

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Background and aims: Sleep disturbances are common after traumatic brain injury (TBI). There are few longitudinal studies that assess patients with sleep disorders after TBI over time. The aim: the assessment of sleep disturbances at 1 year after TBI.
Methods: Prospective study on 57 patients (71.92% males, mean age 43.37±27.39 years). We used a standardised questionnaire which included demographics, sleep quality questions, sleep duration assessment, Center for Epidemiologic Studies Depression Scale (CES-D), The Galveston Orientation and Amnesia Test, Hamilton Anxiety and Depression Scale (HADS), Athens Insomnia Scale, Fatigue Symptom Inventory (FSI), Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale, and Toronto Hospital Alertness Test (THAT).
Results: At baseline, TBI was mild in 21 cases (36.84%), moderate in 27 cases (47.36%), and severe in 9 cases (15.78%). The mean sleep time/24 hours was 7.9±1.9 hours during week days and 8.6±2.1 hours during weekends. Excessive daytime sleepiness (ESS≥10) was reported at baseline by 19 patients (33%), while at 1 year it was reported by 15 patients (26.31%). Insomnia was found in 23 cases (40.35%) at baseline and in 17 cases (29.82%) at 1 year. There were no correlations between EDS and insomnia with GCS, topography or severity of TBI. Fatigue was reported by 34 patients (59.64%) at baseline and by 39 patients (68.42%) at 1-year follow-up.
Conclusion: Sleep disturbances have a high prevalence at 1-year follow-up after TBI.
Disclosure: Nothing to disclose

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Ageing and dementia 1

EPR1001

Annual trends of prevalence and incidence of Alzheimer's dementia and vascular dementia in the entire Korean population: A national cohort study for 10 years

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Background and aims: We investigated annual trends regarding the prevalence and incidence of dementia based on the National Health Insurance System database covering the entire Korean population. In addition, we assessed a cut-off age for dementia diagnosis, and the risk factors for Alzheimer's dementia(AD) and vascular dementia(VD).
Methods: The prevalence and incidence of dementia of the entire Korean population aged ≥40 years was investigated using a database covering 2006 to 2015. The diagnosis was classified by the ICD-10 codes. The Youden index was estimated to determine optimal cut-off age for dementia diagnosis.
Results: The prevalence and incidence of AD showed increasing trends. The age-standardized prevalence of AD was 3.17, 11.28, and 15.75 per 1,000 persons, and the incidence of AD was 1.83, 4.49, and 5.21 per 1,000 persons in 2006, 2012, and 2015 respectively, while the prevalence of VD also showed increasing trends: 0.30, 1.98, and 2.27 per 1,000 persons in 2006, 2012, and 2015 respectively. However, the incidence of VD showed no increasing trends after 2011: 0.24, 0.80, and 0.78 per 1,000 persons in 2006, 2012, and 2015 respectively. The cut-off age for diagnosis of AD or VD are 69 and 65 years old. Vascular risk factors such as diabetes mellitus, hypertension and atrial fibrillation affected the risk of developing dementia.
Conclusion: Contrary to the findings for VD, the prevalence and incidence of AD is still increasing in Korea. The cut-off age for dementia diagnosis and modification of vascular risk factors may be of relevance for early diagnosis and intervention in dementia.
Disclosure: Nothing to disclose

EPR1002

Concordance of amyloid PET and CSF metabolic biomarkers in Alzheimer's disease and how to improve it: data from the Czech Brain Ageing Study

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Background and aims: Current guidelines for Alzheimer's disease (AD) shift the focus from clinical findings to biomarkers. Most widely used metabolic biomarkers are cerebrospinal fluid (CSF) levels of amyloid-β1-42 (Aβ1-42), total-tau (t-tau), and phosphorylated tau 181 (p-tau), as well as amyloid positron emission tomography (PET). However, the concordance between amyloid PET and CSF biomarkers is not well established and interpretation of biomarkers in clinical settings may also be challenged by analytical procedures and cut-off values. Our aim was to investigate the use CSF biomarkers in prediction of amyloid PET positivity, concordance of biomarkers, and propose cut off values in clinical settings.
Methods: 44 patients with mild cognitive impairment or mild dementia classified as possible AD (National Institute on Aging–Alzheimer's Association criteria) underwent MRI, neuropsychological assessment, flutemetamol PET and CSF sampling. PET was evaluated visually and dichotomized. AUCs of ROC curves for Aβ1-42, p-tau and p-tau/Aβ1-42 ratios were compared. Optimal cutoff points were based on the highest Youden's J indices.
Results: Concordance between PET and Aβ1-42 was highest (88%), followed by p-tau (75%). Concordance between both CSF biomarkers combined and PET was 74%. P-tau181/Aβ1-42 ratio (AUC=0.975, P<0.001), followed by Aβ1-42 (AUC=0.905, P=0.001) and p-tau181 (AUC=0.797, P=0.001) levels were found to discriminate PET positive and negative patients. A p-tau181/Aβ1-42 ratio of 0.098 provided 88,0% sensitivity and 100% specificity.
Conclusion: In our cohort 26% patients the results of Aβ1-42 and p-tau combined versus amyloid PET were disconcordant. Therefore we propose p-tau/Aβ1-42 ratio with reasonable sensitivity and specificity for identification of amyloid PET positive patients.
Disclosure: Nothing to disclose

EPR1003

Biomarkers in differential diagnosis of dementia using a data-driven approach

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Background and aims: Despite an increasing number of biomarkers, differential diagnosis in dementia remains challenging. In this study we aim to investigate the value of different biomarkers to diagnose different types of dementia using a data-driven approach.

Methods: We included 844 subjects (302 controls, 356 Alzheimer's disease (AD), 87 frontotemporal lobe dementia (FTLD), 61 dementia with Lewy Bodies (DLB), 38 vascular dementia (VaD)). We used a multivariate model based on the disease state index classifier, to assess the value of 6 cognitive tests, 3 cerebrospinal fluid biomarkers (Beta-amyloid 1-42, total tau, phosphorylated tau) and 14 automated MRI biomarkers (e.g volumes, voxel- and tensor based morphometry) for pair-wise differentiation between the dementia types. As performance metric we used balanced accuracy, defined as the average of sensitivity and specificity, which was computed using 10-fold cross-validation. The optimal sets of determinants were searched by adding one-by-one a determinant that maximized the accuracy.

Results: Analysis of different types and optimal combination of determinants revealed high performance of cognitive tests in separating controls from the dementia subtypes (Table 1). CSF biomarkers performed best for the separation of AD from controls and other types of dementia. Automated MRI features had the highest accuracies for separation of VaD, DLB and FTLD. Combining all tests and biomarkers optimally increased the majority of accuracies, with a balanced accuracy ranging from 82 to 95.

Table 1 Results for optimized sets of determinants, reporting balanced accuracy.

	Controls vs. AD	Controls vs. FTLD	Controls vs. VAD	Controls vs. DLB	AD vs. FTLD	AD vs. VaD	AD vs. DLB	FTLD vs. VAD	FTLD vs. DLB	VaD vs. DLB
Cognitive tests	93	87	95	93	68	63	70	63	65	59
CSF	86	62	58	63	88	76	76	58	61	53
MRI	88	85	94	78	79	86	70	85	81	87
Cognitive tests + CSF	93	87	95	93	88	76	79	64	68	59
Cognitive tests + MRI	95	92	94	94	78	86	74	85	84	87
CSF + MRI	90	85	94	78	88	86	79	85	81	87
Cognitive tests + CSF + MRI	95	92	94	94	88	86	82	85	84	87

NOTE: The table shows the balanced accuracy achieved when using the optimal combination of determinants for cognitive tests, CSF and MRI. Moreover, the balanced accuracy when combining these modalities is reported. Balanced accuracies 85-100 are highlighted in dark green.

Conclusion: The results show that pair-wise differentiation between subtypes of dementia is optimized by different biomarkers. Data-driven approaches like this could contribute to improved use of biomarkers in clinical practice.

Disclosure: Juha Koikkalainen and Jyrki Lötjönen are shareholders and founders of Combinostics Ltd. They are also inventors in the following patents relevant to the subject of the study, for which Combinostics Ltd owns the IPR: 1. J. Koikkalainen and J. Lotjonen. A method for inferring the state of a system, US7,840,510 B2, PCT/FI2007/050277. 2. J. Lotjonen, J. Koikkalainen and J. Mattila. State Inference in a heterogeneous system, PCT/FI2010/050545. FI20125177.

EPR1004

Automatic classification of patients with Alzheimer's disease (AD) and mild cognitive impairment (MCI) who will convert to AD using deep neural networks

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Background and aims: To build and validate a deep learning (DL) algorithm that predicts the individual diagnosis of Alzheimer's disease (AD) and the development of AD in mild cognitive impairment (MCI) patients based on a single cross-sectional brain structural MRI scan.

Methods: 3D T1-weighted images from ADNI (352 healthy controls [HC], 294 AD, 253 MCI converters, 510 MCI stable) and subjects recruited at our Institute (non-ADNI dataset: 55 HC, 124 AD, 27 MCI converters, 23 MCI stable) were used. Deep neural networks (DNNs), which are mathematical representations of the human neural architecture with multiple hidden layers of artificial neurons, were applied. The whole dataset was randomly divided into a training/validation set (90%) and a testing set (10%). DNN performance was improved by adding to the original dataset synthetic images created using data augmentation algorithms, as well as transfer learning to subsequent comparisons.

Results: DNNs with different architectures and parameters were optimized. The results demonstrated that high level of accuracy was achieved in all of the experiments, with the highest accuracy rate of 99.2% achieved in the AD vs HC classification test using ADNI dataset. In a second dataset including ADNI and non-ADNI images, DNNs discriminated AD and HC with an accuracy of 98.2%. The DNN was also able to discriminate c-MCI from nc-MCI with an accuracy up to 75.1% with no difference between ADNI and non-ADNI images.

Conclusion: DNNs provide a powerful tool for the automatic individual patient diagnosis along the AD continuum.

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EPR1005

Changes in functional and structural brain connectome along the Alzheimer's disease continuum

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Background and aims: To investigate structural and functional brain architecture in patients with Alzheimer's disease (AD) and amnestic mild cognitive impairment (aMCI), stratified in converters (c-aMCI) and non-converters (nc-aMCI) to AD, and the relationship between healthy brain network functional connectivity and the topography of brain atrophy in patients.

Methods: Ninety-four AD patients, 47 aMCI patients (25 c-aMCI within 36 months) and 53 healthy controls underwent 3D T1-weighted, diffusion tensor and resting state functional MRI. Graph analysis and connectomics assessed global and local, structural and functional topological network properties and regional connectivity. Healthy topological features of brain regions were assessed based on their connectivity with the point of maximal atrophy (epicenter) in AD and aMCI patients.

Results: Graph analysis properties were severely altered in AD patients. Structural brain network was altered in c-aMCI patients relative to healthy controls in particular in the temporal and parietal brain regions, while functional connectivity did not change. Structural connectivity alterations distinguished c-aMCI from nc-aMCI cases. In both AD and c-aMCI, the point of maximal atrophy was located in left hippocampus (disease-epicenter). Brain regions most strongly connected with the disease-epicenter in the healthy functional connectome were also the most atrophic in both AD and c-aMCI patients.

Conclusion: Progressive degeneration in the AD continuum is associated with an early breakdown of anatomical brain connections and follows the strongest connections with the disease-epicenter. These findings support the hypothesis that the topography of brain connectional architecture can modulate the spread of AD through the brain.

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EPR1006

White Matter Hyperintensities in Alzheimer Disease: a comparison with normal aging.

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Background and aims: Higher white matter hyperintensities (WMH) load has been reported in Alzheimer's disease (AD) patients when compared to controls. Our study assessed possible differences in the spatial distribution of WMH between AD patients and age-matched elderly normals by means of lesion probability maps.

Methods: The present study included MRI scans of 130 probable AD patients (male/female=48/82) from the Prospective Dementia Registry Austria Study (PRODEM-Austria) and 130 age-matched (±0.5/5 years) healthy controls (HC) from the Austrian Stroke Prevention Family Study (male/female=50/80). There were no significant between group-differences in hypertension, hyper-cholesterolemia, diabetes, smoking and WMH volume normalized by intercranial volume. Manually segmented WMH masks were transformed in the MNI152 space using FSL-FNIRT, where voxelwise paired t-test was applied using the General Linear Model framework with FSL-randomise with 5000 permutations.

Results: The result of the voxelwise paired t-test comparison of lesion masks in AD patients versus age-matched HC, overlaid on the T1-MNI brain is shown in the below figure. AD patients showed a significantly higher likelihood of having WMH in a bilateral periventricular distribution than controls ($p=0,05$; threshold-free cluster enhancement corrected).
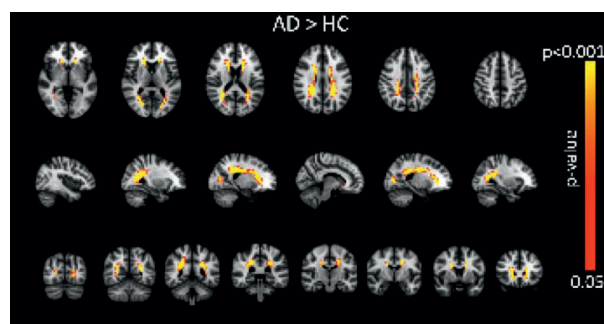
Axial, sagittal and coronal views illustrate the result of voxelwise paired t-test comparison of lesion masks in AD patients versus age-matched HC, overlaid on the T1-MNI brain. Yellow-red colors denote voxels in WMH were significantly more common in AD than in HC with p-values <0.05 (corrected). The color bar indicates the probability range.

Conclusion: The reason for the preferential location of WMH in periventricular brain areas in AD patients described in current study is unclear. Little is known about differential etiologies between periventricular and deep WMH. The MRC Cognitive Function and Ageing Neuropathology Study Group showed that periventricular lesions are related to immune activation resulting from disruption of the blood brain barrier, while the immune response seen in deep and subcortical WMH reflects an innate phagocytic phenotype.

Disclosure: Nothing to disclose

EPR1007

Double-blind argument for a synergistic therapeutic effect of a fixed low-dose combination of acamprosate and baclofen in Alzheimer's disease

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Background and aims: PXT-864, a fixed low-dose combination of acamprosate and baclofen, has shown multiple reversions of pathological alteration in cellular and animal models of AD (Chumakov 2014) in addition of good safety and preliminary evidence of efficacy in early clinical phases (CTAD 2016). If the synergistic profile of PXT-864 in preclinical studies has been clearly established, it remains a challenge in human due to the need of a rdesign including treatment arms under single drugs.

Methods: Patients with mild AD (n=45, progressive decline, no depressive disease) were evenly assigned to one of 3 doses of PXT864, for 36 weeks. The efficacy of PXT864 alone was assessed through cognitive-behavioural tests (per protocol dataset n=32) by dose and compared to historical placebo (Thomas 2016). The exposure to both drugs (Cmax) was measured at each visit evidencing various Cmax groups used to assess the synergy.

Results: On a composite score of 9 clinical endpoints, a synergistic profile using the various Cmax groups at 36 weeks was identified. An improvement on ADAS-Cog11 (1.16 point increase from baseline) in the higher Cmax group for both drugs was observed, whereas by dose, no improvement was observed. The mean change from baseline ADAS-Cog11 was significantly improved for D2 and D3 PXT864 alone vs historical placebo at W36 (p<0.002 and p<0.014, respectively) and for this higher Cmax group vs D3 (p<0.052).

Conclusion: The results provide a synergistic proof-of-action of PXT-864 in AD and our approach could become a key methodology for the development of drug combinations in neurodegenerative disorders.

Disclosure: Peter Schmidt, Viviane Bertrand, Rodolphe Hajj, Serguei Nabrotchkin, Mickaël Guedj, René Goedkoop, Daniel Cohen: Employees Pharnext

EPR1008

LTP-like cortical plasticity is associated with verbal memory impairment in Alzheimer's disease patients

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Background and aims: Experimental studies showed that synaptopathy induced by the neuropathological alterations of Alzheimer's disease (AD) impair synaptic plasticity and memory performance. In humans it is possible to investigate cortical plasticity by applying means of Transcranial Magnetic Stimulation. In AD patients such mechanisms have been widely investigated with TMS protocols such as Theta Burst Stimulation (TBS), showing a clear impairment of Long-Term Potentiation (LTP) cortical-like plasticity consistent with the AD murine models of altered hippocampal plasticity.

Methods: we assessed in 60 newly diagnosed AD patients means of cortical plasticity by applying TBS protocol in order to investigate its relationship with patients' neuropsychological performance.

Results: Long-Term Potentiation (LTP)-like cortical plasticity impairment is associated to a less efficient verbal memory (r=0.45; p=0.002), while neither visual-spatial long-term memory (r=0.08; p=0.53), general intelligence (r=0.11; p=0.45), executive functions (FVF: r=-0.13; p=0.36) or visual-spatial abilities (r=-0.08; p=0.54) showed any association. The relationship between LTP and verbal memory remained significant in a combined model adjusting for gender, disease duration, ApoE e4 status, A-beta, total tau and p-tau (beta=0.05, p= 0.001, 95% CI: 0.02 - 0.08)

Conclusion: These findings suggest that LTP-like cortical plasticity can be assessed non-invasively in vivo as a neurophysiological surrogate of memory in AD patients and reinforce the notion that LTP investigation may represent a valid and reliable tool to evaluate in vivo the weight of sinaptopathy responsible for cognitive dysfunction.

Disclosure: Nothing to disclose.

Cerebrovascular diseases 1

EPR1010

Reasons for Prehospital Delay in Acute Ischemic Stroke: Hints on Increasing the Rate of Recanalization Therapies – a Prospective Cohort Study

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Background and aims: Delays in the prehospital phase jeopardize the chances for stroke patients to be successfully treated with recanalization therapies (RT). Public education campaigns aiming to increase stroke preparedness and reduce prehospital delays showed contradictory results. Therefore, different approaches to optimize processes in the prehospital phase are required.

Methods: In this prospective cohort study, we included patients admitted to the University Hospital Basel Stroke Center, between 2015 and 2017 with an acute ischemic stroke confirmed on Magnetic Resonance Imaging. Trained study nurses interviewed all patients at bedside along a 28-item questionnaire.

Results: Overall, 337 patients were included. 147 (46%) patients arrived at the hospital within 4.5h, 190 (56%) more than 4.5h after symptom onset. 71 of 147 patients (48%) in the first group received RT compared to 11 of 190 (6%) in the delayed group. A general practitioner (GP) was called by one quarter (n=96, 28%) of patients, 16% in the early vs. 38% in the delayed group (p<0.001). In the subgroup who called the GP first, delays occurred due to prehospital face-to-face GP-visits and transportation delays. Calling the GP first was associated with a lower rate of RT (aOR 0.39, 95%-CI 0.19-0.80, p=0.01).

Conclusion: Even in a relatively small urban area, prehospital delay occurred in more than half of stroke patients, and was associated with a lower probability of receiving a RT. Calling the GP first, even within 3h of symptom onset, was associated with avoidable delays. Information campaigns targeted at the GP may increase RT rates.

Disclosure: Nothing to disclose

EPR1011

withdrawn

EPR1012

Quality of life in juvenile stroke

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Background and aims: The incidence of juvenile stroke is increasing. Considering younger age of patients and the potential long-lasting disability, the consequences of juvenile stroke may have a greater societal impact than those of stroke in elder population. We performed a systematic review of studies on quality of life (QoL) in juvenile stroke.

Methods: We have performed a systematic review of all studies on quality of life in juvenile stroke published in PUBMED before January 15, 2018. The search terms were "stroke", "juvenile", "young", "adult", "quality of life" and "resilience". After the abstract evaluation of 555 search results, only six studies we identified as appropriate for the review. The age criterion for juvenile stroke was set as 55 years and younger.

Results: The studies have shown a decline of quality of life in at least 46% of patients with juvenile stroke. On average, QoL was reduced by 37%. The following domains as measured on SF-36 were particularly impaired: physical role, physical functioning and emotional role. The factors influencing the QoL in juvenile stroke were ability to return to work, post-stroke depression, functional outcome, level of education and age of stroke onset.

Conclusion: This systematic review shows a significant decline of QoL in patients with juvenile stroke. Rehabilitation programs should consider the factors influencing QoL in these patients in order to improve outcome of juvenile stroke. Patients who are unable to return to work should receive necessary social support. In addition, our data underline the importance of screening procedures for post-stroke depression in this population.

Disclosure: Nothing to disclose

EPR1013

In-hospital stroke: characterisation in a tertiary hospital

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Background and aims: In-hospital Stroke (IHS) is a stroke that occurs in patients admitted for another diagnosis, and represents 2.2% to 17% of all strokes. Its characterisation is important to identify the circumstances in which occurs and the specific aetiologies.

Methods: Descriptive, retrospective study of IHS occurred between January 2014 and May 2017 at Hospital de Santa Maria. Neurological department and Critical Care Units IHS' were not included. Data was collected from inpatient neurology consultations request forms. Demographic characteristics, inpatient departments, causes of hospital admission, circumstances of stroke occurrence, type and aetiology were analysed.

Results: 64 IHS patients were included (mean age 68.7 years (SD=14.2); 40 (62.5%) males).

The main inpatient department cases distribution was: 16 (25%) in Cardiology; 7 (10.9%) Vascular Surgery; 6 (9.4%) Internal Medicine; 5 (7.8%) General Surgery; 5 (7.8%) Infectious Diseases; 5 (7.8%) Gastroenterology; 4 (6.3%) Cardiothoracic Surgery.

The most frequent causes of admission were elective procedures (18 cases: 8 Interventional Cardiology, 6 Vascular Surgery, 4 other surgeries), cardiac diseases (11), infections (11), gastrointestinal bleeding (5), vascular diseases (4) and kidney failure (4).

55 (85.9%) IHS were ischemic, 5 (7.8%) haemorrhagic and 4 (6.3%) cerebral venous thrombosis.

Besides TOAST aetiologies, multiple mechanisms related to admission (acute myocardial infarction, cardiac/vascular procedure) or associated with hospitalisation (e.g. hemodynamic changes) were identified as potential IHS triggers.

Conclusion: IHS represents a singular population with different risk factors and co-morbidities compared to community-onset strokes. Our findings allow us to organise a prevention-oriented care, to educate staff on stroke recognition and to improve management.

Disclosure: Nothing to disclose

EPR1014

Evaluation of the mechanisms of vascular regulation in middle cerebral artery stenosis using transcranial Doppler

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Background and aims: Stroke due to atherosclerotic intracranial arterial stenoses has high recurrence rate. It is important to identify greater risk patients. We aimed to study cerebral vascular reserve in Caucasian patients with unilateral MCA stenoses through cerebral autoregulation (AR), vasoreactivity (VR) and neurovascular coupling (NVC) tests.

Methods: Case-control study of a cohort of adult patients with unilateral MCA stenosis >50% (MRA), and healthy controls. Carotid stenoses >50% and large white matter lesions were excluded. Blood pressure (Finometer), MCA flow velocity (transcranial Doppler), electrocardiogram and tele-expiratory CO_2 were evaluated. AR was evaluated by transfer function (coherence, gain and phase), VR to hypercapnia response, and NVC by cognitive N-Back test response.

Results: 30 patients and 23 age and gender adjusted controls. 16 had moderate (50-69%) and 14 severe ($\geq$70%) stenosis; in both, efficacy of AR and VR to CO_2 was significantly lower ipsilaterally to the stenosis (p<0.05). AR (phase), VR to CO_2 and NVC were significantly different between controls and patients, only ipsilaterally to the stenosis (p<0.05), although for NVC only in the group of severe stenosis. AR (phase) was worse with higher stenosis degree (p<0.05), similar to that of VR to CO_2 (although not statistically significant).

Conclusion: CO_2 VR test and AR (phase) allow detecting cerebral vasomotor regulation disfunction even for moderate stenosis (50-70%), and also seem useful for measuring stenosis severity effect. NVC, on the other hand, is only altered in severe stenosis, suggesting preservation of functional hyperemia associated with cognitive activity until later stages of intracranial vascular disease.

Disclosure: Nothing to disclose

EPR1015

Association of obesity with other stroke risk factors in young adults of the Republic of Moldova

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Background and aims: Obesity is associated with an increased risk of stroke. Abdominal obesity is a stronger risk factor than body mass index (BMI) with a greater effect among younger persons. We studied the relationship between obesity and other stroke risk factors in the young adult population of the Republic of Moldova.

Methods: In November 2015, we initiated an epidemiological study in 2 villages located in the northern and central regions of the Republic of Moldova. Our study protocol included: questionnaire, clinical examination, electrocardiography, laboratory examinations and Doppler/Duplex ultrasound of the carotid arteries.

Results: In the study were included 412 subjects, 246 (60%) women and 166 (40%) men (mean age 36.6±9.2 years). The most common identified risk factors were abdominal obesity in 237 (57.5%) and obesity of different degrees in 125 (30.3%) subjects. Mean abdominal circumference (AC) in men was 94.02±14.16cm and 87.81±13.79cm in women. Increased total cholesterol, blood pressure (BP) $\geq$140/90 mmHg and carotid atherosclerotic plaques were more frequent in subjects with central obesity then in those with overweight and general obesity. AC significantly correlated with the systolic BP (r=0.395; p<0.0001), diastolic BP (r=0.412; p<0.0001), BMI (r=0.872; p<0.0001) and mean intima media thickness (r=0.401; p<0.0001).

Conclusion: Abdominal obesity was the most common risk factor for stroke in young adult population and was significantly associated with other stroke risk factors. Prevention of obesity and weight reduction need greater emphasis in stroke prevention programs.

Disclosure: Nothing to disclose

EPR1016

Cerebral venous thrombosis in Oslo 2008-2017

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Background and aims: Cerebral venous thrombosis (CVT) is an uncommon cause of stroke that mainly affects adults <45 years of age. Although headache, seizures and focal neurological deficits are the most common symptom, baseline symptoms can vary considerably resulting in challenging diagnostics. The purpose of this study was to assess risk factors and management in patients treated at Oslo University Hospital.

Methods: Patients admitted to Department of Neurology, Neurosurgery or Geriatrics from January 2008 to November 2017 with CVT was identified for patient administrative system by the ICD-codes I67.6 and I63.6. Information on symptoms, risk factors, etiology, diagnostics and management was collected retrospectively from the medical records.

Results: 130 patients with CVT were identified, 26 (20.0%) with traumatic (tCVT) and 104 (80.0%) with non-traumatic CVT (nCVT) Among the patients with nCVT headache was the most common symptom reported by 83.7%. Among female patients <50 years of age, 14% of reported cases occurred during pregnancy/puerperium and 50% on oral estrogen-containing contraceptives. Hereditary thrombophilia was identified as the main cause in 15%, a combination of different causes was identified in 1/3. However, in 1/3 of the cases no pro-thrombotic condition was identified. All patients were treated with anticoagulations. In addition, 10% of the patients with nCVT were treated with endovascular treatment and <5% was neurosurgical interventions.

Conclusion: Prognosis in CVT is generally good. In traumatic brain injury with skull fracture there is a considerable risk of CVT. Both nCVT and tCVT are treated with anticoagulation.

Disclosure: Nothing to disclose

EPR1017

The role of spinal imaging in the management of angioggram-negative spontaneouss subarachnoid haemorrhage: a single-centre experience

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Background: The non-aneurysmal SAH constitute 15% of all spontaneous subarachnoid haemorrhages (SAH), where no intracranial vascular pathology is found despite extensive neuroimaging investigations. Those non-aneurysmal haemorrhages are subdivided into perimesencephalic SAH (PMSAH) and non-perimesencephalic SAH (NPSAH). Searching for a spinal pathology might reveal a spinal arteriovenous malformation (AVM) as a cause of the haemorrhage in about 10% of the cases.

Objective: To evaluate the diagnostic yield of Magnetic Resonance Imaging (MRI) for the spinal column in searching for a spinal aetiology for angiographically-negative spontaneous subarachnoid haemorrhage (AN-SAH)

Methods: A retrospective analysis was conducted in the Walton Centre/Liverpool/UK, which is a tertiary stroke referral centre. The database of the patients who presented with spontaneous nonaneurysmal SAH, diagnosed by computed tomography (CT) or lumbar puncture, and negative CT angiography and digital subtraction angiography (DSA) was reviewed.

Results: There were 1457 patients admitted to The Walton Centre with non-traumatic, spontaneous SAH between January 2009 to December 2015. 300 patients (20.6%) were diagnosed with non-aneurysmal SAH. In 51 patients (17%), an entire spinal axis by standard T1- and T2-weighted MR-imaging was done. While cervical T1- and T2-weighted MR-imaging was conducted in 86 patients (28.7%). In all the 137 patients (45.7%), MR-imaging for the spinal axis did not identify any underlying spinal anomaly that contributing to the SAH formation

Conclusion: In spontaneous nonaneurysmal SAH patients, MR-imaging of the spinal axis has a very low diagnostic yield, and routine radiological investigation of the spinal axis in non-aneurysmal SAH patients' care pathway is therefore not recommended.

Disclosure: Nothing to disclose

Cerebrovascular diseases 2

EPR1018

Occurence and evolution of spasticity in stroke patients – prospective, longitudinal study

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Background and aims: The main aim of the study was to document occurrence and evolution of post stroke spasticity (PSS). Secondary goal was to identify predictors for the increase and the decrease in PSS during 12 months follow up.

Methods: In the longitudinal, multicentric, prospective cohort study assessments were done 7 days (V1), 6 (V2) and 12 (V3) months following the stroke onset. The demographic data, baseline characteristics, the Barthel Index, degree and pattern of paresis and muscle tone were evaluated and recorded. Spasticity was assessed using the Modified Ashworth Scale (MAS).

Results: A total of 402 consecutive patients with first-ever stroke of carotid origin and presence of motor deficit at the day 7 were included. Spasticity was present in 42.3% of patients at V1, 47.3% at V2 and 43.2% at V3. A significant number of patients experienced changes in spasticity between the visits: decrease/disappearance of spasticity was noted in 18.6% (V1 and V2) and 18.3% (V2 and V3) of patients, increase/new occurrence of spasticity in 30.7% (V1 and V2) and 13.6% (V2 and V3) of patients. Number of patients with severe spasticity increased throughout the year from 2.9% to 11.6% (V2) and 12.5% (V3).

Conclusion: Spasticity was noted in almost half of the included patients. The degree of spasticity often changed over time in both directions. The rate of severe spasticity increased steadily during the first year following stroke onset.

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EPR1019

Arterial stenting in echolucent carotid plaques is more frequently asssociated with adverse outcomes: a systematic review and meta-analysis

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Background and aims: Several studies have confirmed that echolucent plaques are associated with higher rates of emboli signals and in-stent restenosis compared to echogenic plaques. There are controversial data according to carotid artery stenting (CAS) interventions on echolucent plaques and recurrent symptoms. In this meta-analysis we aimed to evaluate associations between carotid plaque echolucency and adverse outcomes following CAS.

Methods: Electronic databases (PubMed, EMBASE and Cochrane Center Register) were systematically seaeched up to September 2017. Studies with ultrasound-based characterization of carotid artery plaque echogenicity and its association with adverse outcome after CAS were eligible for this study.

Results: Out of 412 studies found after the first medical databases search, we identified five studies appropriate to be qualitatively and quantitatively analyzed, which evaluated different adverse outcomes in patients with echolucent plaques after CAS. Pooled analysis showed that CAS in echolucent carotid plaques is associated with higher risk of stroke (OR 2.33; 95% CI 1.73-4.65, p=0.015), microembolization (OR 2.77; 95% CI 1.40-5.45, p=0.003), and in stent restenosis (OR 3.8; 95% CI 1.93-7.44, p<0.001). In general, pooled OR of adverse outcomes for CAS performed in echolucent compared to echogenic plaques was 2.92 (95% CI 1.97-4.32), p<0.001.

Conclusion: Compared to echogenic plaques the echolucent ones are more frequently associated with recurrent stroke, distal embolization and in-stent restenosis.

Disclosure: Nothing to disclose

EPR1020

Scale of connective tissue dysplasia signs in patients with spontaneous cervical artery dissection

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Background and aims: Spontaneous cervical artery dissection (sCeAD) is the most frequent cause of ischemic stroke in young adults. Connective tissue dysplasia (CTD) can be considered as a risk factor for dissection, due to dysplastic change of arterial wall.
To assess clinical signs of CTD in patients with CeAD.
Methods: We examined 82 patients (mean age 38.3±13.5; 52 females, 63.4%) with CeAD, verified by MRI/MRA and 40 healthy volunteers (mean age 38.5±6.7; 25 females 62.5%). We evaluated 48 signs included in the Villefranche diagnostic criteria for the vascular type of Ehlers–Danlos syndrome, Ghent criteria for Marfan syndrome, Beighton criteria of joint hypermobility and others, as well as history of headache. Each sign was counted as present or absent.
Results: Signs suggesting CTD were detected more frequently in the group with sCeAD (mean score 7.9±3.6 vs 4.6±2.5; p<0.0039). Regression analysis was performed to determine diagnostic-prognostic value of CTD signs. This allowed us to identify main:history of headache (p=0.022), arterial hypotension (p=0.012), extensive bruising (p=0.011) and additional diagnostic criteria:translucent skin (p=0.034), hight palate (p=0.034), nasal bleeding (p=0.043), blue sclera (p=0.05), predisposition to constipation (p=0.05). In the presence of the 4 main and 2 additional criteria, the predictive value of dissection according to regression model is 77% (ROC analysis: AUC 0.90, 95% CI, 0.84–0.96).
Conclusion: We showed that clinically detectable connective tissue abnormalities are prevalent in patients with sCeAD. The presence of the 4 main and 2 additional diagnostic criteria of CTD has a high predictive value of CeAD and can be used as its diagnostic-prognostic criteria.
Disclosure: Nothing to disclose

EPR1021

Biochemical and Imaging Biomarkers of Atrial Fibrillation in Cryptogenic Stroke Patients

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Background and aims: Ischaemic stroke in atrial fibrillation (AF) patients is often territorial and affecting more arterial areas of blood supply. Elevated blood levels of D-dimer and NT-proBNP were described in AF stroke patients. The aim of the study was to compare the association of selected biochemical biomarkers and MRI imaging characteristics with occurrence of paroxysmal AF and frequent supraventricular extrasystoles (SVES) on 30-days Holter ECG monitoring in cryptogenic stroke patients.
Methods: Retrospective monocentric analysis of consecutive ischaemic stroke patients admitted to comprehensive stroke centre in 2.5 years' period with cryptogenic etiology of stroke at discharge who underwent 30-days Holter ECG monitoring. As potential biomarkers, we compared blood levels of D-dimer and NT-proBNP. MRI was performed within initial hospitalization. SVES were described as frequent if occurred in more than 1% of ECG record.
Results: 178 patients were monitored (average age 60 years, 54% men, 9% had AF, frequent SVES 13%, less frequent SVES 27%). Mean levels of D-dimer differed significantly among the groups (AF 255 ng/ml, frequent SVES 396 ng/l, less frequent SVES 274 ng/l, others 129 ng/ml). Mean levels of NT-proBNP did not differ significantly among the groups. In patients with AF or frequent SVES we found more old ischaemic lesions on MRI (82.9% vs. 61.5%, p=0.003). In occurrence of territorial, lacunar or infarction in more areas of blood supply the groups did not differ.
Conclusion: Cryptogenic stroke patients with detection of AF or frequent SVES on 30-day Holter ECG monitoring had higher levels of D-dimer and significantly more old ischaemic lesions on MRI.
Disclosure: Nothing to disclose

EPR1022

Glucose variability and post-stroke hyperglycemia: the key factors underlying poor outcomes in patients with Diabetes Mellitus

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Background and aims: Diabetes Mellitus (DM) has been identified as a prognosis factor of poor outcome after ischemic stroke (IS) but the mechanism underlying it has not been elucidated yet. We analysed the influence of DM, post-stroke hyperglycemia, glucose variability (GV) and HbA1c in the prognosis of IS.

Methods: Secondary analysis of the GLIAS II study. Acute stroke patients were classified into two study groups: DM group (patients with previous history of DM) and a non-DM group. Capillary finger-prick glucose levels were measured every 4 hours the first 48 hours after an IS. Glycaemia >155mg/dL was the cut-off point of post-stroke hyperglycemia. GV was measured by the standard deviation (SD) of the mean glucose values. HbA1c was tested in all patients. The outcomes were death or dependency and mortality at 90 days.

Results: 213 patients were included. 64 (30%) had a previous history of DM. No differences in death or dependency (mRS score >2: 31.7% DM vs. 26.4% non-DM; P=.500) at three months were found. The DM group showed a trend to higher mortality (12.7% vs. 5.7%, P=.096). The logistic regression analysis adjusted by the stroke severity showed that GV and post-stroke hyperglycemia were independently associated with mortality at three months. Post-stroke hyperglycemia was also associated with higher risk of death or dependency. DM and HbA1c were not related to the outcome.

	Crude OR			Adjusted OR		
	P	OR	95% CI	P	OR	95% CI
Mortality						
NIHSS admission	.009	1.1	1.02 – 1.18	ref	ref	ref
DM	.09	2.4	.8-6.7	.15	2.21	.75-6.59
Glycemia >155mg/dL	.05	2.9	.9-8.7	.04	3.27	1.03-10.36
GV	.06	1.02	.9-1.05	.03	1.03	1-1.06
HbA1c	.22	1.26	.86-1.83	.19	1.29	.87-1.89
Death or dependency						
NIHSS admission	<.001	1.14	1.08 – 1.2	ref	ref	ref
DM	.44	1.29	0.67-2.48	.45	1.32	.64 – 2.7
Glycemia>155mg/dL	.19	1.5	.81-2.78	.04	2.04	1.0 – 4.03
GV	.34	1	.99-1.02	.07	1.02	.99-1.04
HbA1c	.13	1.21	.94-1.55	.08	1.26	.97-1.64

Logistic regresion analysis for mortality and dependency or death adjusted by NIHSS score and each of the following: DM, Glycemix variability, HbA1c and Post stroke hyperglycemia.

Conclusion: The presence of post-stroke hyperglycemia and GV were associated with poor prognosis after IS independent of the diagnosis of DM and HbA1c values.

Disclosure: Nothing to disclose

EPR1023

Can we cut off mortality rates by one third? An analysis of in-hospital acute stroke mortality in a tertiary stroke centre in Romania.

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Background and aims: In-hospital mortality rates in acute stroke patients vary between 3%-20% mainly depending on acute management and quality of stroke-unit care. The aim of this study was to assess the rates and causes of deaths in patients hospitalized for acute stroke.

Methods: We performed a retrospective analysis of prospectively collected data for all patients admitted with acute stroke between January 1st and June 30th 2017. We assessed demographic, clinical characteristics, rates and causes of in-hospital mortality.

Results: During this period, 766 acute stroke patients were admitted in our Department, of which 689 (89.9%) had an ischemic stroke and 77 (10.1%) a haemorrhagic stroke. 99 (12.92%) of the admitted stroke patients died during hospitalization. The mean hospitalization length until the moment of death was 7.5 days. The mortality rate was 11.03% among patients with ischemic stroke and 29.87% among patients with haemorrhagic stroke. 51.5% of in-hospital mortality was attributed to stroke severity, whereas 34.3% of deaths were related to infectious complications (mainly pneumonia and urinary tract infections), 8.08% to cardiac pathology (acute coronary syndromes and cardiogenic shock), 3.03% to massive gastrointestinal bleeding, 2.02% to pulmonary embolism and 1.07% to other causes.

Conclusion: At least 35% of the in-hospital stroke related deaths in our centre are attributable to preventable factors. Improving the measures taken for the prevention of infectious and cardiac complications in these patients could lead to a significant decrease of in-hospital stroke mortality rates.

Disclosure: Nothing to disclose

EPR1026

Atrial fibrillation in patients with first-ever stroke: incidence trends and antithrombotic therapy before the event

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Background and aims: Atrial fibrillation (AF) is the most common cardiac arrhythmia among adults. In this study, we investigated the incidence of AF-related ischemic stroke over the past decade in South Korea and trends of preventive antithrombotic therapy use before stroke in a Nationwide cohort.

Methods: The data source for this study was a Nationwide sample cohort comprising 1,025,340 individuals (2% of the entire population of Korea) that was established by the countrywide health insurance system. A total of 10,215 patients with acute ischemic stroke (AIS) were selected from the cohort between 2004 and 2013.

Results: AF was identified in 1,662 (%) patients, and 979 patients had preexisting AF before AIS. The annual proportion of patients with AIS with AF gradually increased from 13.4% to 22.6% over the studied time period (p for trends <0.001). Only 14.4% of patients with AF with a high risk for stroke were receiving OAC therapy before the stroke. On the other hand, the proportion of patients treated with antiplatelet agents had increased from 17.8% in 2004 to 46.7% in 2013, while that of patients receiving no antithrombotic therapy decreased from 64.4% in 2004 to 42.2% in 2013.

Conclusion: The number of patients with AIS and AF has steeply increased over the last 10 years in Korea. However, a small portion of patients with AF were receiving OAC therapy before the stroke and about half of the patients did not receive any antithrombotic medication.

Disclosure: Nothing to disclose.

Cognitive neurology/neuropsychology 1

EPR1027

Validation of Montreal Cognitive Assessment-Basic Arabic Version in Low Educated Adults with Mild Cognitive Impairment

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Background and aims: Mild Cognitive Impairment (MCI) may be an early sign of dementia. Educational level can affect its accurate recognition by neurocognitive tools. We aimed to evaluate the Montreal Cognitive Assessment Basic (MoCA-B) Arabic version to detect MCI in adults with low education.

Methods: 116 illiterate or low educated (up to 9 years) adult Egyptians; (MCI=46) according to the National Institute on Aging-Alzheimer's Association clinical criteria, and 70 cognitively normal controls were assessed using the clinical dementia rating scale and the MoCA-B-Arabic Scores.

Results: MCI patients scored significantly lower than controls on all subscales and total MoCA-B-Arabic (P <.001). At the cutoff 24/25, the scale has 84.8% sensitivity and 82.9% specificity for MCI detection. Area under the receiver operating characteristic curve (AUC) was 0.886, P <.001. Internal consistency was 0.733 and test retest reliability was 0.972. The total score differed with literacy level. Correction for education yielded 76.1%, sensitivity and 82.9% specificity and AUC was 0.877, P <.001. The suggested total score correction was able to differentiate correctly between patients with MCI and normal controls with an accuracy of 80.1% at a cutoff 24/25.

Conclusion: MoCA-B-Arabic is reliable and valid in detecting MCI among illiterate and low educated Egyptian adults.

Disclosure: Nothing to disclose

EPR1028

Pure word deafness after lesion in the left superior temporal gyrus

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Background and aims: Pure word deafness is a rare neurologic disorder, characterized by selective deficits in auditory speech comprehension with preserved speech production and written language comprehension. Due to the scarcity of published cases, the critical lesion site in the temporal lobe responsible for PWD remains debated.

Methods: We report three detailed cases of pure word deafness that occurred after a stroke. We performed MRI normalization and lesion overlapping to identify common lesion sites in these patients. Furthermore, we mapped their lesions onto a tractography atlas to quantify the severity of white matter tracts disconnection and performed diffusion tension imaging-based (DTI) tractography in one of our patients to identify fiber tracts specifically lesioned in this patient.

Results: Lesion overlap showed a unique cortical region in the middle part of the left superior temporal gyrus (STG), anterior to the classical location of Wernicke's area and postero-lateral to Heschl's gyrus. Regarding white fibers' integrity, all three patients had disruption in the posterior long segment of the left arcuate fasciculus and in the left inferior fronto-occipital fasciculus. Finally, in one of the patients, tractography revealed two main fiber tracts affected, arising from middle STG, one projecting to the left Heschl's gyrus, and the other to the left inferior frontal gyrus.
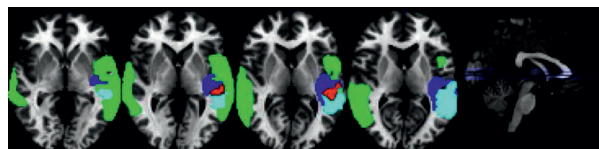
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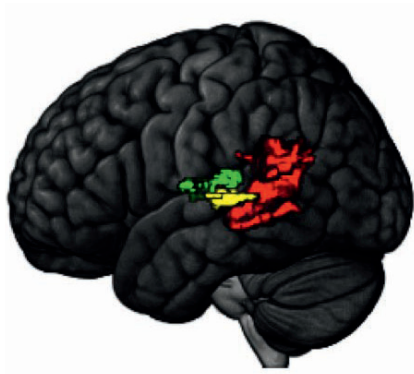
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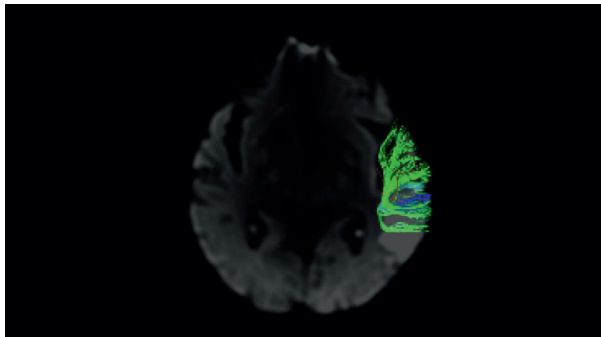
DTI tractography

Conclusion: These cases provide clinical support for recent functional neuro-imaging studies suggesting a causal role for left mid to anterior temporal gyrus in auditory word-form recognition and suggest that lesions of its afferent and efferent projection fibers contribute to the pathology of PWD.

Disclosure: Nothing to disclose

EPR1029

The effect of prolonged-release fampridine on cognitive performance, fatigue, depression and quality of life of MS patients: results from the Ignite study

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Background: Fampridine improves impaired axonal conduction associated with central nervous system demyelination. Long-term effects of fampridine have not been fully explored.

Objectives: To assess cognitive function, quality of life, depression and fatigue in Multiple Sclerosis (MS) patients treated with fampridine after 6 and 12 months of treatment.

Methods: 60 patients (31 female, median EDSS 6.0 (4-6.5), mean age 50.9±9.5) were enrolled in the study. Patients were examined with T25FW and BICAMS battery and were asked to complete MSIS-29, MFIS, BDI-II and MUSIQOL questionnaires. Patients were sub-grouped in responders (n:40) and non-responders (n:20) according to T25FW performance after 2 weeks on treatment.

Results: After 6 months, statistically significant improvement was observed in MSIS29 ($p<0.001$), in T25FW ($p<0.001$) and SDMT($p<0.001$) for responders. After 1 year on treatment, statistically significant improvement was observed in MSIS29 ($p=0.004$), T25FW ($p<0.001$), SDMT (($p<0.001$) and MUSIQOL ($p=0.03$) for responders. Non-responders did not present any statistically significant improvement in all tests during the study duration

Conclusions: According to study results, fampridine may have a beneficial effect on information processing speed though not other domains of cognitive function in MS patients. Study data have provided some evidence that fampridine treatment may reduce the impact of MS in daily activities and improve quality of life but has no effect on subjective fatigue and mood.

EPR1031

Measuring sentence production in primary progressive aphasia

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Background and aims: To test the ability of the Sentence Anagram Test (SAT) in distinguishing non-fluent (nfv) and logopenic variants (lv) of primary progressive aphasia (PPA) which are the two most difficult PPA forms to be distinguished based on speech production.
Methods: We recruited 13 nfvPPA, 9 lvPPA and 4 semantic PPA (svPPA) patients. Participants underwent SAT, which included canonical and non-canonical sentences. Performance accuracy and time for completing total and sub-session items were recorded. Performances at syntax comprehension test were also investigated. Neuropsychological features were compared between nfvPPA and lvPPA groups. The four svPPA were not included in the statistical analysis and were only used for a qualitative example of grammar unaffected performance.
Results: PPA groups took similar time to complete all the SAT sub-sessions. Compared to lvPPA, nfvPPA patients showed worse accuracy for both canonical and non-canonical sentences. Likely due to initial comprehension deficits in lvPPA with longer disease duration, both groups of patients performed similarly in the syntax comprehension test. As expected, svPPA qualitatively performed better than the other groups in all investigated domains.
Conclusion: The SAT is a powerful tool for distinguishing nfvPPA and lvPPA. Although some lvPPA had longer disease duration, the SAT was still able to detect the differences in the two variants. Future studies in larger samples should test the performance of these measures for a correct classification at the single subject level.
Disclosure: The study was supported by the Italian Ministry of Health (grant number GR-2010-2303035).

EPR1032

Behavioral and physiological markers of feigned memory impairment

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Background and aims: The detection of malingering in cognitive performance is an important clinical challenge. The study goal is to explore behavioral and physiological responses in a performance validity test under normal vs. feigning conditions.
Methods: Twenty healthy women (mean age=32±6; mean education=17±1) recruited in the community performed a digital version of Test of Memory Malingering (TOMM) adapted for eye-tracking recording (iView X™ Hi-Speed 1250 System). Half performed TOMM under normal effort and half were instructed to feign memory impairment as if they were in the initial stages of dementia to receive retirement or disability benefits. Number of correct responses (CR), response time (RT), and fixation time (FT) in old vs. new stimuli were recorded. Mann-Whitney test were used for group comparisons and ROC curves were applied for diagnostic test evaluation.
Results: The feigning group produced fewer CR on both evaluation trials and retention trial (p<0.001), had longer RT on evaluation 1 (p=0.007) and 2 (p=0.004), and had shorter total FT (during the 3 seconds visualization period prior to RT) in old stimuli during evaluation 1 (p=0.013) and 2 (p=0.019). No significant other group differences (p>0.05) were identified regarding RT, first FT, and total FT. ROC curves revealed that behavioral measures (CR and RT) had AUC >0.9 on both evaluation trials and that the AUC for total FT was 0.8 on both evaluation trials.
Conclusion: Healthy individuals feigning memory impairment have a distinct behavioral and physiological response pattern, reflecting an increased effort to inhibit a natural response.
Disclosure: Study funded by Bial Foundation research grant 430/14

Epilepsy 1

EPR1033

Short-term risk of recurrence after a first unprovoked seizure

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Background and aims: Our objective are to evaluate the risk of recurrence after a first unprovoked seizure at one month and the associative risk factors of recurrence at 1 month as well as the recurrence risk at 3 months.

Methods: This is a prospective observational study based on a consecutive series of 140 adult patients admitted in Emergency Department (ED) for a first unprovoked seizure during one year. All the included patients were followed in a specialized consultation at 1 month maximum. The collected data was exhaustive including: demographic criteria, clinical examination, recurrence at 1 and 3 months, EEG, Imaging, precipitating factors, type of seizure and prescribed treatment.

	Recurrence at 1 month n=80		P Value
	Yes n=9 (11%)	No n=71 (89%)	
EEG N	5(55.5 %)	46(64.8%)	0.59
EEG Abnormal	4(45%)	19(27%)	0.271
EEG<48H Abnormal	4(45%)	17(23.9%)	0.232
EEG <48 N	3(66.6%)	32(45.1%)	0.724
EEG P	0	5(7%)	1.00
EEG <48 P	0	5(7%)	1.00
EEG FL	4(44.4%)	14(19.7%)	0.109
EEG <48 FL	4(44%)	11(15.5%)	0.058
Imaging anomalies	3(33.3%)	11(15.5%)	0.188
Precipitating factors	1(11.1%)	21(29.6%)	0.432
Age >60 years	4(44.4%)	28(39.4%)	1.00
SEX	M:3(33%) F:6(66.6%)	M:46(64%) F:25(35.2%)	0.082
BDZ	3(3.33%)	3(4%)	0.017
Generalized	2(22.2%)	7(10%)	0.266
Focal	6(66.6%)	19(27%)	0.015

Table 1: Different studied risk factors and their significance.
EEG N: EEG Normal; EEG<48H Abnormal: Abnormal EEG performed in less than 48 hours after the first epileptic seizure; EEG < 48 N: Normal EEG performed less than 48 hours after the first epileptic seizure; EEG P: Paroxysm discharges on EEG; EEG < 48 P: Paroxysm discharges observed on EEG performed less than 48 hours after the first epileptic seizure; EEG FL: Focal slowness on EEG, EEG < 48 FL: Focal slowness on EEG performed less than 48 hours after the first epileptic seizure; BDZ: Benzodiazepine. Generalized: clinical generalized seizure type; Focal: clinical focal seizure type.

Risk factors and their significance

Results: Among the 140 patients diagnosed as first unprovoked seizure by the ED, only 80 patients have their diagnosis confirmed at 1 month. Nine patients had recurrence before one month (11%). We were able to define specific valid risk factors of short term recurrence: focal seizure (p=0.015), abnormal EEG in the first 48 hours as focal slowness (p=0. 058) and imaging abnormalities (p=0.19). The risk of recurrence at 3 months was 16% in a total of 38 patients.

Conclusion: Most patients came in the ED did not have any recurrence seizure in the first month (89%). So, we do not suggest any pre-medication in ED waiting for their first consultation especially without our risks factors. The valid risk factors are: EEG in the first 48 hours, Type of seizure and Imaging. The delay of 1 month is absolutely safe.

Disclosure: Nothing to disclose

EPR1034

Language fMRI in epilepsy: Current standards in practice

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Background and aims: Functional MRI is validated for lateralizing language areas in pre-surgical planning, but teams often remain uncertain about fMRI's strengths and weaknesses. In this talk the key evidence supporting fMRI's use will be summarized through two extensive international surveys of clinicians and analysts completing language fMRI in epilepsy.

Methods: Respondents included 82 clinicians involved in selecting patients for epilepsy surgery, and 63 analysts completing language fMRI. Respondents were typically from academic centers (clinician survey 85%; analysts, 82%) and treated primarily adults (44%/42%), adults and children (40%/36%), or children alone (16%/22%).

Results: Primary findings from the clinical survey included the fact that fMRI is used both for lateralizing language and, frequently (44% of programs), guide surgical margins. Programs reported both cases of unpredicted decline (17%) and unexpected preservation of function (54%). The analytic survey identified the most-commonly used language tasks, which include noun-verb generation, verbal fluency, and object naming. A de-facto standard processing stream is evident, with analysis most often completed in the open-source software SPM. Clinical fMRI is already executed in a wide range of languages.

Conclusion: Language fMRI is well established for presurgical language mapping in epilepsy. These surveys reveal a great diversity in protocols, however, and highlight a need for highly standardized and validated forms of fMRI. They also underscore the importance of not using fMRI maps to guide surgical margins. An ongoing study to validated clinical language fMRI in multiple languages will be discussed, as will key points for successful use of fMRI in the clinic.

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EPR1035

IL-1 signals in epileptogenesis and epilepsy-induced sleep disruptions

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Background and aims: Epilepsy is often associated with sleep disturbance, but the interaction between sleep and epilepsy is not clear. Interleukin-1 regulates sleep and participates in epileptogenesis. NMDA receptor also play a key role in epileptogenesis. Therefore, we herein study the activation of NMDA receptors via the IL-1 signaling pathways, e.g., Src kinase and NF-kappaB, in epileptogenesis and epilepsy-induced sleep disruption.
Methods: Spontaneously generalized seizures were induced by intraperitoneal injection of pentylenetetrazol (PTZ), the sleep-wake activity was analyzed, and the seizure threshold was determined. NR1 and phosphorylated-NR2B were determined by the Western blotting. Activators and inhibitors of Src kinase and NF-kappaB were administered intracerebroventricularly.
Results: Occurrence of spontaneous seizure was higher in the wildtype treated with PTZ than that in the IL-1R1 kockout (KO) mice treated with PTZ. NREM sleep was decreased in wildtype mice treated with PTZ, but it was not altered in IL-1R1 KO mice. The expression of NR1 subunit protein and the phosphorylation of NR2B at Tyr1472 in the hippocampus and the hypothalamus were significantly lower in the IL-1R1 KO mice treated with PTZ when comparing to those in the wildtype mice treated with PTZ. Furthermore, administering inhibitors of Src kinase or NF-kappaB blocked PTZ-induced NMDA activation, and suppressed epileptogenesis and sleep disturbance in wildtype mice. In contrast, activators of Src kinase and NF-kappaB restored the IL-1 signaling in the IL-1R1 KO mice.
Conclusion: Our results indicate that the increase of NMDA receptor activity by the IL-1 signal contributes to the PTZ-induced epileptogenesis and the epilepsy-induced sleep disruption.
Disclosure: Nothing to disclose

EPR1036

TC-G 1008, GPR39 (zinc receptor) agonist decreases seizure threshold in maximal electroshock seizure threshold test and facilitates kindling development in pentylenetrazole kindling model in mice

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Background and aims: Previously described as an orphan, GPR39 receptor was shown to be activated by zinc ions. It was demonstrated that zinc-enriched mossy fiber stimulation-dependent up-regulation of potassium-chloride co-transporter 2 (KCC2), which is indispensable for GABAA receptor function, was not observed in slices from GPR39 knockout animals (Chorin et al. 2011), suggesting that GPR39-dependent up-regulation of KCC2 activity provides homeostatic adaptation to an excitotoxic stimulus by increasing inhibition. Thus, GPR39 has been proposed as a novel target for dampening seizures.
Methods: Using recently synthesized selective GPR39 agonist, TC-G 1008, we assessed the effects of GPR39 activation in vivo, in a seizure test and a model of epilepsy, i.e., maximal electroshock seizure threshold (MEST) test and pentylenetrazole (PTZ) kindling model, respectively.
Results: Liquid chromatography tandem mass spectrometry analysis revealed that TC-G 1008 is brain penetrant, reaching substantial brain concentrations 15–30 min following its administration at a dose of 20 mg/kg. In MEST test, TC-G 1008 (5, 10 and 20 mg/kg) and zinc (8 and 16 mg/kg, given as zinc chloride) decreased seizure threshold, while a common anticonvulsant drug, valproic acid (VPA) (150 mg/kg), exerted the opposite effect. In the PTZ model, TC-G 1008 (10 mg/kg) facilitated kindling development. 93% of mice that received TC-G 1008 and 77% of mice that received zinc (8 mg/kg) exhibited at least three consecutive stage 5 seizures vs. 62% of control mice and none of VPA treated mice.
Conclusion: Our in vivo data obtained using TC-G 1008 argue against GPR39 activation as a therapeutic strategy for alleviating seizures/epilepsy.
Disclosure: The study was supported by a grant from the National Science Centre 2016/20/S/NZ7/00424 (UD).

EPR1037

Coffin-lowry syndrome as a rare cause of X-linked drop attacks

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Background and aims: Coffin-Lowry syndrome (CLS) is a rare X-linked syndrome characterized by psychomotor, intellectual disability and facial dysmorphic features. Non-epileptic drop episodes occur in 3-7% and epileptic seizures in 5-30%. It is unusual for a female present the classic phenotype.

Methods: Case Report

Results: A 21-year-old female, child of non-consanguineous Caucasian parents, with a psychomotor development delay, attention deficit and hyperactivity. The pregnancy was complicated with pre-eclampsia and preterm delivery occurred at 36 weeks. No history of CNS infections or febrile seizures was reported.

When she was 3 years old, she presented multiple episodes of unprovoked sudden falls without loss of consciousness.

At the age of 7, she developed daily motor seizures with nocturnal predominance.

Objective examination showed craniofacial and osteoarticular dysmorphisms with tapering fingers and hyperlaxity.

Cranial MRI showed enlargement of the ventricular system due to subcortical atrophy.

Video-EEG recorded asymmetric tonic seizures in sleep and episodes of non-epileptic falls not external-stimulus induced.

She was treated with carbamazepine, levetiracetam, zonisamide, clonazepam, with partial benefit on epileptic seizures and without any improvement in drop episodes.

The karyotype (46,XX) was determined and exome sequencing analysis was performed and the variant c.1756dup (p.Ala586Glyfs*11) was detected in heterozygous state in the RPS6KA3 gene, confirming the diagnosis of CLS.

Conclusion: This report suggests that CLS should be considered in the differential diagnosis of drop attacks in the presence of the typical phenotype even among females.

Disclosure: Nothing to disclose

EPR1038

A service evaluation of patients attending A&E with seizures

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Background and aims: Epilepsy is the most common, chronic neurological condition with a prevalence of 0.5% and an incidence of 3 to 5%. Despite anticonvulsant use, there are approximately 60,000 A&E attendances and 40,000 hospital admissions in the UK per year. Over EU 15 billion is spent annually on treatment in Europe.

Aims: To clinically characterise patients with seizures attending A&E and audit their management and follow-up with respect to NICE guidance and local hospital guidelines.

Methods: Using A&E triage records a list of all patients attending St George's Hospital in London with a seizure within a six month period was derived. By referring to clinical records, management in A&E and beyond was audited.

Results: 382 adults with seizures were identified. 33% attended A&E in the previous 12 months with a seizure. Of those with epilepsy (n=187), 9% were on no drug. In all seizure cases, documentation was often incomplete and a collateral history was only obtained in 44% cases. 44% of patients were admitted, and of these, 15% were unnecessary according to criteria outlined by Iyer et al. Only 8% were asked if they were a driver, alcohol intake was not documented in 44% and illicit drug use was absent in 57%. Only 37% were referred to a neurologist or epilepsy specialist.

Conclusion: As a third of the patients attended A&E in the previous 12 months, it is clear that thorough history taking to determine factors provoking seizures and better management in the community is necessary to prevent recurrence of seizures.

Disclosure: Nothing to disclose

EPR1039

MMP-2 and disease activity in epilepsy patients

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Background and aims: Various blood-brain barrier (BBB) markers are elevated in epilepsy. In this study we examined levels of MMP-2 and TIMP-2, which are important proteins involved in BBB activation and restoration, in patients with epilepsy after generalized tonic-clonic seizures (TCS) and in the interictal period.

Methods: Serum levels of MMP-2 and TIMP-2 were examined in two groups: I - 50 patients during one hour after TCS; and II - 62 epilepsy patients, seizure-free for a minimum of 7 days, and measured by ELISA. Seizure count for group II was performed for one year before and one month after blood collection. Levels of MMP-2 and TIMP-2 were also examined in control group matched for sex and age, with no history of epilepsy.

Results: Serum levels of MMP-2 were higher in epilepsy patients both in the group after TCS and in the stable group (group I: 216.4 ng/ml±75.3 vs. 186.6±8.7 ng/ml; group II: 374.3 ng/ml±12.5 vs. 193.7±8.5 ng/ml). We also observed a tendency for higher levels of serum TIMP-2 in both groups of epilepsy patients in comparison to controls. Interestingly, in the examined groups of patients we found higher levels of BBB markers in patients in the interictal period.

Conclusion: We observed that epilepsy patients have increased markers of BBB activation both after seizures, suggesting abrupt changes in BBB, and in the interictal period, indicating persistence of neuroinflammation. Due to a noticeable dispersion of obtained data it is necessary to conduct further research.

Disclosure: National Science Centre grant 2012/07/N/NZ4/01969

EPR1040

Transcranial brain parenchyma sonography of basal ganglia in the evaluation of the clinical course of juvenile myoclonic epilepsy

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Background and aims: Abnormal neural networks in the thalamus, limbic areas, brainstem and cerebellum seem to be associated with juvenile myoclonic epilepsy (JME). Cognitive and behavioral difficulties in JME are suggested to relate with alterations in basal ganglia. These structures are implicated in the modulation of epileptic spike-wave discharges generalization in patients with idiopathic generalized epilepsy.

Aim: To evaluate the influence and potential clinical significance of abnormal findings in subcortical structures associated with JME.

Methods: This retrospective study included 40 JME patients who were followed-up from January 1985 to December 2016 at the Clinic of Neurology and Psychiatry for Children and Youth in Belgrade, and received transcranial parenchymal sonography (TPS). Relation of clinical parameters (seizure control, cognitive functioning, behavior) with TPS results was assessed.

Results: Duration of remission for at least one year was achieved in 71% of patients (mean duration of remission 8.9 years), while 10% had pseudo-resistant epilepsy. Dysexecutive syndrome and psychiatric comorbidities were noted in 30.4% and 25% of patients, respectively. Pathologically hyperechogenic substantia nigra (SN) and red nucleus (RN) on TPS were found in 35% and 32.5% of patients, respectively. There was no statistically significant influence of seizure control on TPS findings. However, compared to the control group, hyperechogenicity of the right-sided SN and both RN was significantly more common in JME patients.

Conclusion: To our knowledge, this is the first study to demonstrate structural changes of SN and RN in JME. Our results suggest additional non-lesional abnormalities of BG and midbrain structures in JME patients.

Disclosure: Nothing to disclose

Headache and pain 1

EPR1041

Salivary inflammatory markers in tension type headache and migraine sufferers

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Background and aims: No research has been performed for the role of salivary inflammatory markers in Tension type headache(TTH) and migraine. We studied whether headache attacks are associated with changes in CRP, IL-1β and IL-6 in saliva. We, also investigated whether these markers in TTH and migraine could be influenced by psychiatric comorbidities such as depression and anxiety.

Methods: This is a cross-sectional study of 19 migraine and 19 TTH patients that attended our outpatient headache clinic and 15 healthy controls between January-March 2016. We accessed theirs demographics, headache features, anxiety and depression as measured by the Hamilton Anxiety Rating Scale (HAM-A) and the Beck Depression Inventory (BDI). Salivary IL-6, IL-1β and CRP were collected in distinct time points as A- headache free period, B – during headache, C- one day after headache attack, and measured by ELISA kits

Results: IL-1β significantly decreased from point A to B, while increased from B to C in headache groups. They had greater IL-1β levels at time point B as compared with controls. No significant differences were found in time variation of CRP, IL-1β and IL-6 levels between migraine and TTH (p>0.05). CRP measured at point B was negatively correlated with HAM-A, and BDI scores. IL-6 was negatively correlated with BDI scores at point B (r=0.52, P<0.001)

Conclusion: For the first time, it seems to exist a similar variation of salivary inflammatory cytokines in headache groups. CRP and IL-6 were correlated with higher anxiety and depression scores during headache attack in headache groups.

Disclosure: Nothing to disclose

EPR1042

Retinal fiber layer and choroid thickness are reduced in cluster headache: results from an Optical Coherence Tomography study

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Background and aims: Cluster headache (CH) is the most frequent trigemino-autonomic headache with severe unilateral pain probably due to an increased venous load in the inflamed cavernous sinus.We aimed to evaluate structural abnormalities in the retina of episodic CH patients using Optical Coherence Tomography (OCT).

Methods: This observational and cross-sectional study screened CH patients according to the International Classification of Headache Disorders, referring to the Headache Centre of the University of Catania in the period between 1st September 2016 and 30th April 2017. We also recruited 23 healthy-controls. CH patients previously treated with O2 therapy were excluded. For right (RE) and left eye (LE) we studied the mean retinal nerve fiber layer (RNFL) thickness, single quadrants analysis and choroid thickness (CT).

Results: Out of 42 CH patients, a total of 19 patients diagnosed as CH were enrolled. We found that average RNFL and inferior sector were thinner in CH compared to controls (90.1±7.4 vs 99.3±4.5μm, p<0.01 RE, 90.7±6.8 vs 100.2±6.5μm, p<0.01 LE, 118.5±7.9 vs 127.2±15.1μm, p<0.01 RE, 117.3±8.6 vs 126.3±12.3μm, p<0.01 LE, respectively). Moreover, CH patients showed a significant reduction in CT compared to controls (270.3±5.9 vs 333.2±3.1 μm, p<0.01 RE, 265.8±7.1 vs 334.5±4.1 μm, p<0.01 LE). The eye of the headache side presented thinner inferior sector (114.5±6.8 vs 122.5±9.0μm, p<0.01) and CT (258.6±4.5 vs 282.0±3.9μm, p<0.01) compared to the non-affected side.

Conclusion: We confirmed that retinal profile is affected in CH; in particular, the involvement of CT, especially in the affected side, could be explained by vascular changes of retinal vessel during CH attacks.

Disclosure: Nothing to disclose

EPR1043

Phase-3 safety data from studies comparing galcanezumab and placebo in patients with episodic and chronic migraine

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Background and aims: To evaluate the safety and tolerability of galcanezumab compared with placebo each given monthly (subcutaneous injection) for up to six months for prevention of migraine.

Methods: Data were integrated from three double-blind clinical studies (EVOLVE-1=NCT02614183; EVOLVE-2=NCT02614196; REGAIN=NCT02614261); two galcanezumab dose-groups (120- and 240mg) were pooled. Adverse events (AEs) that were treatment-emergent (TEAEs), discontinuation due to AEs (DCAEs), and serious AEs (SAEs) were analysed. Laboratory results, vital signs, and ECG results were also assessed.

Results: A total of 1,435 patients were treated with galcanezumab and 1,451 with placebo. TEAEs occurring in 1.5% or more of galcanezumab-treated patients, more frequently than among placebo-treated patients, and significantly different between galcanezumab and placebo included nasopharyngitis, injection site reaction, injection site erythema, injection site pruritus, and constipation. The proportion of DCAEs among galcanezumab-treated patients was low, and the proportion of patients who discontinued due to an injection-site related AE was less than 0.5%. None of the TEAEs related to injection site were reported as an SAE, and the majority of patients reported the events as mild or moderate in severity. Fewer than 2.0% of galcanezumab-treated patients reported an SAE. There were no clinically meaningful differences between galcanezumab and placebo in laboratory analytes, vital signs, or ECGs.

Conclusion: Galcanezumab (120- and 240-mg monthly) demonstrated a favorable safety and tolerability profile for the prevention of episodic and chronic migraine.

Disclosure: Sponsored by Eli Lilly and Company.

EPR1044

Efficacy of galcanezumab in patients who failed to respond to preventives previously: results from EVOLVE-1, EVOLVE-2 and REGAIN studies

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Background and aims: Galcanezumab (GMB) is a humanized monoclonal antibody against calcitonin gene-related peptide under development for prevention of migraine. Objective of this subgroup analysis of three Phase 3 studies of galcanezumab was to assess if differential treatment effects exist in patients who failed ≥2 previous preventives versus who had not.

Methods: EVOLVE-1 (NCT02614183), EVOLVE-2 (NCT02614196), and REGAIN (NCT02614261) were randomized, double-blind, placebo-controlled studies in patients with episodic (EVOLVE-1/2) or chronic (REGAIN) migraine. Patients were randomized 2:1:1 to receive placebo/GMB_120mg/GMB_240mg during double-blind treatment period lasting 6 (EVOLVE-1/2) or 3 (REGAIN) months. Subgroup analysis was conducted for change from baseline in number of monthly migraine headache days (MHD) and ≥50% response (reduction in number of MHD) for patients who failed ≥2 prior preventives (yes/no). Subgroup-by-treatment interactions were calculated using linear or generalised linear mixed models.

Results: In EVOLVE studies and REGAIN study, GMB_120mg/240mg statistically significantly improved (p<0.001) overall mean reduction of monthly MHD versus placebo in both subgroups (Table 1). Significant treatment-by-subgroup interactions were seen for GMB_240mg (EVOLVE studies) and GMB_120mg (REGAIN) suggesting better efficacy versus placebo for these doses in patients who failed prior preventives. Mean percentage of galcanezumab-treated patients with ≥50% response were significantly higher versus placebo for both subgroups.

Table 1. Overall change from baseline in number of monthly migraine headache days in patients with migraine who failed ≥2 previous preventives and who did not. Results are least square mean change from baseline (standard error) from integrated analysis of EVOLVE-1 and EVOLVE-2 studies, and from REGAIN study.

		Placebo	GMB_120mg	GMB_240mg
EVOLVE Studies (integrated set)	Failed ≥2 previous preventives	N=85 -0.81 (0.61)	N=43 -3.45 (0.73)	N=44 -3.85 (0.77)
	Did not fail ≥2 previous preventives	N=790 -2.68 (0.17)	N=393 -4.61 (0.20)	N=384 -4.36 (0.21)
REGAIN study	Failed ≥2 previous preventives	N=161 -1.44 (0.62)	N=66 -5.91 (0.79)	N=96 -3.30 (0.71)
	Did not fail ≥2 previous preventives	N=377 -3.69 (0.43)	N=207 -4.82 (0.48)	N=178 -5.77 (0.53)

Table 1

Conclusion: GMB_120mg/240mg is efficacious compared with placebo in reducing monthly MHDs in both patients who failed and did not fail ≥2 prior preventives. Treatment-by-subgroup interactions may be driven by lower placebo response in patients who failed preventives previously as magnitude of change for GMB-treated patients were similar in both subgroups.

Disclosure: Supported by Eli Lilly and Company.

EPR1045

Migraine with visual aura associated with thicker visual cortex

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Background and aims: Until recent years it was believed that migraine with aura (MA) was a disorder with no impact on brain structure. However, recent MRI studies have reported increased thickness of visual and somatosensory cortex in patients with MA, suggesting that such structural alterations were either due to increased neuronal density or result of multiple episodes of cortical spreading depression as part of aura attacks. Subsequent studies have yielded conflicting results, possibly due to methodological reasons, e.g., small number of subjects.

Methods: We recruited women aged 30-60 years from the nationwide Danish Twin Registry. Brain MRI of women with MA (N=166), their co-twins (N=30), and unrelated migraine-free twins (N=137) were performed at a single centre and assessed for cortical thickness in predefined cortical areas (V1, V2, V3A, MT, somatosensory cortex (SSC)), blinded to headache diagnoses. The difference in cortical thickness between patients and controls adjusted for age, and other potential confounders was assessed. Comparisons of twin pairs discordant for MA were also performed.

Results: Compared with controls, patients had thicker cortex in areas V2 (0.032 mm), V3A (0.037 mm), while differences in the remaining areas examined were not statistically significant. We found no association between the regions of interest and active migraine, or number of lifetime aura attacks. MA discordant twin pairs (n=30) only differed in mean thickness of V2 (0.039 mm).

Conclusion: Women with MA have a thicker cortex corresponding to visual areas. Our results indicate this may be an inherent trait rather than a result of repeated aura attacks.

Disclosure: Nothing to disclose

EPR1046

Genetic variants in KCNK18 gene in migraine patients with positive family history of this disease

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Background and aims: Migraine is common neurological disorder divided into two main clinical subtypes: migraine with aura (MA) and migraine without aura (MO). Migraine is multifactorial disease with genetic component. One of candidate gene in families with migraine is KCNK18 encoding TRESK channel. Mutation in KCNK18, leading to the loss of TRESK function, was found in a multigenerational family with MA. Genetic changes in KCNK18 may result in hyperexcitability of trigeminal nerve neurons and an increase in the susceptibility of migraine headache.

The aim of the study was to screen KCNK18 gene for polymorphisms and mutations in migraine patients with positive family history of this disease.

Methods: The study included 90 migraine patients (MA:39, MO:51) and 90 controls. Mean age of participants was 36±13 years. The HRMA and sequencing were used for genotyping.

Results: We identified two rare polymorphisms: c.28A>G, c.691T>C and mutation c.328T>C of KCNK18. The c.28A>G polymorphism was as common in migraine group as in controls and occurs both in MA and MO. c.691T>C was found in one family suffering from MO. The c.328T>C mutation, leading to loss of TRESK function, was found in one family with MO. Interestingly, migraine was not present in all individuals carrying the mutation, thus it suggest that other factors, such as female sex hormones may influence the migraine manifestation.

Conclusion: It seems that both polymorphisms and mutations in KCNK18 gene may be associated with MO. The overexpression of TRESK channels may be a potential target for the development of new migraine therapy.

Disclosure: Nothing to disclose

EPR1047

Idiopathic intracranial hypertension without papilledema (IIHWOP) in chronic refractory headache

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Background and aims: To determine the prevalence of Idiopathic intracranial hypertension without papilledema (IIHWOP) testing revised diagnostic criteria by Friedman in refractory chronic headache (CH) patients.

Methods: This is a prospective observational study. Each patient underwent ophthalmologic evaluation and Optical Coherence Tomography; brain magnetic resonance venography (MRV) and a lumbar puncture (LP) with opening pressure (OP) measurement. CSF withdrawal was performed in patients with CSF OP>200 mmH2O. IIHWOP was defined according Friedman's diagnostic criteria. Effect of CSF withdrawal was evaluated clinically in a 6 month follow-up and with a MRV study at 1 month.

Results: Forty-five consecutive patients were enrolled. Five were excluded due to protocol violations. Analyses were conducted in 40 patients (32 F, 8 M; mean age 49.4±10.8). None had papilledema. Nine patients (22.5%) had OP greater than 200mmH2O, two of them above 250 mmH2O. Two (5%) had neuroimaging findings suggestive of elevated intracranial pressure. One of them (2.5%) met the newly proposed diagnostic criteria by Friedman for IIHWOP. After CSF withdrawal seven (77.8%) of the nine patients improved. No changes in neuroimaging findings were found.

Conclusion: We found a low prevalence (2.5%) of IIHWOP in refractory CH patients according actual diagnostic criteria. In agreement to Friedman's criteria, our result confirm that diagnosis of IIHWOP should be based on CSF OP and the combination of neuroradiological findings. However, where to set the CSF OP upper limit in IIHWOP needs further field testing. Although IIHWOP is a rare clinical condition, it should be considered and treated in refractory CH patients.

Disclosure: Nothing to disclose

EPR1048

Abnormal pattern of intracortical facilitation in migraine without aura. Preliminary results of a paired-pulse TMS study.

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Background and aims: Paired-pulse TMS paradigms can be used to test connectivity within the primary motor cortex in migraine sufferers. Aim of the present study was to provide additional information on short intracortical inhibition (SICI), long intracortical inhibition (LICI) and intracortical facilitation (ICF) using different intensities of the test stimulus (TS) in patients suffering from migraine without aura (MwoA).

Methods: We enrolled 16 patients suffering with episodic MwoA and 16 healthy subjects. Both patients and controls were randomly assigned to two groups: the first group underwent assessment of SICI and LICI, whilst in the second group we evaluated ICF. In each subject we assessed SICI, LICI and ICF by using three different suprathreshold intensities of the TS (intensities eliciting motor evoked potentials of 0.2, 1 and 4 mV). Interstimulus intervals (ISI) of 2 ms and 100 ms were used for testing SICI and LICI respectively, whilst ICF was carried out by using 10 ms ISI.

Results: When testing ICF, maximum increase in conditioned MEP amplitude was observed in migraineurs at the lower stimulation intensity of the TS. This intensity was indeed unable to induce significant facilitation in the healthy subjects, where maximum facilitation was observed at the higher stimulation intensities. No significant differences were observed between patients and healthy subjects as regards SICI and LICI.

Conclusion: Our results strengthen the notion of altered tuning of cortical excitability in migraine. In particular, we provide evidence of hyperresponsivity of the glutamatergic intracortical circuits that could be revealed only by using a low stimulation intensity.

Disclosure: Nothing to disclose

EPR1049

Abnormal peripheral and central visual processing in migraine

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Background and aims: Sound induced flash illusion (SIFI) is an illusory cross modal (audio-visual) phenomenon critically dependent upon excitability of visual cortex. A recent study with SIFI confirmed hyperexcitability of visual cortex in migraine; patients with migraine show abnormality of chromatic perception. Here we explored the relationship between peripheral chromatic and central visual dysfunction in patients with migraine

Methods: 15 migraine patients with aura (MWA) and 15 without aura (MWoA) were studied interictally and compared with 12 healthy controls
all subjects underwent the following examinations:
1. SIFI with flashes and beeps in different combinations to generate illusions of 'fission' (one flash with 2 beeps perceived as 2 flashes) or 'fusion' (2 flashes with one beep perceived as 1 flash); 2. colorimetric test to explore dysfunction in color perception. 3. Multifocal electroretinogram (mfERG) to evaluate the functional contribution of retinal receptor.

Results: MWA and MWoA patients showed significantly reduced SIFI of fission than controls (p<.01). 8 MWA and 9 MWoA patients presented dysfunction of color perception. They showed significantly more reduced SIFI with than those with no abnormality in chromatic perception (p<.05). No significant changes emerged in mfERG when comparing patients vs control; MWA vs MWoA, patients with and without chromatic perception dysfunctions.

Conclusion: results confirmed hyperexcitability of visual cortex in MWA and MWoA. Moreover, greater excitability levels are found in patients with chromatic perception abnormalities suggesting a potential pathophysiological relationship between peripheral and central visual dysfunction. However, results of nornal mfERG response seem to exclude direct dysfunctional involvement of visual receptors, making likely abnormalities at different retinal levels of the neural pathway (bipolar cells?).

Disclosure: Nothing to disclose

Motor neurone diseases 1

EPR1050

Imaging denervation in amyotrophic lateral sclerosis for future clinical trials: 12-month follow-up from a longitudinal cohort study

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Background and aims: A key area-of-need in motor neuron disease/amyotrophic lateral sclerosis (MND/ALS) research is a tool to objectively track disease progression over short timescales, to reduce duration and cost of clinical trials, and facilitate translation of promising novel therapeutics from laboratory to clinic. Previous studies have focused on the central nervous system. The aim of this study was to assess the utility of whole-body MRI to depict muscle denervation changes over 12 months in patients with ALS, and compare radiology to clinical and neurophysiological measures.

Methods: A prospective longitudinal observational cohort study was performed. Twenty-nine ALS patients and 22 age and sex-matched healthy controls were assessed with clinical measures, electrophysiological motor unit number index (MUNIX) and T2-weighted whole-body muscle magnetic resonance imaging (MRI), at first presentation to our clinic, and at 4 months. Patients were reassessed at 12 months. Between-group differences, associations and longitudinal changes were assessed using multivariable linear regression models, adjusted for age and gender.

Results: ALS patients had higher relative T2 signal and lower MUNIX than controls at baseline. Higher relative T2 signal was associated with greater weakness and lower MUNIX. Relative T2 signal in bilateral tibialis anterior increased over 4 months in ALS patients. Further changes in relative T2 signal in leg muscles, clinical scores and neurophysiology were evident at 12 months.

Conclusion: Whole-body muscle MRI offers a new approach to the objective assessment of denervation in ALS and detects progressive changes. Muscles inaccessible to conventional clinical and neurophysiological assessment may be investigated.

Disclosure: This research was supported by charitable funding from grant awards from the British Medical Association (Vera Down Grant) and Neurocare/Ryder-Briggs Trust, and supported by the NIHR Sheffield Biomedical Research Centre for Translational Neuroscience. The funding bodies had no role in the conduct of the study.

EPR1051

Development of ALS therapy using AMPA receptor RNA aptamers

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Background and aims: Failure of RNA editing at the GluA2 Q/R site resulting from downregulation of RNA editing enzyme adenosine deaminase acting on RNA 2 (ADAR2) occurs in motor neurons of sporadic Amyotrophic lateral sclerosis (ALS) patients. Expression of Q/R site-unedited GluA2 triggers a slow death of motor neurons via Ca2+-permeable AMPA receptor-mediated mechanism in conditional ADAR2 knockout mice (AR2 mice), a mechanistic model of ALS. Therefore, amelioration of exaggerated Ca2+ influx by antagonists of AMPA receptors is a potential therapeutic strategy for ALS. Here we report our test of a class of RNA aptamers acting as AMPA receptor RNA inhibitors for their safety and efficacy in AR2 mice.

Methods: After confirming the in vivo stability and local CNS delivery, we have tested the efficacy and safety of the aptamer by continuous cerebroventricular infusion for 2 weeks in AR2 mice. As a short-term measure, changes in the behavior and TDP-43 subcellular localization were examined.

Results: An RNA aptamer FN1040 has effectively normalized the TDP-43 mislocalization in the ADAR2-lacking motor neurons without causing sedative or other adverse effects in the AR2 mice. Because exaggerated Ca2+ influx exacerbates TDP-43 mislocalization, the normalization of subcellular localization of TDP-43 indicates the amelioration of Ca2+ influx through the abnormally Ca2+-permeable AMPA receptors that contain Q/R site-unedited GluA2 in the ADAR2-lacking motor neurons in the AR2 mice.

Conclusion: The efficacy and the lack of sedative effects of an RNA aptamer targeting AMPA receptors indicate a high potential of developing AMPA receptor aptamers into an ALS drug.

Disclosure: Nothing to disclose

EPR1052

Sensory disturbance and sphincter dysfunction in a slowly progressive motor neuron disease caused by a novel SOD1 mutation

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Background and aims: Superoxide dismutase 1 (SOD1) has been the first gene discovered as causative of amyotrophic lateral sclerosis (ALS), accounting for 20-25% of familial cases. The presence of misfolded SOD1 protein suggests a gain of function pathogenic mechanism. Patients carrying SOD1 mutation usually present lower limb onset and predominant lower motor neurons (LMN) involvement; sensory disturbance and bladder dysfunction were reported.

Methods: We describe the case of a 57-year-old patient who developed a slowly progressive gait disorder, preceded by sphincter incontinence with thermal and pain hyposensitivity. Spinal cord magnetic resonance imaging, lumbar puncture and spinal angiography were performed to rule out a spinal cord pathology.

Results: Neurophysiological exams showed neurogenic alterations in lower limbs and pathological central motor conduction, consistent with ALS. Genetic screening for ALS identified a novel point mutation in SOD1 gene at codon 122 (c.365A>G, pE122Q). Mutation Taster and Poly-Phen 2 algorithms predicted the mutation to be likely causative. The patient's brother recently reported left hand weakness and muscle atrophy and was found to carry the same SOD1 variant, increasing the suspicion of a new pathogenic mutation. Induced pluripotent stem cells (iPSCs) were generated from patient peripheral blood and differentiated towards motor neurons; the phenotypic characterization is ongoing. Furthermore, we are planning to study a model of Drosophila melanogaster harboring E122Q mutation in SOD1.

Conclusion: Bladder dysfunction, sensory impairment, slow progression and prevalent LMN involvement were previously reported in association with ALS with SOD1 gene mutations. E122Q mutation seems to represent a new missense mutation of SOD1 gene in ALS patients.

Disclosure: Nothing to disclose

EPR1053

Contribution of rare homozygous variants in ALS in a homogenous population

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Background and aims: Amyotrophic lateral sclerosis (ALS) has multiple etiologies, among them genetic. Disease-causing genes were discovered for over 60% of familial and over 10% of apparently sporadic cases.
The present study aims to detect rare homozygous variants in ALS in a relatively homogenous population.

Methods: We performed whole-exome-sequencing (WES) of 43 patients of North Africa Jewish origin. Filtering identified very rare recessive damaging variants in the gnomAD browser, in genes previously associated with ALS. Two variants were genotyped in an additional cohort of 70 unrelated patients and 400 controls of the same ethnic background.

Results: We identified 32 rare homozygous variants in genes associated with autophagy, mitochondria, RNA-binding and cytoskeleton. These include genes previously reported as upregulated (LZTS3) or downregulated (ARMC4, CFAP54, and MTHFSD) in ALS patients, and genes previously associated with other neurodegenerative or neuromuscular diseases: HTT, ATM, ZFYVE26 and MFN2. The homozygous variants in MFN2 and NEK1 were further evaluated. Their allele frequencies were 11.2 and 1.9 times higher in patients than in controls (p=0.031 and NS), with no homozygotes in controls. Seven ALS patients (16.3%) were homozygotes for more than one variant.

Conclusion: WES homozygosity analysis in our unique homogenous population identified rare homozygous variants, suggesting involvement of new genes and contribution of recessive alleles in ALS. We report for the first time that the MFN2 p.Arg663Cys mutation is associated with ALS, and suggest that the stress granules genes, MTHFSD and EIF4G3, are involved in ALS. Our data also support oligogenic inheritance in ALS.

Disclosure: Nothing to disclose

EPR1054

The HFE H63D (p.His63Asp) polymorphism is a modifier of ALS outcome in Italian and French patients with SOD1 mutations

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Background and aims: In a previous study we found that the HFE H63D polymorphism did not influence ALS phenotype and survival, with the possible exception of SOD1-positive patients. Since the small number of SOD1 patients in that series, we evaluated whether such polymorphism is a modifier of phenotype and survival in a larger series of SOD1-mutated patients.

Methods: 185 Italian and French SOD1-positive patients were included. Mutations were classified as severe or mild according to the median survival of the sample (7.1 years). The adherence to the Hardy-Weinberg equilibrium was tested for the HFE alleles. We used the Student's t-test or ANOVA for comparisons between means, the χ^2 test for the comparison between categorical variables, the Levene's test to confirm the equality of variances. Survival was calculated using the Kaplan-Meier modeling (differences were measured by the log-rank test). Multivariable analysis was performed with the Cox proportional hazards model (stepwise backward).

Results: The following allelic frequencies were found: CC 127 cases (68.6%), GC 53 cases (28.6%), and GG 5 cases (2.7%). They respected the Hardy-Weinberg equilibrium. The H63D polymorphism did not influenced age and site of onset. In univariate analysis, patients carrying the H63D polymorphism had a longer median tracheostomy-free survival (p=0.031). The presence of the H63D polymorphism remained significant in Cox multivariable analysis using as covariates age at onset, site of onset, positive family history, nation, and severity of mutations (hazard ratio, 0.52, 95% CI 0.32-0.85, p=0.01).

Conclusion: In SOD1 patients the HFE H63D polymorphism resulted significantly associated with a longer survival.

Disclosure: Nothing to disclose

EPR1055

Multiparametric unconventional MRI study in early stage of ALS disease

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Background and aims: Great efforts are made to define a typical structural pattern in Amyotrophic Lateral Sclerosis (ALS) by unconventional magnetic resonance imaging (MRI). Although there are various studies, no univocal pattern has been identified. The aim of this study was to evaluate the microstructural changes in a cohort of patients at the time of the diagnosis.

Methods: We enrolled 38 incidental ALS patients who underwent brain MRI at the time of the diagnosis (duration from onset: 13.31±10.08 months) and 19 healthy controls (HC) matched for sex and age. We evaluated Cortical thickness (CTh) in motor and extra motor areas using Freesurfer, Fractional Anisotropy (FA) of the cortico-spinal tracts using FSL, probabilistic tractography of whole brain using TBSS, volumes and shape of subcortical gray matter (SGM) using FIRST.

Results: CTh analysis shows reduction in both precentral gyri (dx p=0.025; sx p=0.026). FA of the cortico-spinal tracts was significantly increased than HC (dx p=0.007, sx p=0.020). Tractography identified white matter changes also in fornix and mid-body corpus callosum. No differences were found in SGM volumes, although shape analysis demonstrated alterations in both thalami, globi pallidi and putamina.
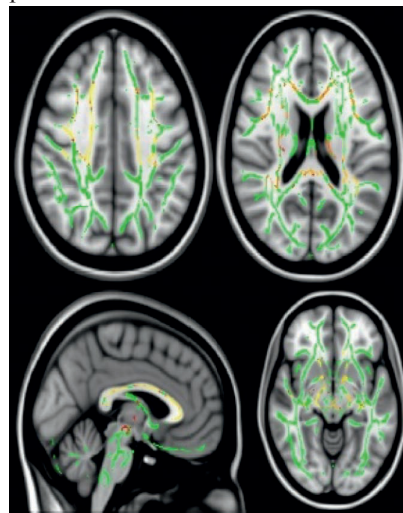
Probabilistic Tractography in ALS patients compared to Healty controls. Yellow, orange and red show white matter (FA) alterations (p<0.005)
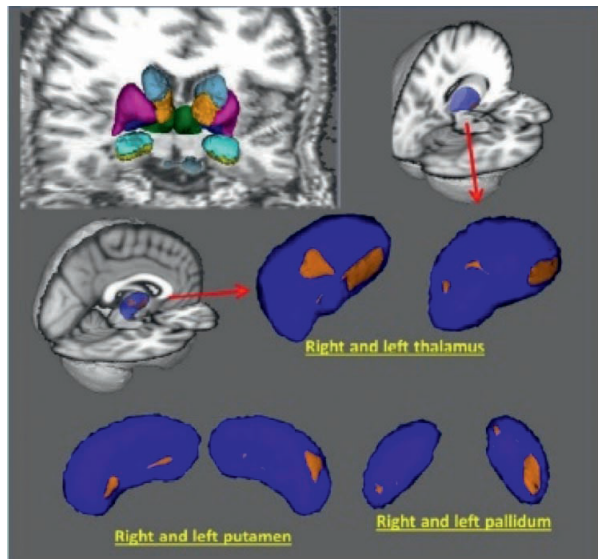
Three-dimensional vertexwise patterns of changes in basal ganglia. Orange colour indicates morphological modification beetween ALS patients and healty controls.

Conclusion: An involvement of the motor system has been confirmed in the early phases of ALS. As suggested by recent studies, we postulate that the dorsal and mid-body of the corpus callosum have a central role in the spread of the disease. SGM are affected by microstructural damage in the early stages.

Disclosure: Nothing to disclose

EPR1056

The relationship between motor phenotypes and cognitive impairment in ALS: a population-based study

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Background and aims: Amyotrophic Lateral Sclerosis (ALS) may present with different motor phenotypes. It is associated with cognitive impairment in half of cases, ranging from frank Frontotemporal Dementia (FTD) to mild deficits. We aimed at evaluating if motor phenotypes differ according to the frequency and severity of cognitive deficits.

Methods: 1,173 incident ALS cases from the Piemonte and Valle d'Aosta Register for ALS were eligible from 2009 to 2016. 63% of patients (N=751) underwent neuropsychological assessment and were enrolled. According to Strong et al (2009), patients were classified as ALS-FTD (19.5%), ALS with cognitive impairment (23.7%), ALS with behavioural impairment (4.5%), ALS with normal cognition (52.3%). Motor phenotype was classified as lower motor neuron prevalent (22.2%), upper motor neuron prevalent (14.7%), classic (33.4%), bulbar (29.7%). The association between cognitive impairment and motor phenotype was assessed by using stepwise backward logistic regression analysis, adjusted for sex, age at onset, education, hypertension, diabetes mellitus, marital status, and C9orf72 expansion.

Results: 54.6% of patients were male, with an average age at diagnosis of 67.0 (SD 10.3). Sixty-one patients carried the C9orf72 expansion (8.8%). Significant associations were detected only for bulbar patients, for whom the likelihood of developing any grade of cognitive impairment was 88% higher than that of non-bulbar patients (OR=1.88; 95% CI=1.30-2.70), while the risk of developing FTD was two-fold than that of non-bulbar patients (OR=2.17; 95% CI=1.40-3.37).

Conclusion: Bulbar patients showed a higher risk of developing cognitive impairment, especially FTD, compared to non-bulbar patients, that seemed relatively less vulnerable to cognitive decline.

Disclosure: Nothing to disclose

Movement disorders 1

EPR1058

Parkinsonism in higher level gait disorders: the role of amyloidopathy

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Background and aims: Parkinsonism is frequently described in older adults with higher level gait disorders (HLGD). However, the neuropathological substrate of parkinsonism and the clinical impact of this parkinsonism have been never studied in these patients. This cross-sectional study aims to compare the CSF total tau, Aβ1-42, and phosphorylated tau levels in older adults with HLGD with and without parkinsonism and to study the clinical impact of parkinsonism on gait parameters and cognitive performances.
Methods: CSF biomarkers (i.e., total tau, Aβ1-42, and phosphorylated tau) were measured by ELISA in 49 non-Parkinson's disease patients with HLGD (77.7±6.6 years; 32.7% women). Gait parameters were quantified with an optoelectronic system and cognitive performances with a comprehensive neuropsychological assessment. Parkinsonism was defined by presence of bradykinesia and at least one of the following signs among muscular rigidity, rest tremor or postural instability.
Results: Fourteen HLGD patients (28.6%) presented a parkinsonism. CSF Aβ1-42 level was decreased in HLGD patients with parkinsonism (β:-189.4; 95%CI [-352.3;-26.6]; p=0.024) even after adjusting for age, gender, comorbidities and total white matter burden; while CSF total tau and phosphorylated tau levels were similar between HLGD patients with and without parkinsonism. HLGD patients with parkinsonism presented decreased cognitive performances in attentional and executive domains but similar gait parameters than those without parkinsonism.
Conclusion: Parkinsonism in HLGD patients represents a clinical marker of amyloidopathy. This phenotype is clinically associated with impaired cognition, but similar quantitative gait parameters in comparison to HLGD patients without parkinsonism.

EPR1059

Variability of vestibular evoked myogenic potentials parameters in different periods of motor fluctuations in Parkinson's disease

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Background and aims: Research of vestibular evoked myogenic potentials (VEMP) can assess the condition of the sacculocervical reflex and objectify the abnormalities in vestibulospinal paths, the disturbances of which contribute greatly to the development of postural instability in PD. Change in severity of postural disorders can be observed in PD patients with motor fluctuation.
Aim: To investigate the VEMP parameters in correlation with the severity of postural instability and to estimate their variability within «on-off»-periods.
Methods: 47 PD patients with motor fluctuation and 30 healthy individuals aged 38 to 65 years were investigated. We evaluated the latent period (LP) P1 (p13) and N1 (n23) of VEMP (module EP25; company Interacoustics (Denmark)). The severity of postural instability was evaluated from 0 point (normal) to 4 (patient cannot stand without help).
Results: We discovered a significant increase in the LP P1 and N1 components in a group of patients with PD in comparison with the control group, it indicated a slowdown of the vestibular-spinal conducting. The correlation analysis revealed a strong correlation between the severity of postural disorders and LP P1, N1 components (RSpearman =0.70; p =0.0005). Statistically significant increase in the LP P1 and N1 components were observed within the «off»-period in comparison with «on»-period (p=0.01) However, variability VEMP parameters within «on-off»-periods was noted only in 20 patients.
Conclusion: Our data show that the study can evaluate the pathophysiological processes underlying postural disorders. Account the variability VEMP parameters with their normalization within «on»-period can help in deciding the feasibility of neurosurgical treatment.

EPR1060

Exposure to environmental factors and clinical presentation of Parkinson's Disease patients in Greece: data analysis of the Hellenic Biobank of Parkinson's Disease

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Background and aims: PD is a multi-factorial disorder with unknown etiology. Epidemiological data about PD in Greece are scant. The aims of this study are to investigate the association between environmental exposure and PD development and to describe clinical features of PD patients in Greece.

Methods: Our data derived from the Hellenic Biobank of Parkinson's Disease, consisting of blood samples, medical and lifestyle information about PD patients and controls during 2006-2017. Cases with A53T mutation in SNCA or mutations in GBA1 gene were excluded. OR and 95% CI were calculated for each factor.

Results: 575 PD patients and 340 controls were included. The mean onset age of PD was 62.87 (±12.311), onset age of dopaminergic treatment 63.71 (±11.990), disease duration 6.13 (±6.125) and dopaminergic treatment duration 5.30 (±5.920) years. The first symptom was tremor (54.4%), bradykinesia (25.6%), gait disturbances (7%), rigidity (4.9%), dystonia (1.7%) and postural impairment (0.9%). The side of onset was right (41.4%), left (32.9%) and bilateral (18.3%). Coffee consumption and pesticide exposure were not associated with PD development. Cigarette smoking was associated with lower risk of PD development in men (OR=0.526, 95% CI=0.324-0.853) and women (OR=0.462, 95% CI=0.296-0.724). Cigarette smoking was associated with lower risk of "normal"-onset PD (>50 years) (OR=0.693, 95% CI=0.512-0.939), but not with early-onset PD (≤50 years).

Conclusion: Cigarette smoking is associated with lower risk of "normal", but not early-onset PD in this Greek population, confirming most studies, but also suggesting that this environmental factor may affect PD development only in specific subgroups.

Disclosure: Nothing to disclose

EPR1061

Differences between familial and sporadic Parkinson's Disease in Greece: data analysis of the Hellenic Biobank of Parkinson's Disease

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Background and aims: The aim of this study is to compare sporadic and familial PD regarding their associations with clinical characteristics and environmental exposures.

Methods: Our data derived from the Hellenic Biobank of Parkinson's Disease, consisting of blood samples, clinical and lifestyle information of PD cases and controls during 2006-2017. Cases with A53T mutation in SNCA or mutations in GBA1 gene were excluded. OR and 95% CI were calculated for each factor.

Results: 160 patients with familial and 407 patients with sporadic PD were included. Early-onset of PD (≤50 years) was associated with family history of PD (OR=1.613 95% CI=1.019-2.555). Coffee consumption was associated with lower risk of PD only in the case of familial PD (OR=0.535, 95% CI=0.303-0.944). Psychotic manifestations and dyskinesias were more common in familial PD (OR=1.685, 95% CI=1.002-2.834 and OR=3.312, 95% CI=1.193-9.199 respectively). Gender, cigarette smoking, pesticide exposure, tremor, bradykinesia, rigidity, gait disturbances, autonomic dysfunction, dystonia, dementia, depression and motor fluctuations were not found to be associated with family history of PD.

Conclusion: Familial PD in this Greek cohort was associated with early-onset of PD, psychotic manifestations and dyskinesias. Coffee consumption was associated with lower risk of PD development only in the case of family history of PD, indicating that the interaction between coffee and specific genetic factors may be needed for the protective influence of coffee consumption on PD development.

Disclosure: Nothing to disclose

EPR1062

Validation of Ambroxol and UDCA treatments in cellular models of autosomal dominant Parkinson's disease

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Background and aims: The genetic findings in Parkinson's disease (PD) shed a light on the pathogenesis and possible therapeutic targets for the disease. In this view, we investigated the function of mitochondrial respiratory chain complexes and the glucocerebrosidase (GCase) activity in LRRK2 (Leucine-Rich Repeat Kinase 2) and GBA (Acid Beta-Glucocerebrosidase) mutated fibroblasts from PD patients. Thereafter, we assessed the efficacy of drugs to rescue the enzymatic activities.

Methods: We used a spectrophotometric assay to measure the activity of mitochondrial respiratory chain complexes in control fibroblasts and in LRRK2 or GBA mutated cells; we compared the results before and after treatment with UDCA (Ursodeoxycholic Acid). GCase activity was assessed before and after the treatment with Ambroxol. p62, LC3 and LAMP1 protein levels were assessed by Western Blot at baseline and after Ambroxol treatment.

Results: Complex III activity was slight reduced in LRRK2-mutated fibroblasts. UDCA did not induce a significant improvement in the mitochondrial function. The GCase activity was reduced in GBA mutated cells and in most lines with LRRK2 mutations. Ambroxol was effective in improving the levels of enzyme activity and determined an increase of all markers of autophagy (p62, LC3, LAMP1), whose pre-treatment levels were pathologically low.

Conclusion: Mitochondrial and GCase function play a relevant role in PD. Therefore, the search for drugs capable of acting on these targets is of primary importance. The in vitro administration of Ambroxol produced promising results and opens the possibility of its use in other cellular models and in clinical trials on GBA-PD and idiopathic-PD.

Disclosure: Nothing to disclose

EPR1063

Progression of Parkinson's disease: 2-year longitudinal study of clinical and MRI changes in patients at different stages of the disease

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Background and aims: To investigate motor and cognitive/behavioural changes, cortical thickness and white matter (WM) alterations over time in patients at different stages of Parkinson's disease (PD).

Methods: 83 early (Hoehn and Yahr [HY] 1-1.5) and 60 mild-to-severe (HY 2-4) PD patients underwent clinical motor and neuropsychological evaluations and MRI at study entry and every year for 2 years. 66 healthy subjects performed baseline assessments. Cortical thickness measures and diffusion tensor (DT) MRI metrics of WM tracts were evaluated.

Results: At baseline, motor disability was greater in mild-to-severe PD relative to early cases, while cognitive/behavioural functions were similar. Over 2 years, both groups showed a deterioration of motor skills, significantly in early PD, and a decline in depression, anxiety and apathy; mild-to-severe PD experienced greater cognitive decline. At baseline, mild-to-severe PD patients showed a more severe and widespread cortical thinning relative to controls and early PD patients; on the contrary, early PD patients showed a significant cortical thinning over time relative to mild-to-severe PD. DT MRI at baseline showed focal WM abnormalities in early PD patients relative to controls; mild-to-severe PD cases showed a more widespread damage than early PD involving also extramotor WM pathways. WM damage progressed over time in both groups of patients in both motor and extramotor circuits.

Conclusion: MRI may be a useful tool to monitor the progression of PD. Cortical thickness investigation is promising to evaluate the early phase of the disease, while the analysis of microstructural WM involvement may represent a potential biomarker for monitoring also advanced PD stages.

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EPR1064

Subthalamic nucleus high frequency and Levodopa treatment effects on effort-based decision-making in Parkinson's disease

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Background and aims: Idiopathic Parkinson's disease (PD) is a neurodegenerative disorder entailing several behavioural dysfunctions. It is now well admitted that Levodopa and, in more advanced PD, high frequency subthalamic deep brain stimulation (STN-DBS), influence motivated behaviours. The aim of the present work was to determine the influence of STN-DBS, Levodopa and the association of both treatments on effort- and reward-based decision-making.

Methods: We recruited 13 PD patients and 13 matched healthy controls (HC). Our experimental task involved taking a decision based on variable rewards (3 levels) and effort (12 levels). If the participants judged that the reward was worth realising the effort, they had to squeeze a dynamometer with the necessary force. All PD patients completed the task in 4 conditions: without treatment, with Levodopa or STN-DBS alone, with both Levodopa and STN-DBS. Using mixed model, we analysed the acceptance rate, decision time and applied force on the dynamometer.

Results: Our results showed a decrease of acceptance rate and applied force for PD patients without treatment in comparison to HC. Taken alone, Levodopa induced no changes in comparison to the condition without treatment. In contrast, STN-DBS, either with and without Levodopa, improved all measures, leading to an undistinguishable profile from HC.

Conclusion: From our results, we can conclude that Levodopa remains insufficient for cost-benefit computation. In contrast, STN-DBS modifies decision-making processes by normalizing all our measures. We can hypothesise that STN-DBS, but not Dopamine, helps to restore the integration of information from cortical territories.

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EPR1065

The effect of exenatide on specific non-motor symptoms in Parkinson's disease – a post-hoc analysis

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Background and aims: Exenatide is a GLP-1 receptor agonist that was recently studied for potential disease-modifying effects in an RCT in patients with Parkinson's disease, showing positive effects on motor severity which were sustained 12 weeks beyond the period of exenatide exposure.

Methods: This post-hoc analysis was conducted to explore the possible effects of exenatide compared to placebo on individual non-motor symptoms. Patients were assessed using the non-motor symptoms-scale (NMS), MDS-UPDRS Part 1, Montgomery–Asberg depression rating scale (MADRS), Mattis Dementia rating scale and the Parkinson's disease questionnaire (PDQ-39).

Results: Compared to placebo, patients treated with exenatide had greater numerical improvements in individual domains assessing mood/depression across all observer-rated outcome measures after 48 weeks including the "mood/apathy" domain of the NMSS, -3.3points (9% CI -6.2, -0.4), p=0.026; the "mood" score (Q1.3+Q1.4 of the MDS-UPDRS Part 1), -0.3points (95%CI -0.6, -0.1), p=0.034; and MADRS total score, -1.7points (95%CI -3.6, 0.2), p=0.071, in addition to improvement in the "emotional well-being" domain of the PDQ-39 of 5.7 points ((95%CI -11.3, -0.1), p=0.047).

Conclusion: There were consistent changes in mood that were of a magnitude that would be subjectively meaningful to patients and were not associated with changes in motor severity or other factors, suggesting exenatide may exert independent effects on mood dysfunction. These exploratory findings will contribute to the design of future trials that will confirm the extent of motor and non-motor symptom effects of exenatide in a larger cohort of patients.

Disclosure: The research was funded in part by the Michael J. Fox Foundation for Research and the Cure Parkinson's Trust

Movement disorders 2

EPR1066

Dyspnea: an underestimated non-motor symptom in Parkinson's disease?

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Background and aims: Among the non-motor symptoms (NMS) associated with Parkinson's disease (PD), dyspnea remains one of the less explored. The aim of our study was to determine the prevalence of dyspnea in a monocentric cohort of 153 non-demented PD patients (mean age: 63.9±7.4 years old; mean disease duration: 9.2±6.1 years), with no history of lung or heart diseases. Then, the clinical features of the dyspneic and non-dyspneic PD patients were assessed.

Methods: The following questions were asked to all the participants: "In the last month, did you suffer from breathlessness?" and "Did you experience difficulty to breath normally?" If the answer was positive for at least one among the two questions, dyspnea was confirmed. Patients with an abnormal cardiovascular and pulmonary clinical examination were excluded.

Results: In our cohort, the prevalence of dyspnea was 39.2% (31.5-47). Adjusted for disease duration, PD patients with dyspnea had a significant higher MDS-UPDRS I (p<0.001), II (p<0.001), III (p<0.001) and IV (p<0.001) scores, a significant lower MoCA (p<0.001) and a higher PDQ8 (p<0.001). Other NMS had a strong associations with dyspnea: cognitive impairment (OR, 7.5; 95% CI [3.9-14.6]), fatigue (OR 6.16; 95% CI [3.30;11.51]) and constipation problems (OR, 4.2; 95% CI [2.4-7.3]).

Conclusion: Dyspnea seems to be a frequent NMS in PD with an impact on autonomy and quality of life. It could also be an early axial manifestation of the disease. Further studies are needed to assess the potential correlation with objective alteration in lung volumes, respiratory muscles strength or response to hypoxia.

Disclosure: Nothing to disclose

EPR1067

Autosomal recessive Hereditary Spastic Paraparesis due to SPG 7 mutation – a case series

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Background and aims: Autosomal recessive hereditary spastic paraparesis is rare. SPG7 mutation accounts for 1.5-7% of all the HSP but it is the cause of undiagnosed ataxia in 18.6% in a recent case series. We present a case series of slowly progressive ataxia due to SPG 7 mutation.

Methods: We collected the details of 4 confirmed cases of HSP due to SPG7 mutations. We analysed their clinical presentation, family history, outcome of the radiological and genetic investigations.

Results: All patients had gradual onset slowly progressive spastic ataxia but family history of undiagnosed ataxia was present in one. External ophthalmoplegia, optic atrophy and peripheral neuropathy were also common. One had peripheral neuropathy.

80% of the patients showed some degree of cerebellar atrophy in Magnetic resonance imaging.

One had homozygous mutation in exon 11 of the SPG7 gene (c1529C>T pAla510Val). One of the heterozygous mutatnts showed a novel c1617delC ,p(Val540fs) frameshift mutation in exon 12 of the SPG 7 gene. . Since this mutation led to frameshift it is likely to be pathogenic though we could not study the full family to ascertain pathogenicity beyond doubt. One had compound heterozygous mutation (exon 12,14) of c1529C>T pAla510Val and c1672A>T p(Lys558). The last person had heterozygous c1529c>T,p(Ala510Val) mutation in exon 11 and the c1672A>T ,p(Lys 558) mutation in exon 13 of the SPG 7 gene

Conclusion: SPG7 mutation should be remembered as an important cause of undiagnosed ataxia especially where next generation sequencing is not widely avaialbale or affordable.

Disclosure: Nothing to disclose

EPR1068

Neurostructural alterations associated with Rapid Eye Movement Sleep Behavior Disorder in Parkinson's disease

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Background and aims: Rapid Eye Movement (REM) Sleep Behavior disorder (RBD) is a parasomnia observed in up to 60% of Parkinson's disease (PD) patients and associated with a more severe phenotype of this disease. The pathophysiology is partially elucidated. It is known that brainstem play a central role, but more and more evidence appear for a limbic involvement.

The aim of current study was to evaluate the volumetry of subcortical structures in PD patients and to compare results between PD patients with and without RBD.

Methods: Sixty-six participants were included: 22 PD withRBD (PD-RBD), 22 PD without RBD (PD-noRBD), 22 healthy control. RBD was diagnosed by videopolysomnographic recording according to the ICSD-3 criteria. Subjects with impulse control disorders, depression or apathy were excluded. Normalized brain structure volumes were measured on T1-weighted-MRI with volBrain software. The subcortical structures considered were the brainstem, the caudate, the putamen, the thalamus, the globus pallidus, the amygdala, the nucleus accumbens and the hippocampus.

Results: PD patients with RBD showed smaller volume than PD without RBD in the left nucleus accumbens (0.209 mm3 versus 0.233 mm3, p=0.036) and a tendency to be smaller in the left globus pallidus in PD patients with RBD compared to healthy control (0.823 mm3 versus 0.766 mm3, p=0.05).

Conclusion: There is a specific atrophy of the left nucleus accumbens in PD-RBD compared to PD-noRBD. This observation underlines the hypothesis of a more severe PD-RBD phenotype and supports the hypothesis of potential mesocorticolimbic involvement in the pathophysiology of RBD.

Disclosure: Neurodis Fondation

EPR1069

Perinatal insults and neurodevelopmental disorders may impact age of diagnosis of Huntington's disease

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Background and aims: The objectives of this study were to determine whether early-life factors, like perinatal insults or neurodevelopmental disorders, are associated with the age of diagnosis of Huntington's disease (HD).

Methods: We used data from 13,863 participants from REGISTRY and Enroll-HD, two large international multi-center observational studies. Disease-free survival analyses of mutation carriers with an HTT CAG repeat expansion size above 36 were computed through Kaplan-Meier estimates of median survival time until a diagnosis of HD. Between groups, comparisons were computed using a Cox proportional hazard survival model adjusted for the CAG-repeat expansion length. All tests were two-sided with a significance level of 0.05.

Results: Our results showed that insults in the perinatal period were associated with an earlier median age of diagnosis of 45.00 years (95%CI: 42.07-47.92) compared to 51.00 years (95%CI: 50.68-51.31) in the reference group, with a CAG-adjusted hazard ratio of 1.61 (95%CI: 1.26-2.06). Neurodevelopmental disorders were also associated with an earlier median age of diagnosis of 47.00 years (95%CI: 43.63-50.36) with a CAG-adjusted hazard ratio of 1.41 (95%CI: 1.15-1.73).

Conclusion: These results, derived from large observational datasets and using robust survival analysis methods, show that perinatal insults and neurodevelopmental disorders are associated with earlier ages of diagnosis of magnitudes similar to the effects of known genetic modifiers of HD. Given their clear temporal separation, these early events may be causative of earlier HD onset. Even with a survival analysis, this association does prove causation. Further research is needed on the basis of this interaction.

Disclosure: Nothing to disclose

EPR1070

Stay in motion with Parkinson's Disease – a 12-week rehabilitation program for People with Parkinson's Disease

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Background and aims: Many clinical studies have proven the benefits of physiotherapy on both motor and non-motor symptoms of Parkinson's patients. Different rehabilitation programs are being used, ranging from conventional physiotherapy with or without dual tasking, over training in a virtual reality setting to even dancing, tai chi and boxing.
Methods: We - a team of two physiotherapists, two occupational therapists, a rehabilitation specialist and a neurologist - started a 12-week, twice weekly training program designed for PD patients. During these 12 weeks, four sessions of occupational therapy and four educational moments were organized. Before and after the training course we evaluated motor (MDS-UPDRS-III, mini BESTest, 6 minute walk test, 10 meter walk test) and non-motor (PDQ-39, NMSS and BDI) symptoms.
Results: In this pilot study we included 9 patients with idiopathic Parkinson's disease of whom six were male. The median age was 67 years and a median disease duration was 4 years. A Hoehn and Yahr scale of 1 was the median for this group with a levodopa equivalent daily dose was 450 mg. We observed a positive trend in both motor and non-motor symptoms but due to the small sample size the differences did not reach statistical significance.
Conclusion: Many different rehabilitation techniques are being used to treat Parkinson's Disease. We present a pilot study with a multidisciplinary approach, which shows positive trend for both motor and non-motor symptoms. More studies with a larger sample size should be done to establish which rehabilitation regime is most desirable.
Disclosure: Nothing to disclose

EPR1071

Breakdown of Affective-Cognitive Network in Functional Dystonia

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Background and aims: To explore the role of affective-cognitive network (ACN) in two clinical phenotypes of functional dystonia (FD): fixed (FixFD) and mobile dystonia (MobFD).
Methods: Resting state (RS) fMRI was obtained from 40 FD patients (12 FixFD; 28 MobFD) and 43 healthy controls (14 young FixFD-age-matched [yHC] and 29 old MobFD-age-matched [oHC]). Functional connectivity (FC) was assessed using a seed-based approach with ventromedial prefrontal cortex (vmPFC), right temporoparietal junction (rTPJ), dorsal anterior cingulate cortex (dACC), bilateral medial dorsal nucleus (MDN) of thalamus and cognitive part of cerebellum (Cog-cerebellum) as seeds.
Results: Compared to HC, both FD groups showed enhanced FC between the right Cog-Cerebellum and the bilateral associative parietal cortex, with greater enhancement in FixFD compared with MobFD. Compared to oHC, MobFD showed reduced FC between vmPFC, left MDN and the bilateral anterior PFC; and enhanced FC between bilateral MDN and the bilateral associative parietal and visual cortices. Compared to yHC, FixFD showed reduced FC between vmPFC, right MDN, rTPJ, dACC and bilateral PFC and premotor cortex; and between dACC and right primary motor cortex and insula. Compared to MobFD, FixFD patients showed enhanced FC between dACC and primary and premotor cortices.
Conclusion: The two FD phenotypes showed similar ACN altered connectivity in PFC reflecting patient difficulties in cognitive control and motor inhibition. Sensorimotor connectivity was more disrupted in the FixFD group, with unique involvement of dACC and rTPJ, crucial for emotion regulation, awareness and sense of agency. These findings suggest that brain functional architecture could modulate the phenotypic expression of FD.
Disclosure: Study supported by the Ministry of Education and Science Republic of Serbia (Grant #175090).

EPR1072

The Faroese PD cohort: Clinical and epidemiological data from the longitudinal study

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Background and aims: The Faroe Islands, a geographic population isolate in the North Atlantic with ~50,000 inhabitants, is well suited for complex trait mapping given its isolation and reduced heterogeneity (genetic and environmental), excellent genealogic records dating back >400 years and large pedigrees. An elevated risk of PD and high exposure to environmental risk factors has previously been established. Data from three previous cross-sectional studies (1995, 2005 and 2011) have highlighted clusters of multi-incident pedigrees. Complex segregation analysis of PD on the islands, based on clinical diagnoses and genealogic data, is suggestive of a strong genetic contribution. However, so far known pathogenic mutations and rare coding variability in loci linked to PD have largely been excluded. The aim of the longitudinal study, commenced in 2015, is to 1) prospectively describe clinical phenotypes and quantify trait components associated with prodromal and manifest disease; 2) to assess the contribution of known (and perhaps novel) genes and environmental factors influencing susceptibility and/or progression of PD or trait components.

Methods: Recruitment to cohort via national hospital registries ongoing. Standardized neurologic evaluation (UK Brain Bank Criteria), UPDRS, Hoehn& Yahr staging, assessment of non-motor features, including standardized testing for autonomic failure, depression, hyposmia, and sleep disturbance.

Comparative exome analyses are currently ongoing.

Results: As of January 2018, the Faroese PD cohort for the longitudinal study consists of approx. 300 PD patients, 253 controls, and 156 unaffected relatives. The first clinical and epidemiological data from the study will be presented.

Conclusion: Conclusion will be presented at the congress.

Disclosure: The study is supported by grants from the Faroese Research Foundation and the Danish Parkinsons Disease Foundation.

EPR1073

Evaluation of non-motor fluctuations in Parkinson's disease by a visual analogue scale in Surgical Candidates

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Background and aims: In Parkinson disease (PD) despite the high impact of non-motor symptoms, evaluation of non-motor fluctuations (NMF) is not part of the presurgical evaluation for deep brain stimulation (DBS). Our aim was to evaluate the severity of non-motor symptoms in OFF and ON state compared to motor scores obtained in the same conditions.

Methods: Data from PD surgical candidates were collected in three centers. NMF were assessed using a visual analogue scale. The scale was made up of the 11 most frequent fluctuations that we have detected in previous studies (Witjas et al, 2002), each item being rated from 0 to 10. The scale was obtained in OFF and ON state during the presurgical evaluation as the UPDRS III, the QUIP and the PDQ 39.

Results: 77 patients (58 men; 19 women) were included. The mean score of the NMF in OFF state was 36.8 and improved by 49% after levodopa intake (19). The UPDRS III improved by 68% (from 31 to 10). No correlation was found between the non-motor and the motor scores in OFF state neither between the OFF non-motor score and the PDQ 39 or the QUIP. The degree of dopa sensitivity of the motor and the non-motor scores were not correlated.

Conclusion: NMF were present in all the patients in OFF state and improved dramatically after levodopa intake but less than the motor score. The study will be continued on a larger population of patients, and we will evaluate the effect of STN-DBS on the NMS.

Disclosure: Nothing to disclose

Movement disorders 3

EPR1074

DYT5a – phenotypic variability and anticipation in a Portuguese family

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Background and aims: Dopamine responsive dystonia (DYT5) is characterized by childhood onset dystonia and a sustained response to low doses of levodopa. The DYT5a variant results from a mutation in the GCH1 gene, with autosomal dominant transmission and greater penetrance in females. It is typically manifested by foot dystonia with diurnal fluctuation and later development of parkinsonism. We aim to characterise a three generations family with diagnosis of DYT5a.

Methods: Clinical analysis of 20 individuals from a Portuguese family with DYT5a.

Results: We present a family of three generations (n=20) where thirteen individuals present deletion in GCH1 gene, with greater penetrance in females (83.3% vs 28.6%). Seven are symptomatic. The matriarch (90 years old) started with classic parkinsonian syndrome in her 50's. Two women (B1,B2) in the second generation manifested disease also in 50's: painful feet and hand dystonia (B1), restless legs syndrome, parkinsonian signs and foot dystonia (B2). The men of second generation are asymptomatic carriers. Four elements in the third generation are symptomatic: a 19-year-old girl with severe foot dystonia and pyramidal signs since the age of 8; a 13-year-old girl with painful episodes of foot and hallux dystonia since the age of 4; a 40-year-old man with mild foot dystonia started at age 39; a 25-year-old man with paroxysmal hand dystonia started at age 24. All showed improvement with levodopa even after decades of treatment.

Conclusion: In this family with DYT5a is evident a variable phenotype among three-generations, a predominance of female involvement and a phenomenon of anticipation. To our knowledge this is the biggest family reported.

Disclosure: Nothing to disclose

EPR1075

WTX101 – A novel copper-protein-binding agent for Wilson Disease demonstrates long-term neurological improvement in an ongoing extension of a Phase-2 study (WTX101-201)

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Background and aims: WTX101 (bis-choline tetrathiomolybdate) is a first-in-class copper-protein-binding agent that reduces plasma non-ceruloplasmin bound copper (NCC) by forming tripartite complexes with albumin and increases biliary copper excretion. Here, we present preliminary 72-week data from the ongoing extension of a Phase-2 study in patients with Wilson Disease (WD).

Methods: All 22 patients who completed the 24-week open-label, single-arm study opted to continue once-daily WTX101 treatment in the extension. Assessments up to 72 weeks included disability and neurological status using the Unified Wilson Disease Rating Scale (UWDRS), copper control, hepatic status and safety.

Results: At study entry, 86% of patients had various degrees of WD-related neurological symptoms. From baseline to week 72, mean (SD) UWDRS disability score improved from 6.6 (10.0) to 1.2 (2.1) and neurological score from 22.8 (21.0) to 9.9 (10.7). UWDRS neurological score improved by ≥4 points in 12 patients, stabilised (±3 points) in 5 patients and worsened by ≥4 points in 2 patients . Mean (SD) NCC level corrected for copper in tripartite complexes was 3.6 (2.1) µM at baseline and decreased to 0.5 (0.7) µM at week 72. Liver function tests and Model for End-Stage Liver Disease (MELD) score improved or remained unchanged at week 72. Two discontinuations were considered unrelated to WTX101 treatment.

Conclusion: Once-daily WTX101 treatment improved neurological status and disability, and controlled free copper in patients with WD over 72 weeks. WTX101 was generally well tolerated and, together with its simplified dosing, WTX101 has the potential to address unmet needs in WD.

Disclosure: This study was funded by Wilson Therapeutics AB

EPR1076

Rationale and design of an open-label, randomised, 26-week study comparing levodopa-carbidopa intestinal gel to optimized medical treatment on non-motor symptoms in patients with advanced Parkinson's disease – INSIGHTS study

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Background and aims: To examine levodopa-carbidopa intestinal gel, LCIG (also known as carbidopa-levodopa enteral suspension in the US), on non-motor symptoms (NMS) compared with individually-optimised, conventional PD therapies, ie optimised medical treatment (OMT) in advanced Parkinson's disease (APD).

With conventional therapies, many APD patients experience inadequate motor control and complications. Despite decreased "off" time and increased "on" time without troublesome dyskinesia and reports of NMS improvement, no studies compare the effect of LCIG vs OMT on NMS, including sleep [ref1,2].

Methods: INSIGHTS is a phase-3b, randomised, open-label, multicenter, 26-week study comparing the effect of LCIG vs OMT on NMS in APD (NCT02549092). The study population includes levodopa-responsive APD patients with motor fluctuations no longer controlled by oral PD medications and who experience sleep disturbances as confirmed by a score >18 on the modified Parkinson's Disease Sleep Scale (PDSS-2). Approximately 88 patients will be enrolled and randomised in a 1:1 ratio to either LCIG or OMT. Primary endpoints include changes from baseline in the Non-Motor Symptoms Scale (NMSS) and the PDSS-2 total scores. Key secondary endpoints measure activities of daily living, quality of life, and safety assessments.

Results: At the current cut-off date, 37 patients have been randomised in the study. Nearly all patients are white and ≥60 years of age.

Conclusion: This is the first study comparing the effects of LCIG and OMT on NMS and sleep, and it will provide important information for physicians, patients, and caregivers when assessing the benefits of APD treatment.
1.Fernandez. Mov-Disord. 2015. 2.Antonini. Parkinsonism-Relat-Disord. 2015.

Disclosure: This work was funded by AbbVie Inc. AbbVie participated in the study design, research, data collection, analysis and interpretation of data, writing, reviewing, and approving the publication.

EPR1077

A long-term study on effectiveness of levodopa-carbidopa intestinal gel treatment in advanced Parkinson's disease patients

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Background and aims: To present the design and baseline characteristics from an ongoing global study assessing long-term effectiveness of levodopa-carbidopa intestinal gel, LCIG (also known as carbidopa-levodopa enteral suspension in the US), treatment in Advanced Parkinson's disease (APD) patients under routine clinical care.

LCIG, delivered via percutaneous gastrojejunostomy, has been shown to improve "Off" time, dyskinesia, non-motor symptoms (NMS), and quality of life (QoL) in APD patients. However, prospective, long-term data on LCIG effectiveness in routine clinical practice are limited.

Methods: This global, multi-center, single-arm, open-label observational 3-year study, examines APD patients treated with LCIG under routine clinical care (DUOGLOBE), and is the first observational study of LCIG conducted in the USA. Approximately 200 patients from over 50 global centers are being enrolled according to local product label. Primary efficacy outcome is the mean change in "Off" time. Secondary endpoints include dyskinesia duration/severity (UPDRS IV and the Unified Dyskinesia Rating Scale), Activities of Daily Living (UPDRS-II), motor function (UPDRS-III) and fluctuations (UPDRS item 39), QoL (8-item PD Questionnaire), and NMS, including sleep/daytime sleepiness assessed with the NMS Scale, PD Sleep Scale (PDSS-2) and the Epworth Sleepiness Scale. Caregiver burden will be measured and adverse events monitored.

Results: As of September 14, 2017, baseline demographics and disease characteristics were available for 121 patients (Table 1).

Table 1. Baseline patient demographics and disease characteristics

Demographics and Disease Characteristics	N = 121
Age, years, mean (SD)	70.6 (8.0)
Gender, female, n (%)	43 (35.5)
Race, white, n (%)	117 (96.7)
PD duration, years, mean (SD)[a]	11.2 (4.6)
Dyskinesia duration, hours, mean (SD)[a,b]	4.1 (3.51)
"Off" time, hours, mean (SD)[a,b]	5.8 (3.46)

[a] N=106; [b] Normalized to a 16-hour waking day

PD = Parkinson's disease

Conclusion: Long-term effectiveness data on LCIG in the treatment of APD patients under routine clinical care is limited. The current study is designed to provide a better understanding of the long-term effectiveness profile of LCIG for the treatment of APD.

Disclosure: AbbVie **Disclosure:** This work was funded by AbbVie Inc. AbbVie participated in the study design, research, data collection, analysis and interpretation of data, writing, reviewing, and approving the publication.

EPR1079

Radioactive copper incorporation in the diagnosis of Wilson's disease

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Background and aims: Wilson's disease (WD) is an inherited disorder of copper metabolism that leads to accumulation of copper in the liver and other tissues. Early diagnosis of WD enables the initiation of effective treatment, which is crucial for prognosis. However, routine diagnostic methods do not always provide a final diagnosis. The aim of the study was to evaluate radioactive copper incorporation in the diagnosis of WD.

Methods: We retrospectively analyzed data of patients diagnosed with WD based on radiocopper testing; later, the diagnosis was confirmed by DNA analysis. Incorporation of 64Cu was measured at 2, 24 and 48 h following intravenous injection. Diagnostic accuracy (area under the receiver operating characteristic curve [AUC]), sensitivity, specificity and predictive value were assessed for 24 h/2 h and 48 h/2 h 64Cu ratios and compared with serum measurements of ceruloplasmin, copper, non-ceruloplasmin-bound copper and urinary copper excretion.

Results: Patients having two pathogenic ATP7B mutations (n=74) had significantly lower 24 h/2 h and 48 h/2 h 64Cu ratios than heterozygote (having only one mutation) controls (n=21) (mean 0.14 and 0.12 vs 0.49 and 0.63, respectively; both P<.001). Of note, 24 h/2 h and 48 h/2 h 64Cu ratios had excellent diagnostic accuracy, with AUCs approaching 1, and only urinary copper excretion displayed similar positive features. Other copper metabolism tests had lower accuracy, specificity and sensitivity.

Conclusion: The radioactive copper test had excellent diagnostic accuracy to distinguish homozygote/compound heterozygote and heterozygote WD carriers and may be useful to monitor the efficacy of new therapies for WD.

Disclosure: Nothing to disclose

EPR1080

Motor and cognitive progression in GBA-related PD patients submitted to Deep Brain Stimulation

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Background and aims: Parkinson's disease (PD) patients carrying a glucocerebrosidase gene mutation (GBA-related PD) have been associated to worse cognitive decline after Deep Brain Stimulation (DBS), although the overall response to DBS is still poorly understood. We aimed to evaluate the motor and cognitive outcome after DBS in GBA-related PD.

Methods: Comparison of motor and cognitive outcomes between GBA-related PD and idiopathic PD (iPD) patients after subthalamic nucleus (STN)-DBS. Pre- and post-DBS MDS-UPDRS and MMSE were assessed. Post-DBS evaluations were performed in 4 conditions concerning ON/OFF medication and/or stimulation.

Results: 8 GBA-related PD and 10 iPD patients, with no significant differences in gender, age at disease onset (AO), time to DBS, pre-DBS levodopa response, follow-up post-DBS and pre- and post-DBS levodopa equivalent daily dose. Post-DBS MDS-UPDRS-III MedON/StimON was significantly different between groups (40.1±9.1 GBA-PD; 28.8±11.2 iPD; P=0.05). In GBA-related PD, post-DBS MDS-UPDRS-III MedON/StimON was worse than pre-DBS MDS-UPDRS-III MedON (40.1±9.1 vs 24.5±8; P=0.017). MMSE did not differ significantly between groups. 6/8 GBA-related PD patients were evaluated in the 4 post-DBS conditions. Stimulation significantly improved MDS-UPDRS-III (MedOFF/StimOFF 57.7±14.8 vs MedOFF/StimON 36.7±14.3; P=0.026), but the benefit with stimulation (post-DBS MDS-UPDRS-III MedOFF/StimOFF vs MedOFF/StimON) was worse compared to benefit from levodopa pre-DBS (pre-DBS MedOFF vs MedON)

Conclusion: GBA-related PD patients benefit from acute STN-DBS stimulation, although less than iPD patients. Motor symptoms of GBA-related PD seem to worsen 4.5 years after STN-DBS, whereas we found no cognitive decline. More data is warranted but available evidence do not support excluding GBA-related PD patients from DBS.

Disclosure: Nothing to disclose

EPR1081

Study protocol: Care of Late-Stage Parkinsonism (CLASP): A longitudinal cohort study

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Background and aims: Parkinson's disease (PD) is a chronic progressive disorder leading to increasing disability. While the symptoms and needs of patients in the early stages of their disease are well characterized, little information is available on patients in the late stage of the disease.

Methods: The Care of Late-Stage Parkinsonism (CLaSP) study is a longitudinal, multicenter, prospective cohort study to assess the needs and provision of care for patients with late stage Parkinsonism and their carers in six European countries (France, Germany, Netherlands, Portugal, Sweden, UK). In addition, it will compare the effectiveness of different health and social care systems. Patients with Parkinsonism with Hoehn and Yahr stage ≥IV in the "On"-state or Schwab and England stage 50% or less in the "On"-state are evaluated at baseline and three follow-up time-points. Standardised questionnaires and tests are applied for detailed clinical, neuropsychological, behavioural and health-economic assessments. A qualitative study explores the health care needs and experiences of patients and carers, and an interventional sub-study evaluates the impact of specialist recommendations on outcome using the UPDRS-ADL part.

Results: For the baseline evaluation of the cohort study, at least 70 patients will be recruited per country.

Conclusion: Through the combined assessment of a range of quantitative measures and qualitative assessments of patients with late stage parkinsonism, this study will provide for the first time in-depth and reliable information on the clinical presentation, needs and the health care provision in this population in Europe, and lay the foundation for improved outcomes in this population

Disclosure: This project was supported by a grant from JPND

MS and related disorders 1

EPR1083

Disease activity as assessed by the MAGNIMS score predicts long-term clinical disease activity (CDA)-free status and disability progression in patients treated with subcutaneous interferon beta-1a

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Background and aims: Post-hoc analysis of the MRI in MS (MAGNIMS) score at Year (Y)1 with long-term CDA-free status and disability progression in scIFNbeta-1a-treated patients using data from PRISMS.

Methods: In PRISMS-2, relapsing-remitting MS patients were randomised to scIFNbeta-1a 22 or 44mcg, or placebo, tiw for 2 years. Placebo patients were randomised to scIFNbeta-1a 22/44mcg at Y3. Patients were followed to Y15 post-randomisation (22mcg n=95; 44mcg n=95; placebo n=100). We classified scIFNbeta-1a patients by Y1 MAGNIMS score: 0, 1 or 2. CDA-free was defined as no relapses or disability progression (increase of 1 point from baseline in Expanded Disability Status Scale [EDSS] score, or 1.5 points in patients with EDSS 0). Median times (95% confidence interval [CI]) to first CDA event and EDSS progression from Y1, and retrospective hazard ratios (HR[95% CIs]) versus MAGNIMS score of 0, are presented.

Results: At Y1, 129, 108 and 130 scIFNbeta-1a-treated patients had a MAGNIMS score of 0, 1 and 2, respectively. Median time to CDA event was longer in patients with Y1 MAGNIMS score of 0 vs 1 and 2 (Figure 1). Median time to EDSS progression was longer in patients with Y1 MAGNIMS score of 0 (7.5 years) vs 1 (4.0 years) and 2 (2.5 years). Using MAGNIMS score of 0 as a reference, risk of EDSS progression was higher in patients with Y1 MAGNIMS scores of 1 and 2 (Table 1).
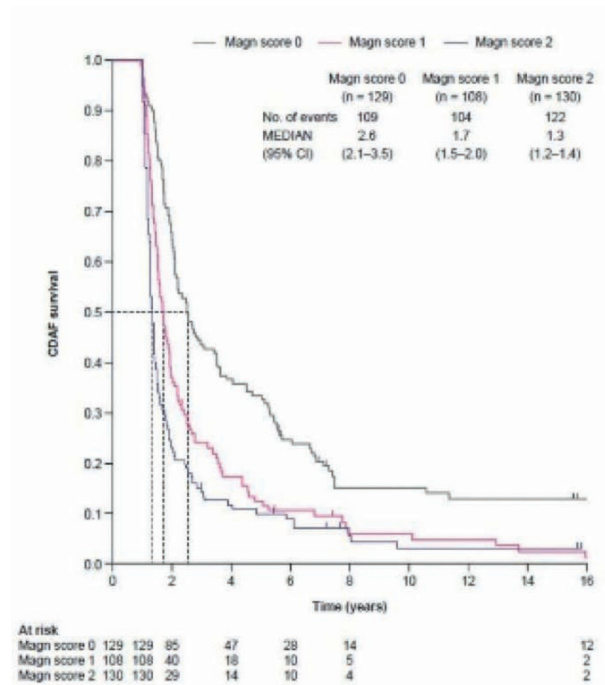
Figure 1: Median time to CDA event after Y1 by MAGNIMS score

	Hazard Ratio	Lower confidence limit	Upper confidence limit	P value
CDA				
MAGNIMS 1 vs 0	1.73	1.32	2.27	<0.0001
MAGNIMS 2 vs 0	2.43	1.87	3.17	<0.0001
EDSS progression				
MAGNIMS 1 vs 0	1.54	1.12	2.11	<0.0001
MAGNIMS 2 vs 0	2.14	1.58	2.89	<0.0001

Table 1: Hazard ratios for CDA and EDSS progression after Y1 by MAGNIMS score

Conclusion: In PRISMS, Y1 MAGNIMS score predicted risk of CDA event or disability progression in scIFNbeta-1a-treated patients.

Disclosure: Funded by Merck KGaA, Darmstadt, Germany

EPR1084

Infections seem to be more frequent before onset of pediatric multiple sclerosis: A Danish nationwide nested case-control study

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Background and aims: Infections are suspected environmental triggers for multiple sclerosis (MS). The relationship between the timing and cumulative number of childhood infections regarding pediatric MS risk is uninvestigated. The aim was to investigate whether childhood infections contribute to pediatric MS.

Methods: A nationwide nested case-control study with detailed MS case ascertainment including chart review was undertaken. For each MS case, we selected five control children using density sampling from the entire Danish population, matching controls to children with MS by sex and birthdate. We analyzed data with the cumulative number of childhood infections as exposure and MS as outcome. Hazard ratios (HR) including 95% confidence intervals (CI) were estimated using Cox regression.

Results: We identified 212 children with MS and 1,060 controls. Median age at MS onset was 15.3 years (range: 7.6–17.8 years); 72% were girls. Each infection during the preceding three years increased the hazard for MS by 11% (95% CI=1.01–1.22, p=0.04); having 5+ infections compared with 0-4 infections the preceding three years doubled the hazard for MS (HR 2.18; 95% CI=1.12–4.30, p=0.02).

Conclusion: Children with MS had more infections in the three years preceding MS clinical onset than age- and sex-matched control children; accordingly, immune response to infections may influence MS pathogenesis.

Disclosure: The study was supported by grants from the Danish MS Society, TEVA, Novartis and Genzyme.

EPR1085

Brain and spinal cord imaging features in neuromyelitis optica spectrum disorders

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Background and aims: Brain and cord MRI features of neuromyelitis optica spectrum disorder (NMOSD) are variable, with typical white matter (WM) lesions and atypical findings (short transverse myelitis, [STM]).
We evaluated the prevalence of typical/atypical hyperintense lesions of brain and spinal cord in a multicentric cohort of NMOSD patients and assessed differences of lesions distribution between NMOSD vs relapsing remitting multiple sclerosis (RRMS) patients.

Methods: Brain and spinal cord MRI scans were obtained from 116 NMOSD and 60 RRMS patients from 3 European centers. A qualitative (typical/atypical findings, cortical/temporal pole lesions and 2010 McDonald criteria fulfillment) and a quantitative (T2-lesion probability maps) analysis were performed.

Results: Cortical lesions did not occur and temporal pole involvement was infrequent (1%) in NMOSD vs RRMS patients (p<0.0001). 22% of NMOSD patients had typical encephalic lesions (18% brainstem periventricular/periacqueductal; 7% large hemispheric; 4% diencephalic; 7% cortico-spinal tract), 55% had long transverse myelitis (vs only one RRMS patient) and 28% had STM (vs 67.5% of RRMS, p<0.0001). 40% of NMOSD and all MS patients satisfied 2010 McDonald criteria for dissemination in space. In NMOSD, lesions were mostly located in periventricular, subcortical insular and periacqueductal regions. Compared to NMOSD, RRMS patients had higher occurrence of lesions in corpus callosum, periventricular zone and inferior longitudinal fasciculus, bilaterally.

Conclusion: Typical brain and cord lesions occur in a minority of NMOSD patients. A relatively high percentage of NMOSD patients satisfies 2010 McDonald criteria, prompting the development of better algorithms for the differential diagnosis of WM conditions.

Disclosure: Nothing to disclose

EPR1086

Correlations between amyloid-beta and white matter damage in multiple sclerosis: a 18F-florbetapir positron emission tomography study

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Background and aims: Positron emission tomography (PET) with amyloid-beta (Aβ) tracers is a promising tool to evaluate white matter (WM) damage in multiple sclerosis (MS). Recent findings showed a link between Aβ and myelination and suggested CSF Aβ levels as prognostic biomarker in MS. Aim of this study was to investigate 18F-florbetapir uptake in normal appearing (NA-) and damaged WM and to evaluate possible correlations with CSF Aβ levels.

Methods: Twelve patients with relapsing-remitting or progressive MS were divided according to clinical/radiological evidence of disease activity (n=8 active; n=4 not active). All patients underwent CSF analysis, brain MRI and 18F-florbetapir-PET. MRI and PET images were co-registered and WM-mean-standardised uptake values (WM-SUV) were calculated for each patient. We obtained brain volumes and calculated WM-lesion load (WM-LL) using SPM12.

Results: WM-SUV resulted lower in patients with active MS compared with not active MS (p=0.0081). Considering only active patients, CSF Aβ levels predicted WM-SUV (p=0.005) and were lower in patients with WM-SUV<1.0 compared to those with WM-SUV>1.0 (p=0.029). Notably, both WM-SUV and CSF Aβ levels correlated with NAWM volume (NAWMV; p=0.0047), but not with WM-LL.

Conclusion: We found a reduced 18F-florbetapir uptake in MS patients with active inflammation compared with not active patients. We discovered that NAWMV was a better predictor of WM-SUV compared to WM-LL. Interestingly, CSF Aβ levels correlated to NAWMV and were also found to be a predictor of WM-SUV. These findings suggest that the prognostic role of Aβ in MS may be directly linked to myelin microscopic damage.

Disclosure: Nothing to disclose

EPR1087

Risk of Becoming Wheelchair-Confined in Patients with Primary Progressive Multiple Sclerosis: Data from the ORATORIO Trial and a Long-Term Real-World Cohort from MSBase Registry

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Background and aims: Ocrelizumab is an approved treatment for relapsing or primary progressive multiple sclerosis (PPMS). We aimed to: (1) assess ocrelizumab's effect on time to wheelchair-confinement including the extended controlled period of ORATORIO (ORATORIO+ECP; NCT01194570); (2) understand long-term benefits by extrapolating results; (3) contextualise results using an MSBase registry cohort.

Methods: In ORATORIO+ECP, we: (1) analysed time to onset of 24-week-confirmed progression (24w-CP) to Expanded Disability Status Scale (EDSS)≥7.0; (2) conducted a Weibull extrapolation until patients reached median time to EDSS≥7.0. In MSBase, we analysed time to initial unconfirmed progression to EDSS≥7.0 and time to onset of 24w-CP to EDSS≥7.0, in PPMS patients with baseline EDSS 3.0–6.5, similarly to ORATORIO.

Results: In ORATORIO+ECP, ocrelizumab significantly reduced the risk of onset of 24w-CP to EDSS≥7.0: 30 (6.2%) of 488 ocrelizumab and 24 (9.8%) of 244 placebo patients reached the milestone (HR=0.54, 95% CI=0.31–0.92, p=0.022). Extrapolated median time to 24w-CP to EDSS≥7.0 was 12.1 years for placebo and 19.2 years for ocrelizumab (expected 7.1-year delay). In MSBase, 238 (30.7%) of 775 PPMS patients progressed to EDSS≥7.0 (median 12.4 years). Of these, 37 had no further visits, 35

regressed and 166 (69.7%) had 24w-CP to EDSS≥7.0 (median 12.0 years).

Conclusion: Ocrelizumab significantly delayed time to wheelchair-confinement in ORATORIO+ECP. The extrapolated median time to reach this disability milestone was similar to that in MSBase, suggesting ORATORIO patients, if left untreated, would progress similarly to a real-world population. The observed benefit with ocrelizumab potentially translates to a meaningful long-term benefit for PPMS patients.

Disclosure: Sponsored by F. Hoffmann-La Roche Ltd.

EPR1088

CADASIL and multiple sclerosis: an unexpected association

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Background and aims: Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) represents a major differential diagnosis with multiple sclerosis (MS), as they share demographic, clinical and, especially, MRI findings. We present the exceptional case of a patient with both disorders.

Methods: To describe a case report.

Results: A 40-year-old healthy female developed over three years two acute partial myleitis and an optic neuritis. No migraine history was reported. Based on a cervical and brain MRI (showing myelitis and an extensive leukopathy affecting the anterior temporal poles and juxtacortical and corpus callosum typical lesions of MS) (images 1,2 and 3) and the finding of oligoclonal bands (OCB) in CSF, the patient was diagnosed with remittent-recurrent MS and treatment with interferon beta 1-b was initiated. Due to a later discover of an Arg332Cys mutation of the NOTCH3 gene in his father and cousin and a subsequent positive genetic analysis in our patient, a MS diagnosis was doubted in favor of a CADASIL. However, the acute-onset of typical clinical syndromes and the findings of OCB and MRI lesions reinforced both diagnoses. During its course, new acute worsening episodes with partial response to corticosteroids overlapped, so the treatment was changed to glatiramer acetate and, later, teriflunomide, remaining relapse-free during 3 years but with a significant disability (EDSS 6.5 after 12 years of disease) and a progressive cognitive decline.
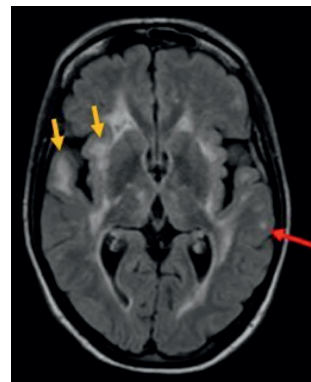
Image 1. Axial Cranial MRI. FLAIR. Anterior temporal lobe and diffuse extensive leukopathy suggestive of CADASIL (yellow arrow). Juxtacortical lesions (red arrow) typical in MS.
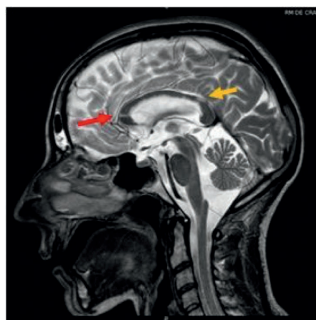
Image 2. Sagittal Cranial MRI. T2.   Red arrow: lesion affecting the entire perpendicular axis of the corpus callosum, typical of CADASIL. Yellow arrow: lesion of the ependymal caudal part of the corpus callosum, typical of MS.
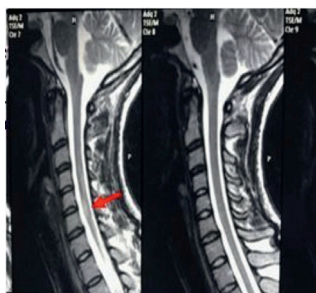
Image 3   Sagittal cervcial MRI. T2. Red arrow : typical MS myelitis.

Conclusion: To distinguish CADASIL and MS is a major differential diagnostic challenge. In an exceptional case with both diagnoses, an extreme difficulty is also observed in taking therapeutic decisions.

Disclosure: Nothing to disclose

EPR1089

Effect of Ocrelizumab on Relapse Rate, and Disability Progression and Improvement in Relapsing Multiple Sclerosis Patients in the Open-Label Extension of the Pooled OPERA Trials

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Background and aims: Efficacy and safety of ocrelizumab (OCR) in relapsing multiple sclerosis (RMS) were demonstrated in the 96-week double-blind control period of OPERA I/II (NCT01247324/NCT01412333). The efficacy of OCR therapy on clinical measures of disease activity, progression and improvement in the open-label extension (OLE) period was assessed.

Methods: At the start of the OLE, patients continued (OCR-OCR) or were switched from interferon-beta-1a (IFN-beta-1a) to OCR (IFN-OCR). Adjusted annualised relapse rate (ARR), time to onset of 24-week-confirmed disability progression (CDP) and time to onset of 24-week-confirmed disability improvement (CDI) were analysed.

Results: More than 89% of patients who entered the OLE period completed OLE Year 2. Among IFN-OCR patients, ARR decreased from 0.20 in the year pre-switch to 0.10 and 0.08 at Years 1 and 2 post-switch (p<0.001 Year 1 versus pre-switch; p=0.31 Year 1 versus Year 2). OCR-OCR continuers maintained the low ARR through the year pre-switch and the 2 years of the OLE (0.13, 0.11 and 0.08). OCR-OCR continuers versus IFN-OCR switchers had lower proportions of patients with CDP and higher proportions with CDI in the year pre-switch and Years 1 and 2 of the OLE (CDP: 7.7%/12.0%, 10.1%/15.6% and 13.8%/18.1%; p<0.05, all within visit comparisons. CDI: 16.8%/13.3%, 20.6%/16.6% and 23.7%/18.9%; p<0.1, all within visit comparisons).

Conclusion: Switching from IFN-beta-1a to ocrelizumab was associated with a consistent and robust reduction in ARR which was maintained through the OLE. The benefits of ocrelizumab on ARR, CDP and CDI as seen in the 2-year double-blind phase were maintained after 2 years in the OLE.

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EPR1090

Reduced expression of the IL7Ra signaling pathway contributes to T-cell pathogenesis in NMO.

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Background and aims: Identification of NMO-associated genes and their involvement in pathogenic pathways could provide a more comprehensive understanding of NMO etiology and the rationale for developing new drugs.

Objective: To characterize the abnormal immunological pathways involved in NMO pathogenesis.

Methods: An immunological gene expression array was performed on blood samples of NMO patients and HCs, followed by validation assays. The patient cohort included 65 NMO patients, 32 MS patients and 37 HCs.

Results: Two major clusters of genes were found associated with NMO: T-cell-associated genes and the TNF/NF-kB-signaling pathway. Analysis confirmed significantly reduced expression of IL7Ra in the peripheral blood of NMO patients (NMO376.4 vs HCs691.7, p=0.00005). IL7Ra expression was significantly lower in the NMO patients vs those in HCs and MS at both the mRNA and protein levels (1RQ;1.5RQ;2.09RQ p=0.01, 9ng/ml; 12.5ng/ml;12.2ng/ml NMO, HCs and MS). IL7Ra upstream transcription factors Foxo1 (0.67RQ vs 1.13RQ, p=0.003) and Ets1 (625.5 vs 851.25 counts, p=0.02), were also markedly reduced. In line with the essential role of IL7Ra in T cell survival, a significantly lower number of naïve T-cells (NMO19.4%; HCs32.9% p=0.05), and reduced T-cell survival signaling mediated by increased apoptosis was observed.

Conclusion: Two gene clusters were identified which distinguished NMO patients from HCs and revealed a major role for the IL7Ra pathway in the pathogenesis of NMO. This could provide a tool for better understanding of the disease and boost the development of new therapeutic approaches.

Disclosure: Nothing to disclose

MS and related disorders 2

EPR1091

Disease modifying treatment in paediatric-onset multiple sclerosis: A Danish nationwide population-based observational study

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Background and aims: Patients with paediatric-onset multiple sclerosis (MS) have a higher relapse rate and carries a worse prognosis than adult-onset MS. Early initiation of disease modifying treatment (DMT) may be beneficial for these children. The treatment pattern of DMT in paediatric-onset MS has never been described in Denmark. The aim of the study is to characterize the treatment of paediatric-onset MS since 1996, when DMT became available.

Methods: Data on DMT for paediatric-onset MS during 1996–2017 were sourced from the Danish Multiple Sclerosis Registry. All persons in the registry have a medical record validated MS diagnosis.

Results: We identified 195 children diagnosed with paediatric-onset (<18 years) MS during 1996–2017. Among these children, 123 (63%) received DMT before 18 years of age. The median age at treatment start was 16 years (range: 4–17 years), and the mean number of DMTs per child was 1.4 (initiated before 18 years of age). Interferons were the most common first-line treatment. Six children (11%) received natalizumab as first treatment. During follow-up, 107 (87%) children switched DMT or discontinued treatment. Fingolimod was prescribed more frequently than natalizumab as escalation therapy.

Conclusion: Taken together, 63% of children with MS were treated with DMT before the age of 18. Of this group, 87% switched DMT or discontinued treatment before 18 years of age. Future studies should focus on reasons for delay in initiating DMT, as well as causes of discontinuation and effectiveness of DMT in paediatric-onset MS.

Disclosure: Nothing to disclose

EPR1092

The role of metabolomics in the clinical parameters of Multiple Sclerosis: serotonin, tyrosine and metabolites

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Background and aims: Studying specific metabolomic pathways in Multiple Sclerosis (MS) patients can provide valuable clinical information to monitor the disease progression and form therapeutic protocols.

Methods: The authors attempted to quantify low molecular weight potential biomarkers for MS progress monitoring, by developing and validating a novel fast and sensitive analytical method in patients' serum.

Pre-treatment sera were obtained from 30 Relapse Remit MS patients (RRMS) during a clinical relapse, 20 patients with Clinical Isolated syndrome (CIS) and 20 healthy individuals age and gender matched. Disease duration, relapse rate (rr), number of Gadolinium enhanced lesions (GdE+), EDSS score and MSFC clinical subscales (Paced Auditory Serial Addition Test-PASAT, 9 Hole Peg Test-9HPT and 25 Feet test-25F) were recorded for each MS patient. High performance liquid chromatography coupled to tandem mass spectrometry (HPLC-MS/MS) was applied for the simultaneous detection and quantification of the following suspected biomarkers: serotonin, tyrosine and its metabolite epinephrine

Results: Serotonin was significantly elevated in the RRMS group ($F(2,67)=4.963$, $p=0.010$) when compared with the control group. In addition, there was a moderate positive partial correlation between PASAT score and serotonin where the lower the serotonin serum concentrations the lower the PASAT score. Moreover, serum tyrosine and epinephrine concentrations act as confounding variables and seem to strengthen the serotonin-PASAT positive correlation. (Par= (9)0.660, p=0.027)

Conclusion: Our results strengthen the already established knowledge on serotonin effects in Th2 diseases, provide useful data on the possible role of serotonin on the pathophysiology of MS and some indications on the synergistic effect of the tyrosine and its metabolites.

Disclosure: Nothing to disclose

EPR1093

CSF β-amyloid predicts prognosis in patients with multiple sclerosis

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Background and aims: The importance of neurodegeneration in multiple sclerosis (MS) has being increasingly recognised. Hence, there is a need to identify reliable biomarkers of the process. This study aimed to investigate the potential prognostic role of cerebrospinal fluid (CSF) amyloid beta 1-42 (Aβ) levels; to evaluate their possible association with white matter (WM) and grey matter (GM) damage; to determine a cut-off of the CSF Aβ levels, in order to classify patients into low and fast disability accumulation groups.

Methods: Seventy patients with a new diagnosis of RRMS were recruited and followed-up. All patients underwent clinical assessment, brain MRI and lumbar puncture. We used T2-weighted scans to quantify WM lesion loads and voxel based morphometry to investigate relative cortical atrophy. Aβ levels were determined in CSF samples from all patients. Between-group comparisons and multiple regression analyses have been performed.

Results: We found lower CSF Aβ levels in patients reporting a worse follow-up EDSS score (p<0.001). Multiple regression analysis confirmed CSF Aβ concentration as a predictor of patients' EDSS increase at follow-up (p<0.001). Patients with a relative reduction of GM at 1-year follow-up had lower CSF Aβ levels than those with a stable GM volume (p<0.05). We identified the cut-off of 813 pg/ml for CSF Aβ levels to identify the patients with worse prognosis.

Conclusion: This study suggests that CSF Aβ levels may be represent a crucial feature in MS, as it may be a predictive biomarker of progression. To this aim, we proposed a new cut-off.

Disclosure: Nothing to disclose

EPR1094

Plasmapheresis as rescue therapy of relapses in multiple sclerosis. A retrospective clinical practice survey.

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Background and aims: Multiple sclerosis (MS) relapse treatment is usually based on intravenous high-dose steroid therapy as first choice. However, in case of poor response or worsening of symptoms, plasmapheresis, a procedure able to remove inflammatory molecules from the blood circulation, should be considered as alternative to a second chance with steroids. The aim of the present study was to investigate the impact of plasmapheresis as relapse rescue therapy in a cohort of MS patients.

Methods: We retrospectively investigated all MS patients with at least one relapse treated at the apheresis centre of Parma in the past ten years (2007-2017), collecting clinical data and considering as primary outcome EDSS score one- and six-month post-apheresis respect to pre-apheresis score.

Results: We analysed a total of 43 relapses from 37 patients (67.6% female, mean age 42.1±11.9 years, mean EDSS on relapse 4.9±1.6, 75.7% with relapsing-remitting course, 95.3% previously treated with steroids). We found an improvement with complete or partial regression of EDSS worsening in 83.8% of patients. At multivariate analysis, improvement after plasmapheresis was associated with female gender (96% vs 58% in males, p=0.004) and with a shorter interval between relapse and apheresis (36.7 vs 70.8 days, p=0.02). Regarding safety, we recorded only six, mainly mild or moderate. adverse events during treatment (14%).

Conclusion: We confirmed that plasmapheresis is an effective and safe rescue therapy of MS relapses not adequately responding to high-dose steroids.

Disclosure: Nothing to disclose

EPR1095

Is an intrathecal kappa-chain oriented immune response typical of Multiple Sclerosis (MS)?

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Background and aims: Intrathecal immune responses in MS prompted to develop assays in cerebro-spinal fluid (CSF) including detection of oligoclonal bands and Link (for IgG) or K indexes (for free light chain kappa). This study explores the occurrence of kappa-chain oriented response as typical of MS.

Methods: 137 patients were enrolled: 45 MS, 57 non-inflammatory neurological disease (NID), 29 neurological inflammatory disease other than MS(ID). Free light chain kappa (KFLC), lambda (LFLC) and IgG were measured in serum and CSF by nephelometry

Results: Serum KFLC/LFLC ratio in MS was 0.98±0.51, comparable to NID (0.81±0.29) and ID (1.23±0.66) whereas in CSF was 12.7±21.7 in MS significantly (p<0.001) higher than NID (0.84±0.58) and ID (1.65±1.84). Serum IgG/KFLC ratio was 809±270 in MS, comparable to NID (687±237) and ID (778±369). The CSF IgG/KFLC ratio was 23±25 in MS, significantly lower (p<0.001) than NID (151±92) and ID (128±98). Serum IgG/LFLC ratio was 737±366 in MS, comparable to NID (618±235) and ID (708±536). The CSF IgG/LFLC ratio was 96±108 in CSF, comparable to NID (101±54) and ID (148±123). The K index (Ki, ratio between KFLC and albumin quotient) was markedly (p<0.0001) higher in MS (80±96) than in NID (4.6±9.0) and ID (13.1±25), the L index was only slightly higher (p=0.017) in MS (16.4±17.7) than in NID (3.7±4.04) but not different from ID.

Conclusion: The high KFLC/LFLC ratio and low IgG/KFLC ratio in CSF suggest that a KFLC- oriented immune response occurs intrathecally in MS thus confirming the powerful diagnostic value of Ki.

Disclosure: Nothing to disclose

EPR1096

Effect of long-term Teriflunomide Treatment on Lymphocyte Counts and Infection Rates in Pooled Data From TEMSO, TOWER, TOPIC, and TENERE Core and Extension Studies

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Background and aims: In TEMSO (NCT00134563) and TOWER (NCT00751881), teriflunomide treatment was associated with early lymphocyte count reductions, whereas mean counts remained within normal range. In long-term extensions (TEMSO, NCT00803049), lymphopenia was uncommon, no higher than Grade 2, and not associated with increased infections. We pooled data from 4 teriflunomide phase 3 core studies (TEMSO, TOWER, TOPIC [NCT00622700], TENERE [NCT00883337]) plus extensions to evaluate lymphocyte counts and infection rates during long-term treatment.

Methods: Patients with relapsing forms of MS or a first clinical event suggestive of MS were treated for up to 11 years. Analysis included all patients exposed to teriflunomide 14 mg. Lymphocyte counts were obtained over the course of each study. Lymphopenia (2 consecutive lymphocyte counts <LLN) was graded by CTCAE, v4.0.

Results: Cumulative duration of exposure to teriflunomide 14 mg was 6055 patient-years. In pooled core and extension studies (n=1895), few patients experienced Grade 1 (4.9%; n=92/1895) or 2 (2.2%; n=42/1895) lymphopenia. Infections were reported in 62.0% (57/92) and 54.8% (23/42) of patients with Grade 1 or 2 lymphopenia, respectively, vs 56.9% (1002/1761) without lymphopenia. Serious infections occurred in 3.3% (3/92) and 7.1% (3/42) of patients with Grade 1 or 2 lymphopenia, respectively, vs 3.7% (66/1761) without lymphopenia.

Conclusion: In this pooled analysis of phase 3 studies, long-term treatment with teriflunomide 14 mg was not associated with high-grade lymphopenia, and low-grade lymphopenia was uncommon. Infection rates were similar in patients with or without lymphopenia, consistent with an immunomodulatory mechanism of action of teriflunomide with limited impact on protective immunity.

Disclosure: Study supported by Sanofi.

EPR1097

Serum neurofilament light chain levels are increased at the onset of PML in natalizumab-treated MS patients

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Background and aims: The monoclonal antibody natalizumab is a highly effective treatment for patients with multiple sclerosis (MS). However, the drug is associated with increased risk of progressive multifocal leukoencephalopathy (PML), a severe infection of the CNS caused by the reactivation of JC virus. Huge efforts have been made to improve risk stratification algorithms and to facilitate early disease recognition, but no serum biomarker is currently available for the condition.

The aim of the study was to assess whether serum neurofilaments light chains (Nfl) are a reliable biomarker for the early recognition of PML during natalizumab treatment.

Methods: Patients were recruited from 2 European cohorts of 304 patients with MS. The cohort comprised 25 patients developing PML under natalizumab treatment, 128 natalizumab treated and 151 untreated MS patients. Serum NfL concentration was assessed using an ECL immunoassay.

Results: Natalizumab-treated patients had similar NFLs 16.1 pg/ml (IQR 13.4-22.2) to other MS patients. At the onset of PML, serum Nfl were 10-fold higher than in the pre PML condition and in other natalizumab treated patients (266.2 pg/ml (IQR 63.5-354.2), and they continued to grow till the onset of immune reconstitution inflammatory syndrome (1000 pg/ml (IQR 303.5 - 1218), p<0.0001).

Conclusion: If replicated in future studies, serum NfL may represent a reliable and easily accessible biomarker of early PML detection in natalizumab treated MS patients.

Disclosure: Nothing to disclose

EPR1098

Ongoing neurodegeneration in the cervical cord of patients with early primary progressive MS

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Background and aims: We reported abnormal Q-space imaging (QSI)-derived indices in the cervical cord of early primary-progressive (PP) MS patients at baseline, suggesting reduced structural integrity of neurons and demyelination (i.e., neurodegeneration).

To investigate if changes in QSI measures occur over 3 years and correlate with clinical changes; to explore the predictive value of baseline MRI measures.

Methods: 23 PPMS patients and 23 healthy controls (HCs) underwent spinal cord MRI at 3T, and after 1 and 3 years. Cord cross-sectional area (CSA) and QSI metrics of the whole cord and four columns were obtained. Patients were scored on several clinical scales, including the Expanded-Disability-Status-Scale (EDSS), 9-hole-peg (9-HPT) and timed 25-foot walk (T25-FW). Mixed-effect linear regression models assessed differences in MRI measures between groups and their association with clinical changes over 3-years, corrected for age and gender.

Results: Patients deteriorated clinically over 3-years (Table.1). They showed a faster rate of decline in CSA than HCs (RC=-0.96, [95%CI=-1.51,-0.14], p=0.001). In patients, there was an increase in the indices of perpendicular diffusivity in the lateral columns, which was associated with a deterioration in 9-HPT, and a decrease in parallel diffusivity in the anterior columns (all p values<0.05). A smaller CSA and higher perpendicular diffusivity of the whole spine and posterior columns at baseline predicted higher disability at 3 years (all p values<0.05) (Fig.2).

	Baseline		1-Year		3-Year	
	PPMS	HC	PPMS	HC	PPMS	HC
Number	23	23	20	18	22*	14
Age, mean (SD) (years)	51 (9.1)	44 (12.6)	52 (9.3)	46 (11.9)	53 (8.8)	46.3 (12.3)
Sex (M:F)	11:12	5:18	10:10	5:13	10:12	6:8
Disease duration, mean (SD) (years)	3.4 (1.7)	-	4.5 (1.8)	-	6.4 (1.7)	-
EDSS, median (range)	5.5 (2.5-6.5)	-	6 (4.5-7)	-	6.5 ^ (3.5-8)	-
9-hole peg test (9-HPT), mean (SD) (z-score)	-0.61 (1.10)	-	-0.99 (1.16)	-	-1.26 ^ (1.20)	-
Timed 25-foot walk test (T25-FW), mean (SD) (z-score)	0.26 (0.24)	-	0.18 (0.33)	-	-1.36 ^ (1.54)	-
Grip strength, mean (SD) (lbs force)	46.17 (23.90)	-	40.22 (24.81)	-	14.76 ^ (9.65)	-
CSA mean (SD) (mm²)	76.99 (9.58)	81.65 (8.62)	75.41 (9.40)	81.42 (8.59)	73.23 * (8.31)	81.59 (9.11)

*=16/22 completed MRI and clinical assessment, 2/22 completed clinical assessment only, 4/22 telephone EDSS

^= Significant deterioration over 3 years, p<0.05

*=Faster reduction in CSA in PPMS patients than HCs

Cohort description
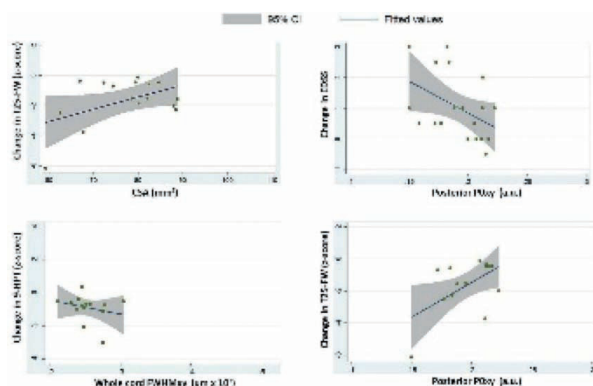
Scatter plots of baseline CSA and QSI-derived perpendicular diffusivity indices, predictor of changes in clinical scores over 3 years.

Conclusion: Progressive spinal cord neurodegeneration, as detected by changes in QSI metrics and development of cord atrophy on MRI, underlies disability worsening in PPMS.

MS and related disorders 3

EPR1099

Pooled analysis of the efficacy of cladribine tablets 3.5 mg/kg in patients with EDSS ≥3.5 or

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Background and aims: In the CLARITY and ONWARD studies, cladribine tablets (CT) demonstrated efficacy across a spectrum of patients with relapsing multiple sclerosis (RMS). Patients with Expanded Disability Status Scale (EDSS) scores ≥3.5 are at higher risk of conversion from relapsing-remitting multiple sclerosis (RRMS) to secondary progressive multiple sclerosis (SPMS) with relapses. Combining data from the double-blind study periods enables the effects of 2 years' treatment with CT (3.5mg/kg cumulative dose) to be assessed in patients with higher EDSS at study entry.

Methods: Data from the 2-year, double-blind periods of CLARITY and ONWARD (n=1,067) were used to analyse the effect of CT 3.5mg/kg on annualised relapse rate (ARR) by comparing patients who entered the study with a baseline EDSS ≥3.5 (n=414) and the complementary subgroup with baseline EDSS ≤3.0 (n=653). ONWARD compared cladribine+interferon-beta and placebo+interferon-beta.

Results: Compared to placebo, CT reduced relapse rate by 60% and 53% for EDSS subgroups ≤3.0 and ≥3.5 respectively (Figures 1, 2). The treatment effect of CT 3.5 mg/kg versus placebo was similar between EDSS subgroups (subgroup by treatment interaction, your own>0.5). The treatment effect in both subgroups was nominally significant (p<0.0001).
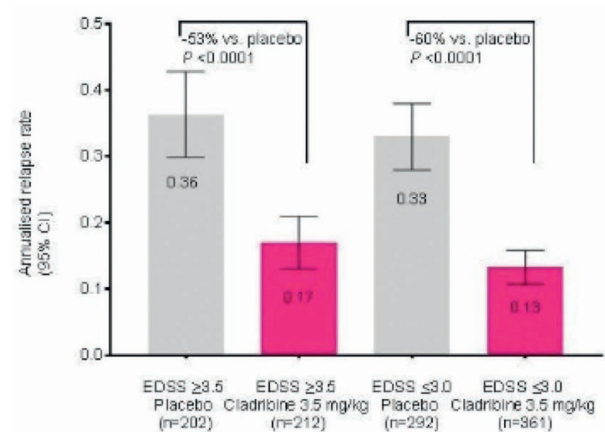
Figure 1: Mean Annualised Relapse Rates at 96 Weeks
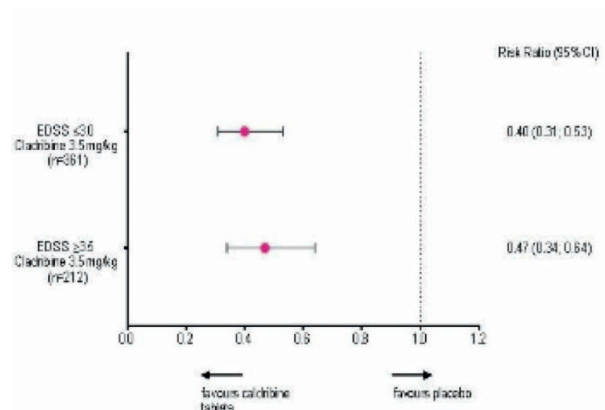
Figure 2: Forest Plot of Annualised Qualifying Relapse Risk Ratio

Conclusion: There was no meaningful difference in the observed ARR between EDSS subgroups supporting the concept that cladribine tablets 3.5 mg/kg is effective for patients with RMS, including those with higher EDSS and increased risk of conversion to SPMS with relapses.

Disclosure: This study was sponsored by EMD Serono Inc, a business of Merck KGaA, Darmstadt, Germany (in the USA), and Merck Serono SA, Geneva, an affiliate of Merck KGaA Darmstadt, Germany (ROW).

EPR1100

Pregnancy outcomes during the clinical development of cladribine in multiple sclerosis: an integrated analysis of safety for all exposed patients

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Background and aims: During clinical trials of cladribine in patients with multiple sclerosis (MS), contraception was specified for men and women of child-bearing potential. Despite these precautions, pregnancies occurred during the clinical trial programme. Here, we report pregnancy outcomes from an integrated safety analysis of patients exposed to cladribine during the clinical development programme in MS.

Methods: Pregnancy outcomes were recorded from an integrated analysis of safety of all exposed patients (cladribine n=1976, placebo n=802). Data on pregnancies recorded as adverse events were included from studies that involved treatment with parenteral cladribine or cladribine tablets.

Results: Overall, 64 pregnancies occurred among 57 women (44 pregnancies were in 38 women with exposure to cladribine; 20 in 19 women who received placebo). Proportions of live births, induced abortions (patient's decision), spontaneous abortions, and medically indicated abortions are presented in Table 1. Spontaneous abortion rates were consistent with epidemiological data on pregnancy outcomes. Three medically indicated abortions were carried out in 2 women who had received cladribine treatment; 2 were for ectopic pregnancies (occurring twice in the same patient), and 1 was for choriocarcinoma. Female partners of 9 cladribine-treated males experienced 10 pregnancies; 9 resulted in live births (1 unknown outcome). Female partners of 2 placebo-treated males experienced 2 pregnancies (unknown outcomes).

Number of pregnancies	Placebo (n=20)	Cladribine (n=44)
Live birth, n (%)	9 (45)	18 (41)
Induced abortion *, n (%)	4 (20)	14 (32)
Spontaneous abortion, n (%)	5 (25)	9 (20)
Medically indicated abortion, n (%)	1 (5)	3 (7)
Unknown, n (%)	1 (5)	0
* Patient's decision		

Table 1: Pregnancy outcomes in the all exposed cohort

Conclusion: In this limited population of pregnancies with potential exposure to cladribine, no congenital malformations were identified. Because of the potential for teratogenicity, further study is warranted to better understand any risks that might be associated with cladribine in pregnancy.

EPR1101

Efficacy of cladribine tablets 3.5 mg/kg in patients ≤50 and >50 years of age with relapsing-remitting multiple sclerosis (RRMS): a post hoc analysis from CLARITY

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Background and aims: In the CLARITY study, treatment with cladribine tablets (CT) significantly improved clinical outcomes vs. placebo in RRMS patients. Compared to older MS patients, younger patients with MS generally have a shorter disease duration and tend to have more inflammation and active disease. This post hoc analysis of CLARITY investigated whether the beneficial effects of CT are consistent in older and younger patients.

Methods: CLARITY patients randomised to CT 3.5 mg/kg or placebo were retrospectively stratified and analysed according to age; ≤50 years (n=761) and >50 years (n=109). Data for ARR and MRI outcomes (mean number of new T1 Gd+ and active T2 lesions) were compared between age subgroups.

Results: At baseline, the subgroup of patients aged >50 years had longer disease duration, higher EDSS score, larger T2 lesion volume, and lower incidence of ≥3 relapses in the previous year. In both the ≤50 and >50 years of age subgroups, CT reduced relapse risk compared to placebo by 59% and 52%, respectively (Figures 1 and 2). For placebo-treated patients, there were higher mean numbers of new T1 Gd+ and active T2 lesions for those aged ≤50 years compared to patients aged >50 (Figure 3). Despite the differences between the placebo-treated age groups, CT treatment demonstrated significant effects on MRI measures in both age groups (P<0.0001).
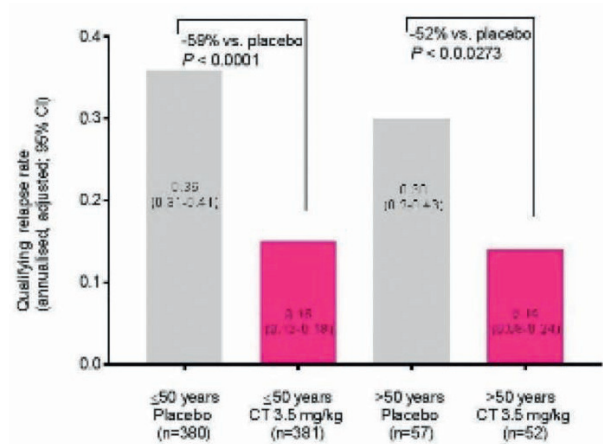
Figure 1: Estimated annualised relapse rates in patients with RRMS aged ≤50 or >50 years treated with cladribine tablets 3.5 mg/kg or placebo for 96 weeks in CLARITY
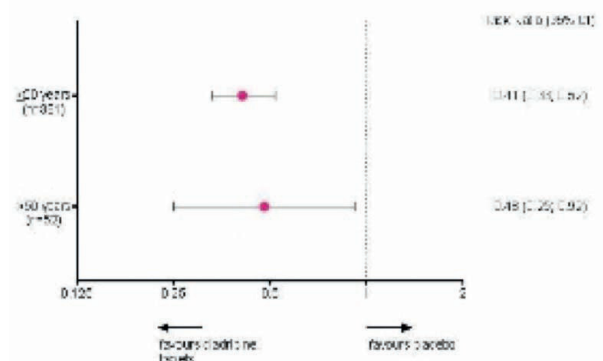
Figure 2: Annualised qualifying relapse risk ratio in patients with RRMS aged ≤50 or >50 years treated with cladribine tablets 3.5 mg/kg or placebo for 96 weeks in CLARITY

Conclusion: The results of this post hoc subgroup analysis suggest beneficial clinical and MRI effects of CT in RRMS patients aged ≤50 and >50 years, with improvements observed in ARR and MRI outcomes vs. placebo.

Disclosure: This study was sponsored by EMD Serono Inc, a business of Merck KGaA, Darmstadt, Germany (in the USA), and Merck Serono SA, Geneva, an affiliate of Merck KGaA Darmstadt, Germany (ROW).

EPR1102

Efficacy of cladribine tablets 3.5 mg/kg in patients with highly active relapsing multiple sclerosis (RMS): Pooled analysis of the double-blind cohort from CLARITY and ONWARD

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Background and aims: In the CLARITY (cladribine tablets [CT] vs. placebo) and ONWARD (CT added to interferon-beta vs. placebo added to interferon-beta) studies, CT demonstrated efficacy across a spectrum of patients with relapsing multiple sclerosis. Patients with high disease activity (HDA) are at higher risk of disability progression. Combining data from the double-blind (DB) periods of each study allowed the effects of 2 years' treatment with CT 3.5 mg/kg (CT3.5) to be assessed in these patients.

Methods: CLARITY and ONWARD patients randomised to CT3.5 or placebo were retrospectively analysed using two different HDA definitions based on relapse history, prior treatment, and MRI characteristics: high relapse activity (HRA) and HRA plus disease activity on treatment (HRA+DAT) (Figure 1).

Figure 1: HDA definitions

HRA	HRA+DAT
Patients with ≥2 relapses in the year before study entry, regardless of treatment status	Patients with ≥2 relapses in the year before study entry, regardless of treatment status
	*
	Patients with 1 relapse in the year before study entry while on DMD therapy and ≥1 T1 Gd+ or ≥9 T2 lesions
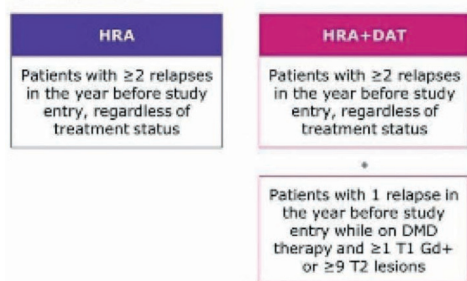
DMD, disease-modifying drug; Gd+, gadolinium-enhancing; HDA, high disease activity; HRA, high relapse activity; HRA+DAT, high relapse activity plus disease activity on treatment

Figure 1: HDA Definitions

Results: In the overall combined DB cohort, CT3.5 reduced the risk of relapse and 3- and 6-month confirmed EDSS progression vs. placebo, an effect observed in both HDA subgroups. In the overall cohort and both HDA subgroups, patients receiving CT3.5 had a reduction in annualised relapse rate and in the number of new T1 Gd+ lesions, compared to patients receiving placebo. Compared to placebo, CT treatment increased the odds of achieving no evidence of disease activity (NEDA) in the overall population (OR, Cl: 3.95; 2.90-5.37), as well as in HRA and HRA+DAT subgroups (OR, CI: 6.94, 3.67-13.12 and 4.28, 2.62-6.99 respectively)

Conclusion: Both HDA and non-HDA patients receiving CT3.5 experienced significantly better relapse, MRI and NEDA outcomes, compared to placebo. HDA patients generally experienced better outcomes compared to non-HDA patients.

EPR1103

Fingolimod may prevent RNFL thinning in multiple sclerosis when compared to first-line injectable treatments independently from disease activity

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Background and aims: Optical coherence tomography-OCT is used in multiple sclerosis-MS to measure retinal nerve fiber layer-RNFL and ganglion cell-inner plexiform layer (GCL-IPL) thickness as a marker of axonal-neuronal loss. A recent study suggested a protective role for Natalizumab on neuroretinal damage; we explored the role of Fingolimod-FTY in this field.

Methods: 90 patients with MS, 45 receiving FTY (mean treatment duration 2.59±1.2years) and 45 (mean treatment duration 4.19±3.6years) Interferon-IFN (n.24) or Glatiramer acetate-GA (n.21), underwent OCT with RNFL and GCL-IPL thickness measurement, with 1 year follow-up.

Results: No significant differences were found comparing IFN vs GA subgroups, so they were combined (IFN-GA). Over one year, patients under FTY had significantly lower RNFL thinning vs IFN-GA group (0.00±0.16µm vs -0.83±0.23µm; p=0.003), despite significantly lower baseline values (81.6±15.2µm vs 88.6±13.9µm; p=0.025). GCL-IPL thickness did not significantly differ between the two groups, both at baseline (IFN-GA 64.2±8.6µm vs FTY 61.1±9.7µm; p=0.097) and over time (-0.44±1.1µm for IFN-GA vs -0.09±1.3µm for FTY; p=0.303). Similar rates of disease activity (new relapses or new T2/Gd enhancing lesion at brain MRI) were found both in the year before baseline (24.3% for IFN-GA vs 28.8% for FTY; p=0.642) and during follow-up (15.3% for IFN-GA vs 13.3% for FTY; p=0.790).

Conclusion: These results suggest a neuroprotective role for FTY at the retinal level, independently from clinical and neuroradiological evidence of disease activity. Although a longer follow-up is warranted to confirm these observations, our findings appear consistent with experiences reporting reduced brain volume loss in patients receiving FTY.

Disclosure: part of this work was supported by NOVARTIS AG - Basel - Switzerland

EPR1104

Disability Outcomes in Young Adult Patients Treated with Fingolimod for up to 96 Months from Pooled FREEDOMS/FREEDOMS II Extension Phases

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Background and aims: In the short-term, fingolimod demonstrated greater treatment benefits on disease activity in patients with relapsing remitting multiple sclerosis (RRMS) vs. placebo. Here we assessed disability outcomes in young adult patients (≤30 years) treated with fingolimod for up to 8 years.

Methods: Young adult patients from the pooled FREEDOMS core/extensions who were followed up for 8 years and received fingolimod 0.5mg (continuous group; N=163) or switched to fingolimod 0.5mg from placebo at Month (M) 24 (switch group; N=147), were included. The time-to-event outcomes: confirmed disability improvement (CDI; decrease in 6-month confirmed Expanded Disability Status Scale [EDSS] by ≤1.0/≤0.5 from baseline scores ≤5.5/≥6.0, respectively), CDI+ (CDI or 6-month confirmed 20% improvement in 9-hole peg test or the timed 25-foot walking test), 6-month confirmed disability progression (6m-CDP), EDSS score ≥4 and ≥6, and progression to secondary progressive MS (SPMS), were analysed using Kaplan-Meier estimates and Cox regression analyses.

Results: At baseline, young adults (vs. patients aged >30 years) had a shorter disease duration (4.5 vs. 10.5 years), lower EDSS (1.9 vs. 2.6), and larger brain volume (Table 1). At M96, a significantly higher proportion of patients in the continuous group (vs. switch group) achieved CDI (58.2% vs. 30.5%) and CDI+ (70.6% vs. 42.3%); a significantly lower proportion had 6m-CDP (20.1% vs. 34.7%) and reached EDSS ≥4 (24.1% vs. 34.1%), with no difference in EDSS ≥6 (10.2% vs. 10.3%). A very small number of patients reached SPMS in both groups (Table 2).

Table 1. Baseline characteristics of young adult patients aged <=30 years and patients aged >30 years in pooled FREEDOMS/FREEDOMS II

Characteristic	Young adult patients aged <=30 years (N=475)	Patients aged >30 years (N=1880)
Age, years	25.8±3.34	41.9±6.57
Duration of MS since first symptom, years	4.5±3.49	10.5±7.62
Number of relapses in previous 2 years	2.3±1.37	2.2±1.44
EDSS	1.9±1.19	2.6±1.31
9-HPT	21.1±5.95	22.7±9.84
T25FWT	5.5±4.64	6.1±4.30
Number of Gd+ T1 lesions	2.7±6.74	1.1±2.94
Volume of T2 lesions, mm³	5904.2±7373.41	5873.4±7840.79
Normalized brain volume, cm³	1571.2±75.38	1504.7±80.44

Data presented are mean±SD.
9-HPT, 9-Hole Peg Test; EDSS, Expanded Disability Status Scale; Gd+, gadolinium-enhancing; MS, multiple sclerosis; SD, standard deviation; T25FWT, Timed 25-Foot Walk Test.

Table 1. Baseline characteristics of young adult patients aged ≤30 years and patients aged >30 years in pooled FREEDOMS/FREEDOMS II

Table 2. Kaplan-Meier estimates for time-to-event outcomes at Month 96

Disability outcome (M96 KM estimates, %)	Continuous group (Fingolimod 0.5mg)	Switch group (Placebo/Fingolimod)
n/N	36/82	17/78
CDI*	58.2	30.5
HR (95% CI), p-value	2.00 (1.11, 3.61), 0.0206	
n/N	42/82	22/78
CDI*	70.6	42.3
HR (95% CI), p-value	1.82 (1.14, 3.23), 0.0149	
n/N	22/163	33/147
6m-CDP*	20.1	34.7
HR (95% CI), p-value	0.46 (0.27, 0.80), 0.0053	
n/N	26/148	38/141
EDSS>=4	24.1	31.1
HR (95% CI), p-value	0.46 (0.28, 0.80), 0.0044	
n/N	10/163	12/147
EDSS>=6	10.2	16.3
HR (95% CI), p-value	0.49 (0.21, 1.14), 0.0971	
n/N	6/163	1/147
SPMS*	4.9	1.8
HR (95% CI), p-value	4.29 (0.48, 38.55), 0.1930	

9-HPT, 9-Hole Peg Test; CDI, confirmed disability improvement; CDP, confirmed disability progression; CI, confidence interval; EDSS, Expanded Disability Status Scale; HR, hazard ratio; KM, Kaplan–Meier; M96, month 96; N, number of subjects included in the analysis; n, number of subjects with the event; SPMS, secondary progressive multiple sclerosis; T25-FWT, Timed 25-Foot Walk Test.

*CDI is defined as 6-month confirmed EDSS decrease of >=1.0 from baseline EDSS >=5.5, or by >=1.5 from baseline EDSS=5.0.

*CDI is defined as CDI or 6-month confirmed 20% improvement in 9-HPT or T25FWT.

*6m-CDP is defined as 6-month confirmed EDSS worsening (>=1.5 if baseline EDSS=0, >=1 if baseline EDSS between 1 and 5, >=0.5 if baseline EDSS>5).

*Episode of SPMS implies an initial EDSS >=4 followed by a relapse-free EDSS progression (>=1.0 if the EDSS was between 3.5 and 5.0, or of 0.5 if the EDSS was >=5.0) that was confirmed after 6 months.

Table 2. Kaplan-Meier estimates for time-to-event outcomes at Month 96

Conclusion: Early initiation of fingolimod in young adults with RRMS improved long-term disability outcomes.

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personal compensation for activities with Bayer Schering, Merck Serono and Teva. Silva and Häring: of Novartis Pharma AG, Basel, Switzerland. Meinert: nothing to disclose

EPR1105

Safety of Ocrelizumab in Multiple Sclerosis: Updated Analysis in Patients with Relapsing and Primary Progressive Multiple Sclerosis

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Background and aims: Ongoing safety reporting on disease-modifying therapies for multiple sclerosis (MS) is crucial to understanding the long-term benefit–risk profile. Data are reported from patients receiving ocrelizumab (OCR) in the Phase II study in relapsing-remitting MS (RRMS; NCT00676715) and in Phase III trials in relapsing MS (RMS; OPERA I/II [NCT01247324]/[NCT01412333]) and primary progressive MS (PPMS; ORATORIO [NCT01194570]). The purpose of the analyses was to report ongoing safety evaluations from OCR clinical trials and open-label extensions (OLEs).

Methods: Patients received intravenous OCR 600mg/24 weeks for 96 weeks in OPERA I/II and ≥120 weeks in ORATORIO. In the Phase II study, patients received 600mg or 2,000mg infusions through Week 24; treatment through Week 96 was OCR 600mg (patients receiving OCR 600mg, placebo or interferon-beta-1a) or 1,000mg (patients receiving OCR 2,000mg). Comparators were placebo (ORATORIO and Phase II) and interferon-beta-1a (subcutaneous/three times weekly [OPERA] or intramuscular/weekly [Phase II]). Patients completing controlled-treatment periods could enrol in the OLE with OCR 600mg/24 weeks. Data presented are from OCR recipients including those switching from comparators.

Results: As of February 2017, 2,301 patients with MS received OCR, resulting in 7,748 patient-years of exposure. Reported rates per 100 patient-years (95% confidence interval) were: adverse events (AEs), 226 (222-229); serious AEs, 7.18 (6.59-7.80); infections, 71.3 (69.5-73.2); serious infections, 1.86 (1.57-2.19); and malignancy 0.454 (0.316-0.632). Updated cross-trial information using a September 2017 data-cut will be presented.

Conclusion: The updated safety profile in the ocrelizumab MS all-exposure population is generally consistent with the controlled-treatment period for the RMS and PPMS populations.

Disclosure: Sponsored by F. Hoffmann-La Roche Ltd; writing and editorial assistance was provided by Articulate Science, UK.

EPR1106

Participant perspectives of a home-based palliative approach for people with severe multiple sclerosis: a qualitative study nested in a randomized controlled trial

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Background and aims: We undertook a multicenter randomized controlled trial to assess the effectiveness of a home-based palliative approach for adults with severe multiple sclerosis (MS) and their caregivers. Concurrently, we performed a qualitative study to investigate the experiences of the patients, their caregivers, patient referring physicians, and the teams who delivered the intervention. Our aim was to explore the strengths/ challenges of the intervention, and circumstances that may have influenced its efficacy.

Methods: We performed semi-structured interviews with 12 patients and 15 informal caregivers (maximum variation strategy), two focus groups with patient referring physicians (four participants each), and one with the teams (nine participants).

Results: From data analysis (framework method) 38 sub-categories emerged, grouped into 12 categories and 3 themes: 'expectations,' 'met and unmet needs', and 'barriers'. Intervention benefits were improved control of symptoms and reduced sense of isolation of the patient-caregiver dyads. Limitations were: factors related to the experimental design; to the intervention; team issues; and external factors. The referring physician focus groups provided little experiential data.

Conclusion: The intervention reduced patient symptoms and sense of isolation of the dyads. The indirect role of the teams, and insufficient length of the intervention were key limitations. The experimental design imposed additional burdens on the dyads. Key barriers were the paucity of available services, demanding administrative procedures, and lack of networking facilities. These findings suggest two major requirements for home palliative care to be effective in this patient population: teams well-connected with MS rehabilitation services, and care delivered over the long-term, with variable intensity.

Muscle and neuromuscular junction disease 1

EPR1107

Complement C5 Inhibitor RA101495 for the Treatment of Myasthenia Gravis

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Figure 1, Pharmacokinetic Analysis: Plasma concentration of RA101495 in healthy volunteers dosed with 0.2mg/kg RA101495 daily

Background and aims: Antibodies against acetylcholine receptor (AChR) activate the classical complement cascade in patients with myasthenia gravis (MG), and induce both, membrane attack complex (MAC) formation and tissue damage at the neuromuscular junction. Inhibition of C5 is a therapeutic target with a strong biological rationale for AChR-antibody positive MG. RA101495 is a subcutaneously-administered macrocyclic peptide that binds to C5 and inhibits its cleavage into C5a and C5b, thus preventing production of MAC. Phase 1 data supported initiation of a Phase 2 study with RA101495 in MG patients.

Methods: Healthy volunteers were randomized to receive single doses (n=14) or 7 daily doses (n=4) of RA101495 or placebo (n=10). Complement inhibition was evaluated using a validated antibody-sensitized sheep red blood cell lysis assay. Based on these data, a multi-center, randomized, double-blind, placebo-controlled Phase 2 study in AChR-antibody positive MG patients was initiated.

Results: In Phase 1, drug levels were consistent with predictions from in-silico modeling, i.e. steady increase over 7 days with daily dosing. The terminal half-life was approximately 7 days [Figure 1]. Near-complete inhibition of complement activity (≥95%) was achieved within 3 hours after the first dose and maintained for >24h [Figure 2]. No safety concerns were identified. Three RA101495-treated healthy subjects experienced mild, transient and self-limiting injection site erythema. The Phase 2 study design will also be discussed [Figure 3].

Conclusion: Subcutaneous self-administration of RA101495, if shown effective, may carry less treatment-related burden than currently available C5 inhibitor therapy and enable a broader population of MG patients to potentially benefit from this treatment modality.
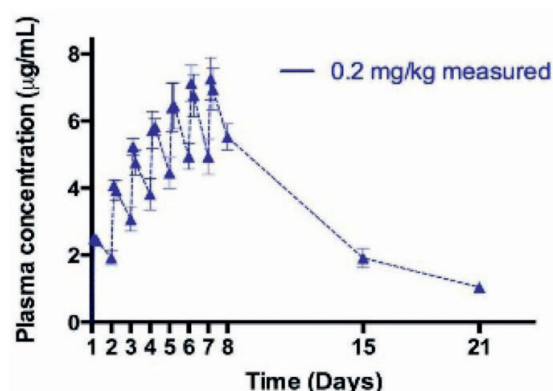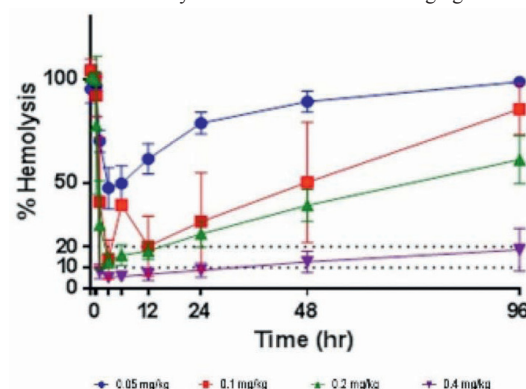
Figure 2, Pharmacodynamic Analysis: Hemolysis as assessed in sheep red blood cell lysis assay after single doses of RA101495 in healthy volunteers (placebo group had complete hemolysis throughout, not shown)
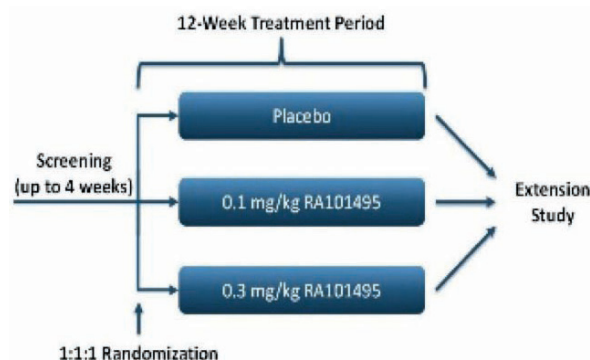
Figure 3, Study Design: RA101495 Phase 2 clinical trial in patients with myasthenia gravis

Disclosure: RA101495 clinical trials are sponsored by RA Pharmaceuticals, Inc.

EPR1108

Glycogenosis type V (McArdle's disease): Successful therapy with vitamin B6

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Background and aims: Mc Ardle's disease is characterized by exercise intolerance, muscle weakness and cramps. To date, no causal treatment is available and patients have to confine themselves to symptomatic therapy. Positive effects of vitamin-B6, an essential cofactor of myophosphorylase, on muscular endurance have been described in individual cases.

A patient with a previously undescribed homozygous mutation in the PYGM gene was treated with vitamin B6. The aim of this study was to verify clinically and biochemically an improvement reported by the patient.

Methods: We performed serial clinical examinations of muscle strength and endurance as well as forearm ischaemic exercise testing, with determination of lactate and ammonia in the presence and absence of vitamin B6 supplementation.

Results: Besides cessation of his muscle cramps, the patient's maximum walking distance doubled and plasma creatine kinase levels dropped significantly on vitamin B6. In the forearm exercise test, a normal increase of plasma lactate and ammonia was seen with vitamin B6, whilst only an insufficient response was recorded in the absence of vitamin B6. Molecular modelling of the myophosphorylase protein indicated that the mutation was located in the vicinity of the pyridoxine-binding site of the enzyme with a putative negative effect on pyridoxine binding.

Conclusion: The patient's mutation in the PYGM gene is located in the vicinity of the pyridoxine-binding site of the myophosphorylase protein and thus explains the favourable clinical and biochemical response to vitamin B6. A trial of vitamin B6 therefore seems justified in McArdle's disease, particularly if the mutation is located near the pyridoxine-binding site of myophosphorylase.

Disclosure: Nothing to disclose

EPR1109

Evaluating the usefulness of new line immunoassays for myositis antibodies in clinical practice: a retrospective study

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Background and aims: Myositis-associated(MAA) and myositis-specific antibodies(MSA) are detected in patients with inflammatory myopathies(IM) and are considered useful diagnostic biomarkers. Aim of our study was to assess the accuracy of MSA/MAA in diagnosing IM in our neuromuscular patients.

Methods: We have retrospectively analysed patients tested for myositis antibodies in our centre (2014-2017). The kit "Euroline:myositis 16Ag" has been used to assess the presence of: Mi-2alpha, Mi-2beta, TIF1gamma, MDA5, NXP2, SAE1, Ku, PM-Scl100, PM-Scl75, Jo-1,SRP, PL-7, PL-12, EJ, OJ, Ro-52. Data on symptom at onset, CK, muscle biopsy and diagnosis were collected.

Results: 1232 patients were identified. Muscle biopsy was performed in 583 patients (47%). 148 patients had a confirmed IM, other diagnoses included: myopathy (n=356), other neuromuscular diseases (n=141), no neuromuscular diseases (n=587). The specificity was for MSA 95% and for MAA 89%, whereas the sensitivity was 21% and 22%. The positive predictive value was higher for MSA (54%) compared to MAA (37%) whereas the negative predictive value was the same for both MSA/MAA (80%). A positive test increases the post-test probability of having myositis of 30% (LR+=4) for MSA and 15% (LR+=2) for MAA, whereas a negative test does not significantly decrease the probability of having myositis (LR-=0.8 for both). In 154 patients the test was repeated at least twice and a high agreement between repeated measurements was found (82%).

Conclusion: Commercial immunoassays for myositis antibodies show low sensitivity and high specificity, they should therefore be used for confirmatory rather than screening purposes and repeating the test doesn't seem necessary. Combining antibody findings with clinical features will help developing specific diagnostic algorithms for IM.

Disclosure: Nothing to disclose

EPR1110

Neonatal cases of congenital myopathy due to RYR1 mutations: early findings at muscle biopsy and muscle MRI

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Background and aims: Mutations in RYR1 gene, encoding ryanodine receptor, are responsible for congenital myopathies (CM). These forms may be widely heterogeneous regarding inheritance, histopathological features, age of onset, clinical severity and evolution.

Methods: We selected a cohort of 9 patients affected by CM with pathogenic RYR1-mutations detected through Sanger sequencing or Next Generation Sequencing techniques. Phenotype spanned from paucisymptomatic hyperCKemia to severe neonatal presentation. Among them we focused on 4 severe congenital cases. All subjects underwent neurological evaluation, muscle biopsy and muscle Magnetic Resonance Imaging (MRI).

Results: Patients presented at birth with severe hypotonia and weakness, some of them even requiring long-term artificial ventilation (2) and percutaneous endoscopic gastrostomy (3). We identified 3 different and novel RYR1 mutations. Muscle biopsies showed an heterogeneous pattern, occasionally with unusual features (mitochondrial oxidative activity deficiency, neurogenic signs). Interestingly two biopsies were performed at a very young age, respectively at 5 and 37 days of life, and revealed abnormalities at ultrastructural analysis, leading to the diagnosis of congenital myopathy. Muscle MRI evidenced predominant involvement of gluteus maximus, adductor magnus, vastus and soleus muscles, with relative sparing of rectus femoris. One patient underwent intrauterine brain MRI.

Conclusion: Since now only few cases of neonatal RYR1-related myopathies with early muscle biopsy and MRI have been described. We report four neonatal cases with precocious evaluations. Muscle biopsy was not always specific, but typical features can be detected at electron microscopy examination. Instead, muscle MRI generally showed a typical pattern. These findings further enlarge our knowledge on this heterogeneous disorder.

Disclosure: Nothing to disclose

EPR1111

Myofibrillar myopathies: state of the art and new phenotypical features in a Parisian cohort

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Background and aims: Myofibrillar myopathies (MFM) are chronic neuromuscular disorders sharing common histological features, including myofibrillar disorganization beginning at z-disk, abnormal accumulation of protein aggregates and filamentous myofibrillar degradation products, and the presence of vacuoles. To date, DES, MYOT, CRYAB, ZASP, FLNC, BAG3, FHL1 and DNAJB6 are considered as the main genes responsible for MFM.

Methods: We retrospectively reviewed the clinical history, imaging, EMG, biological and histopathological characteristic of 75 patients with a diagnosis of MFM referred to the Institute of Myology in Paris.

Results: We characterized 29 patients with desminopathies, 10 patients with alpha-β-crystallinopathies, 11 patients with ZASP mutation, 5 patients with myotilinopathies, 13 patients with filaminopathies, 1 patient with a BAG3 mutation and 6 patients with DNAJB6 mutations. Beside the confirmation of previously described phenotypes, we report several unusual presentations: a bag3pathy, with an onset at childhood presented a rigid spine syndrome, a severe axonal sensorimotor neuropathy and no cardiac involvement; DNAJB6 mutation patients displayed predominantly a proximal phenotype (LGMD1D) in one family and a distal myopathy in the other.

Conclusion: MFM represent a clinically heterogeneous group of muscular disorders. This spectrum is expanding, leading to consider the diagnosis in conditions such as rigid spine syndrome or predominantly axial myopathies. MRI confirms its interest as a useful diagnostic tool especially in desminopathies.

Disclosure: Nothing to disclose

EPR1112

Serum anti-Mullerian hormone as a marker of fertility in women with myotonic dystrophy type 1 and 2

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Background and aims: Myotonic dystrophy (DM) represents the most common type of muscular dystrophy in adult age. Clinical signs and symptoms in type 1 (DM1) and type 2 (DM2) overlap. DM is a multisystem disorder that, among others, affects endocrine system and thus may have a negative impact on fertility. Recent studies suggest an impairment of fertility in female patients with DM1, while few data are available on female fertility in DM2.

One of the most important factors for fertility impairment is supposed to be decreased ovarian reserve. Anti-Mullerian hormone (AMH) is a peptide hormone that represents a simple and widely available measure of ovarian reserve unrelated to the menstrual cycle. The aim of our study was to compare ovarian reserve expressed as AMH values in women with DM1, DM2 and healthy volunteers.

Patients: A total of 15 reproductive-age females (mean age 36.0 ± 8.6) with DM2, 11 age-matched females with DM1 (mean age 35.1 ± 6.0) and 16 healthy controls (mean age 33.2 ± 7.3) were included in this case control study.

Methods: An enzymatically amplified two-site immuno-assay was used to measure serum AMH level.

Results: Mean AMH levels were similar in females with DM2 (2.8 ± 2.0 ng/ml) and healthy controls (2.9 ± 1.7 ng/ml) ($p=0.84$), but were significantly lower in patients with DM1 (1.27 ± 0.4) ($p=0.02$).

Conclusion: Our study confirms that decreased ovarian reserve represents one of the factors that may negatively influence fertility in women with DM1, but not in DM2.

Disclosure: Nothing to disclose

EPR1113

Clinical characteristics, management, and outcomes of Danon disease: A nationwide survey in Japan.

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Background and aims: Danon disease, an X-linked dominant vacuolar cardiomyopathy and skeletal myopathy, is caused by primary deficiency of lysosome-associated membrane protein-2 (LAMP-2). However, the clinical characteristics, management, and outcomes of Danon disease have not been well established.

Methods: Here, we sent questionnaires on Danon disease to 2,617 hospitals in Japan that have departments of neurology, cardiology, or pediatrics. We reviewed clinical histories, muscle specimens, and genetic analyses of the LAMP-2 gene.

Results: As a result, we identified 39 Danon disease patients (17 men and 22 women) from 20 families. Cardiomyopathy and ECG abnormalities were evident in all patients with Danon disease. Among the 20 patients who had died, 19 (95%) died of cardiac failure or sudden cardiac arrest. Hypertrophic cardiomyopathy (HCM) was documented in most patients. Wolf-Parkinson-White syndrome was noted at a relatively high incidence (25%). Heart transplantation, the most effective therapy, was performed in only one woman and is just now required by four patients. Some were supported by left ventricular assist devices, permanent pacemakers, and/or implantable cardioverter defibrillators. Pathologically, all patients showed autophagic vacuoles with sarcolemmal features in muscles. All patients had LAMP-2 gene mutations. Half of the probands showed de novo mutations.

Conclusion: In conclusion, Danon disease is a very rare muscular disorder and may be primarily caused by lysosomal dysfunctions. Cardiomyopathy is the most important prognostic factor and the main cause of death among Danon disease patients. Danon disease may be overlooked in patients with HCM, since other clinical features including myopathy can be mild, particularly in women.

Disclosure: Nothing to disclose

EPR1114

Reducing emergency hospital admissions in England: the importance of the co-ordination of care at specialised neuromuscular services

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Background and aims: A 2 part project conducted over a 6-year period aimed to identify the reasons for preventable unplanned admissions in order to improve care and reduce emergency admissions in patients with neuromuscular diseases (NMDs) in the South-East England.

Methods: Two NHS audits (retrospective case note studies) on unplanned admissions in patients with NMDs in the South-East of England were performed 5-years apart. Inclusion criteria were emergency admission codes and NMD diagnosis ICD-10 codes. Exclusion criteria were incomplete medical notes, elective admissions, absence of a NMD and obstetric admissions.

Intervention: In between both audits, recommendations and a partnership approach project were developed to co-ordinated care and to prevent known NMDs complications in the analysed regions.

Results: Audit 1 showed a substantial proportion of preventable admission in this patient population. Positive impacts of implemented changes included more referrals to specialised centres and more admissions under Neurosciences care (77% in 2014-2016, as compared to 14.9% in 2009-2011). Improvements also included a reduction in preventable admissions directly related to previously known NMDs (from 63% to 32.8%) and reduction in re-admissions (from 25.1% to 12.4%). Mortality rate dropped from 4.5% to 0.3%. Patients known to NMD specialised services had shorter hospital stay and fewer ITU admissions than patients who were not known to such services.

Conclusion: Audit 1 suggested issues related to patients' care contributed to the high frequency of unplanned admission in this patient population. Improvement in the provision of NMD services reduced emergency admissions and improved outcomes, which were successfully documented in Audit 2.

Disclosure: Nothing to disclose

Neurogenetics 1

EPR1115

Micro RNA in Muscular Dystrophies and Metabolic myopathies are useful biomarkers

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Background and aims: To investigate microRNAs (miRNAs) that are small non-coding RNAs that modulate a wide range of biological functions in various metabolic and myopathologic conditions we studied thhe circulating microRNAs in Becker and FSHD muscular dystrophy as well in lipid storage myopathies MiRNAs can be actively released by muscle, carried by exosomes, microparticles and apoptotic bodies or released after sarcolemmal damage.

Methods: We have particulary studied "Canonical myomiRs" (miR-1; miR-206; miR-133a and miR-133b), they are considered as markers of muscle regeneration, myogenesis, fiber type differentiation, degeneration, injury and might represent indicators of residual muscle mass consequent during chronic atrophy of muscle or its metabolic dysfunction in lipid storage myopathies.

Results: Circulating miRNA have been studied in several muscular dystrophy cases and myopathies such as FSHD and Becker muscular dystrophy, LGMD, Lipid Storage Myopathies. We investigated their level observed in various LGMD (transportinopathies, sarcoglycanopathies),BMD and FSHD as well a series of metabolic myopathies (i.e. NLSD-M, ETF dehydrogenase deficiency).Different level of micro RNAs were found while an upregulation of MiR 206 was seen in the course of FSHD and LGMD, MiR 133a and Mir133b were elevated in BMD and ETF dehydrogenase deficiency. In NLSDM an upregulation of all myo-MiRNA correlated with muscle imaging.

Conclusion: In neuromuscular disorders MiRNAs act as negative regulators, we have found a significantly higher expression of miR-206 in serum of several and metabolic and primitive genetic dtstrophies we observed differential serum expression of myomiRNA in a number ofl muscular dystrophies and metabolic myopathies.

Disclosure: Supported by Telethon GGP14066

EPR1116

Quality of life and modifiable lifestyle factors in Leber's Hereditary Optic Neuropathy mutation carriers

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Background and aims: Leber's Hereditary Optic Neuropathy (LHON) is the most frequent mitochondrial disease, leading to bilateral central vision loss and disability. LHON is caused by mitochondrial DNA point mutations, with incomplete penetrance. Risk of disease for carriers differs significantly between genders, with genetic and environmental factors modifying this risk.

Methods: 71 participants of the Munich prospective study on LHON mutation carriers, recruited between 2014 and June 2015, 16 years and older, were included. Systematic neurological and ophthalmological examinations were performed yearly. At each visit, questionnaires on smoking, alcohol, depression and quality of life (QoL) were completed. Nominal data were compared by chi-square tests and continuous data by t-tests, stratified by gender.

Results: 34 (48%) patients (28 male, 82%), and 37 asymptomatic LHON mutation carriers (7 male, 19%) were included. Median age at onset was 26.9 years (range 9.4-71.8), median disease duration was 2.5 years (range 0.4-36.6). The proportion of smokers before onset was significantly higher among patients than for the general population. 60% of LHON patients, who smoked before onset, reduced or stopped smoking after onset. In spite of scoring higher on physical health QoL subscales, asymptomatic female LHON mutation carriers showed worse results in mental health QoL subscore, compared to female LHON patients and female general population ($p < 0.001$).

Conclusion: This study provides insights on LHON mutation carriers, with female asymptomatic carriers showing increased frequency of depressive symptoms and decreased mental health-related QoL, while highlighting modification of lifestyle factors in this population as potentially significant prophylactic measures.

Disclosure: Nothing to disclose

EPR1117

A case of adult-onset leukoencephalopathy with axonal spheroids and pigmented glia, presenting with young dementia and allodynia revealing a novel mutation.

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Background and aims: Adult onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP), mainly caused by mutations in the colony stimulating factor-1 receptor (CSF1R) gene, is an underestimated progressive degenerative white matter disease with a wide spectrum of phenotypes that encompasses hereditary diffuse encephalopathy with spheroids (HDLS) and pigmentary orthochromatic leukodystrophy (POLD)[1]. We report a novel mutation of CSF1R in a 45-year-old woman presenting with a spastic hemiparesis, left-sided allodynia, gait ataxia, dysarthria and cognitive deterioration.

Methods: Case report and review of the literature.

Results: A 45-year-old woman without familial history developed allodynia, a left hemiparesis, cognitive impairment and depression. Examination showed a spastic hemiparesis, gait ataxia and dysarthria. Neuropsychological testing revealed frontal dysfunction. Brain MRI showed confluent periventricular white matter lesions, corpus callosum atrophy and diffusion-restricted lesions (figure 1), characteristic for ALSP. Brain CT showed periventricular calcifications with a typical stepping stone appearance (figure 1), brain FDG-PET showed hypometabolism frontoparietal and in the basal ganglia. Genetic analysis of the CSF1R-gene revealed a novel mutation (c.2466G>A, p.Met822IIe Mayoclinic, R. Rademakers). Progressive neurological deterioration with a tetraparesis and bedridden state evolved and she eventually died 3 years after symptom-onset. Brain autopsy including electron microscopy of the frontal deep white matter showed axonal spheroids, swollen axons containing neurofilaments and residual bodies and macrophage containing pigmented lipofuscin, hallmark features of ALSP (figure 2).
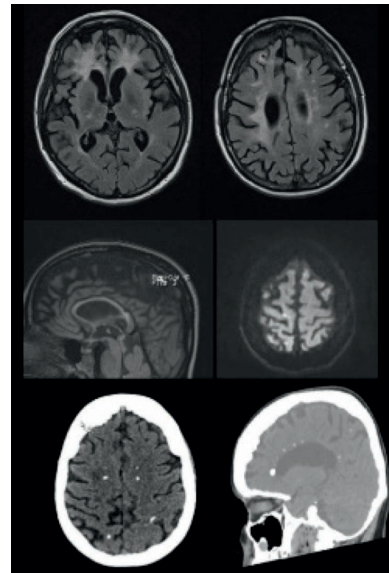
Figure 1: a-d.: Confluent white matter lesions periventricular, corpus callosum atrophy and diffusion-restricted lesions, e-f.: Calcifications, sparing basal ganglia, with stepping stone appearance
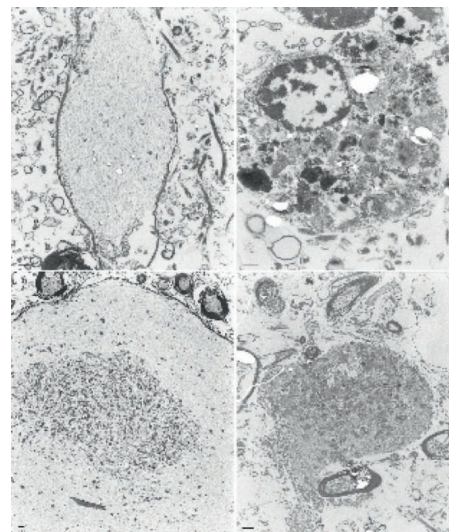
Figure 2: Electron Microscopy of frontal lobe, deep white matter. a. Swollen Axon b. Macrophage containing pigmented lipofuscin c. Swollen axon containing neurofilaments and residual bodies d. Axonal Spheroid

Conclusion: This report highlights the importance of considering ALSP in the differential diagnosis of adult-onset leukoencephalopathy and adds to the growing list of CSF1R-mutations in ALSP.

Disclosure: Nothing to disclose

EPR1118

Utility of Whole Exome Sequencing as a diagnostic tool in different neurologic phenotypes

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Background and aims: Next generation sequencing methodologies, including whole exome sequencing (WES), are transforming the way neurology is practiced. Our aim here was to evaluate the utility of WES in various phenotypes in a cohort of Greek patients.

Methods: Patients presenting with neurological disorders deemed genetic in origin were offered WES based on prespecified criteria. After obtaining informed consent, WES was performed on 109 patients (46 females; mean age=19.5±2.0 years, range 1-73 years). Sequencing was performed at Otogenetics, Norcross, GA, USA, using the Illumina HiSeq2000/25000 platform aiming at a 50X coverage. Variant annotation was performed in the Neurology Laboratory, University of Crete, Greece, using the Ingenuity (Qiagen, USA) software and taking into consideration clinical and bibliographic information.

Results: The most common indications for ordering WES were epilepsy/epileptic encephalopathies (29.3%), muscle disorders (19.3%), developmental disorders (13.8%) and motor neuron disease/spastic paraparesis (8.3%). The overall diagnostic rate of WES was 46.8% (causative genetic defects identified in 51/109 patients). Per diagnostic category, the diagnostic rate was: epileptic syndromes 34.4% (11/32), muscle disorders 66.7% (14/21), developmental disorders 60.0% (9/15), motor neuron disease/spastic paraparesis 55.5% (5/9), cerebellar ataxia 14.3% (1/7), metabolic disorders 66.7% (4/6) and polyneuropathy 50.0% (2/4). In most instances, WES provided final diagnosis after several tedious and expensive diagnostic tests were inconclusive.

Conclusion: In our cohort of neurological and pediatric neurology patients, WES showed high diagnostic efficiency. These data offer support to the value of WES when applied in clinical practice to end the diagnostic Odyssey of patients with heterogeneous neurogenetic disorders.

Disclosure: Nothing to disclose

EPR1119

Novel, likely pathogenic, sequence variants in hereditary neuropathy genes

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Background and aims: Hereditary neuropathy is caused by a large number of genes involved in different cellular mechanisms. Charcot-Marie-Tooth (CMT) disease is the most prevalent inherited neuropathy. Next-generation sequencing (NGS) has during the last five to ten years entered the clinical diagnostics. NGS has proven to be efficient in the diagnostics of disorders where multiple genes can be involved.

Methods: Our NGS-based targeted gene panel consists of 99 hereditary neuropathy genes, i.e. mostly CMT genes. This study is a retrospective study of clinic samples received between May 1 2014 and October 1 2017.

Results: We describe the identified novel likely pathogenic sequence variants, according to International Guidelines. In this period we identified novel, not previously described, likely pathogenic sequence variants in the following genes: AARS, ANO5, BSCL2, FGD4, GAN, GJB1, HINT1, HSPB1, IGHMBP2, LITAF, LRSAM1, MME, MPZ, NEFL, PMP22, POLG, SBF1, SH3TC2 and YARS.

Conclusion: There is now a wide range of genes causing hereditary peripheral neuropathies and many likely pathogenic sequence variants. Likely pathogenic sequence variants are identified in old well established neuropathy genes as well as in the newer genes. The affected in a hereditary neuropathy family share the unique sequence variant causative for the familial disorder.

Disclosure: Nothing to disclose

EPR1120

Genetic analysis of a dementia patients' cohort: experience from Coimbra center in Portugal

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Background and aims: The Dementia outpatient clinic of the University Hospital Center of Coimbra, the largest hospital in the central region of Portugal, is a reference centre on dementia diagnosis and with the support of the Neurogenetics Laboratory has been focused on the genetically mediated dementia forms. We aim to analyse the known causative dementia genes and ApoE genotype in our patient's cohort representative of this region with 2 millions.
Methods: The genetic analysis included: PSEN1 and 2, APP, MAPT, GRN, C9orf72 and SQSTM1 as well as the major genetic AD risk factor, ApoEε4 allele.
Results: A cohort of 2273 patients was recruited: 963 AD, 377 MCI, 248 FTLD, 17 CBD, 11 PSP, 151 LBD, 149 VD or mixed dementia; the remainder have other diagnosis. We identified 4 mutations in PSEN1, PSEN2 and APP in AD patients, 13 C9orf72 expansions, 16 GRN, 3 MAPT and 5 SQSTM1 mutations in FTLD, CBD and LBD patients. In AD patients 45% were ApoEε4 carriers.
Conclusion: In AD patients, the overall low mutation frequency (0.4%) suggests that other yet unknown genes must be involved. ApoEε4 frequency is in accordance with the previously reported. In FTLD cohort, C9orf72 and GRN are the major genetic causes followed by MAPT and SQSTM1 genes. However, mutations in GRN and SQSTM1 genes are also associated with CBD and LBD, respectively. Interestingly, some of the mutations found are novel and are shared by several unrelated patients, reflecting the specific genetic background of the Portuguese population, although we cannot rule out a common ancestor in these families.
Disclosure: Nothing to disclose

EPR1121

Targeted sequencing for the diagnosis of familial dementias

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Background and aims: Genetics is intricately involved in the etiology of degenerative dementia. Indeed, familial occurrence varies between 2% and 50%, depending on the dementia subtype. The current clinical approach is to test a single gene or a limited group of genes using Sanger sequencing, according to specific flow-charts. However, identifying a specific genetic cause of dementia can be difficult due to phenotypic overlap between the different forms of dementia subtypes, locus heterogeneity, and variability in accessibility of genetic tests.
Methods: In this study, we conducted targeted sequencing of 300 heterogeneous patients, mainly with early-onset and/or familial neurodegenerative dementia, using a custom-designed Next Generation Sequencing (NGS) panel covering 27 genes known to harbor mutations that can cause different types of dementia, in addition to the detection of C9orf72 repeat expansions. Novel variants were classified according to the standards and guidelines for the interpretation of sequence variants.
Results: We identified pathogenic and novel likely pathogenic variants in 55 patients (18.33%), in common (presenilin 1, presenilin 2, C9orf72, and granulin) and rare genes (optineurin, serpin family I member 1 and protein kinase cAMP-dependent type I regulatory subunit beta). Additionally, we found one patient with a novel possible risk factor, seven with known genetic risk factors, and ten with previously reported variants of uncertain significance.
Conclusion: Our results support the use of an extended NGS panels as a quick, accurate and cost-effective method for diagnosis in clinical practice. This approach could have a significant impact on the proportion of tested patients, ideally all with early onset disease.
Disclosure: Nothing to disclose

Neuroimaging 1

EPR1122

Functional connectivity changes in relation to dopaminergic decline in Parkinson's over time: a resting-state fMRI and 11C-PE2I PET imaging study

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Background and aims: Resting-state functional magnetic resonance imaging (fMRI) has demonstrated that basal ganglia functional connectivity is altered in Parkinson's disease (PD) as compared to healthy subjects. However, such functional connectivity alterations have not been related to the dopaminergic decline that occurs in PD over time. To evaluate the functional connectivity patterns of basal ganglia subdivisions in relation to dopamine transporter density, as assessed with Positron Emission tomography (PET) and the specific tracer11C-PE2I, and motor features in patients with PD at baseline and over time.

Methods: We assessed functional connectivity of the basal ganglia subdivisions during resting-state fMRI and dopamine transporter density using 11C-PE2I PET in thirty PD patients at baseline. Of these, 15 PD patients were rescanned after 19.9±3.8 months. A seed-based approach was used to analyse resting-state fMRI data. 11C-PE2I binding potential (BPND) was calculated for each participant with the seed regions-of-interest.

Results: At baseline, functional connectivity between striatum and substantia nigra/supplementary motor area (SMA) was significantly correlated with striatal 11C-PE2I BPND. Moreover, substantia nigra-caudate/putamen functional connectivity was significantly correlated with nigral 11C-PE2I BPND. Over time, reduction in posterior putamen functional connectivity with substantia nigra and SMA was significantly correlated with decreases in posterior putamen 11C-PE2I BPND.

Conclusion: Our findings suggest that basal ganglia functional connectivity is related to the integrity of the dopamine system in patients with PD. Application of resting-state fMRI in a large cohort and longitudinal scanning may be a powerful tool to study functional connectivity changes in PD over time.

Disclosure: Nothing to disclose

EPR1123

Natural history of brain inflammatory lesions in multiple sclerosis: a FLAIR and T1w post contrast MRI volumetric analysis

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Background and aims: To characterize the pathology of new MS lesion formation using monthly FLAIR and post contrast T1w scans.

Methods: The volume of brain white matter (WM) lesions was evaluated monthly on FLAIR and T1w after a single (T1wGdSD) and triple (T1wGdTD) dose of gadolinium based contrast agent.A kinetic time course analysis was applied to the post contrast FLAIR and T1w volumes and a two-random-walks model to the FLAIR volume kinetic.

Results: RRMS patients(n=26) underwent a monthly MRI follow-up. The highest volume recorded on FLAIR images was superior to the T1wGdTD one that in turn was superior to the one observed on T1wGdSD, showing similar bell shape profiles. The FLAIR volume kinetic was described by two two-random-walks curves: a rapid onset one, with similar shape compared to the T1wGdSD-TD curves and a second one beginning at the same time but slowly increasing and decreasing. Both nodular(n=84) and ring enhancing lesions(n=16) were described by this model with high fitting quality.

Conclusion: FLAIR MRI resulted to be sensitive to both acute and later stages of lesion pathology: the rapid onset random walk curve, similar in shape to the T1wGdSD-TD ones, describing the acute inflammatory phase marked by overt BBB disruption and the second random walk curve, slowly increasing and decreasing, mirroring the demyelinating process. The mathematical analysis of FLAIR volume kinetic (second random walk curve) may help to monitor remyelinating treatments efficacy in MS. This biological model was valid for both nodular and ring enhancing lesions suggesting a similar physiopathological substrate.

Disclosure: Nothing to disclose

EPR1124

Brain glucose metabolism and connectivity support current diagnostic criteria for Lewy Body Dementia

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Background and aims: Dementia with Lewy bodies (DLB) is a common neurodegenerative condition characterized by a prevalent neurodegeneration of occipital brain regions. Although a posterior brain hypometabolism, as assessed by [18F]FDG-PET, is a supportive feature in the DLB diagnostic criteria, the relationship with clinical features are yet to be elucidated. We aimed to characterize [18F]FDG-PET brain metabolism alterations in a large cohort of patients, in conjunction with detailed clinic-neuropsychological evaluations.

Methods: In a cohort of probable DLB patients (N=72), we applied to [18F]FDG-PET data: i) a validated voxel-wise analysis to obtain brain hypometabolism maps in single-cases, ii) hierarchical cluster analysis to investigate the presence of brain dysfunctional subtypes within our group, iii) seed-based interregional correlation analysis to assess the resting-state networks.

Results: The temporo-parietal and occipital hypometabolism was highly consistent in each included single-case. According to the hierarchical cluster analysis, the severity of occipital hypometabolism varied among patients: a more severe occipital hypometabolism was associated with worse global cognitive status, in particular visuo-perceptual performances, and presence of visual hallucinations.

Network analysis revealed local and long-distance connectivity alterations converging to the posterior brain networks. We found an association between presence/amount of hallucination and alterations in the attentional and visual resting-state networks, and between rapid eye movement sleep behavior disorder and alterations of the subcortical networks.

Conclusion: The disease-specific brain metabolism signature in single-subject supports the FDG PET role in the current consensus criteria for DLB diagnosis. The underlying connectivity dysfunction and network-level alterations, differentially associated with the core clinical manifestations, may promote clinical heterogeneity within the disease.

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EPR1125

Globus pallidus and red nucleus T2 signal differences in idiopathic and LRRK2-related Parkinson's disease

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Background and aims: In both idiopathic and some monogenic forms of Parkinson's disease (PD), increased iron deposition in the substantia nigra has been described, resulting in lower signal intensity in T2-weighted magnetic resonance (MR) images. In other areas of the brain findings are controversial. Our aim was to characterize signal changes in the globus pallidus (GP) and red nucleus (RN) in PD patients with LRRK2 gene mutations (LRRK2-related PD) and idiopathic PD (iPD), using T2-weighted MR imaging.

Methods: Comparative cross-sectional study including iPD and LRRK2-related PD patients and healthy controls with no known family history of neurodegenerative disorders. Imaging data was acquired using a 3.0 Tesla MR scanner. Regions of interest were manually drawn in the GP and RN and semi-automatically delineated. Mean signal intensity was obtained for each group and used for non-parametric analysis. A p-value below 0.05 was considered significant.

Results: Eleven iPD patients, 12 LRRK2-related PD patients (9 G2019S; 3 R1441H) and 9 healthy controls were included. Using manual segmentation, we identified significantly higher signal intensity in the posterior segment of the GP of the iPD group (462±82) compared to controls (404±76) and significantly higher signal intensity in the RN of the LRRK2-related PD (509±80), compared to controls (450±88). Using semi-automatic segmentation methods, a similar trend was noted. No significant differences were found when comparing iPD and LRRK2-related PD.

Conclusion: T2 signal differences found between iPD and LRRK2-related PD may indicate decreased iron deposition in the GP in iPD and in the RN in LRRK2-related PD.

Disclosure: Nothing to disclose

EPR1126

From minimally conscious state minus to minimally conscious state plus: A multiple case study

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Background and aims: The minimally conscious state (MCS) has been sub-categorized in MCS minus and plus, based on language-related behaviors (i.e., command-following, intelligible verbalization or intentional communication [Bruno et al., 2011]). We here aim to describe behavioral and neuroimaging data of severe brain-injured patients who evolved from MCS minus to MCS plus.

Methods: Four patients (23-56 years old, 2 TBI, time since onset: 8 months to 5 years) were assessed at two time points using the Coma Recovery Scale-Revised. During their first week of assessments, they were diagnosed as MCS minus. They later recovered language-related behaviors (i.e., MCS plus), when reassessed during their second week of evaluations. All patients underwent a positron emission tomography (PET-scan) and magnetic resonance imaging (including voxel-based morphometry – VBM) exams during both assessments. We here compared the neuroimaging differences between the two exams in these four patients.

Results: PET-scan results showed that all patients presented partial recovery of metabolism in temporal lobules, reflecting compensation either from left-sided language areas or from their contralateral regions. VBM results showed that two patients presented a significant increase of
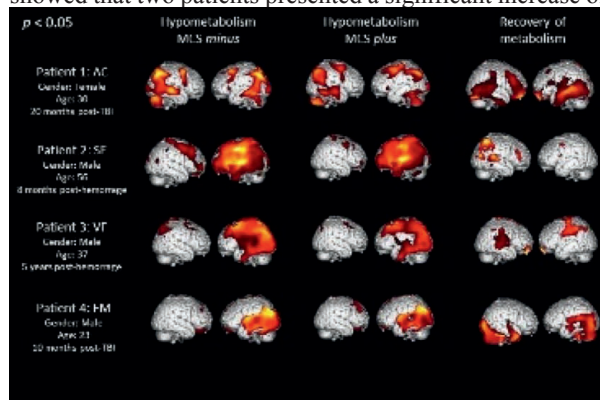
Brain metabolism of the four patients who evolved from MCS minus to MCS plus. Results are significant at p<0.05.

Conclusion: The clinical evolution of patients from MCS minus to MCS plus suggests the reappearance of language-based behavioral signs, but also the partial recovery of metabolism and grey matter structure in cerebral regions that were previously associated to language processing. These neuroimaging results highlight the remaining neuroplasticity in chronic MCS.

Disclosure: Nothing to disclose

EPR1127

Association between abnormal functional connectivity of thalamic sub-regions and clinical disability in CIS patients: a longitudinal study

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Background and aims: No study has explored thalamic connectivity abnormalities in early stages of multiple sclerosis (MS). We investigated sub-regional thalamic resting-state (RS) functional connectivity (FC) abnormalities in patients with clinically isolated syndrome (CIS) suggestive of MS and their correlation with disability.

Methods: Structural and RS fMRI data were acquired from 59 CIS patients and 13 healthy controls (HC) at baseline (within 3 months from first attack), year 1 and year 2. Five thalamic sub-regions (frontal, motor, postcentral, occipital, temporal) were parcellated according to their cortico-thalamic structural-connectivity, and used for seed-based RS FC analyses. Thalamic RS FC abnormalities were assessed and correlated with EDSS at follow-up.

Results: Forty-nine (83%) patients developed MS at year 2. At baseline, compared to HC, CIS patients had reduced thalamic RS FC with frontal cortices and cerebellum, for the frontal and motor sub-regions. During follow-up, there was a progressive reduction of thalamic RS FC with: 1) the cerebellum, for the whole thalamus, motor, postcentral, occipital, and temporal sub-regions; 2) some areas of the default-mode network, for occipital and postcentral sub-regions; and 3) temporal cortices, for the whole-thalamus, frontal and temporal sub-regions. Sub-regional thalamic RS FC abnormalities correlated with higher EDSS at follow-up.

Conclusion: Dynamic alterations of thalamic sub-regional connectivity abnormalities with frontal, temporal, default-mode and cerebellar regions characterized CIS patients. Regional thalamic connectivity abnormalities with the frontal cortex and cerebellum at baseline contributed to explain disability after two years, highlighting the role of thalamic involvement in the first stages of the disease for subsequent clinical outcome.

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EPR1128

What does clinical language fMRI look like? Results from a survey of 63 analysts

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Background and aims: Functional MRI is validated for lateralizing language areas in pre-surgical planning, but anecdotally the protocols used across sites vary markedly. Here we report the first comprehensive survey of analysts undertaking clinical fMRI for presurgical planning in epilepsy.

Methods: Respondents included 63 analysts completing language fMRI and were primarily from the US (44%), Europe (32%), and Australia (11%). They were typically from programs in academic centers (82%) treating primarily adults (42%), adults and children (36%), or children alone (22%).

Results: Over 18 cognitive tasks were reported as being in use, with the most frequent including noun-verb generation, verbal fluency, and object naming. Over 75% of programs complete three or more protocols, with runs having a modal duration of 5 minutes. Nearly all aspects of the tasks used differ among programs, including stimulus modality and control conditions, and fMRI has been adapted formally and informally to a range of languages. A de-facto standard data processing stream is evident, with analysis most often using open-source analytic software SPM.

Conclusion: While language fMRI is well established for presurgical language mapping in epilepsy, the protocols used across sites vary markedly and some of the best-validated protocols appear to be rarely used. There is a strong need for comprehensive, accessible guidelines for clinical fMRI and for open, freely available, replicable approaches that can be adopted at any site. Key points for successful use of fMRI in the clinic are noted.

Neuroimmunology 1

EPR1130

Neurological complications of antiTNF therapies: 16 years tertiary University Hospital experience

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Background and aims: AntiTNF therapies (infliximab, etanercept, adalimumab, golimumab) are widely used in Rheumathology (rheimatoid arthitis, RA, ankylosing spondylitis, AS, psoriatic arthritis, PA), and Gastroenterology (inflamatory bowel disease, IBD). Increased risk of infection and malignancy are common concerns, but neurological complications are considered rare.

Methods: Retrospective analysis of the electronic database of our tertiary university hospital Neurology Department, from 2002-2017, with the search terms antiTNF, infliximab, etanercept, adalimumab, and golimumab. Patients with neurological complaints while on active treatment with these agents were included, clinical variables analysed with appropriate statistical tests.

Results: 15 episodes of 14 patients, 53.4% female with a mean age of 53 years (±8.1DE), on treatment with infliximab (9), adalimumab (6) and golimumab (1) because of IBD (7), RA (5), SA (4), PA (1) and pyoderma gangrenosum (1) were included. No neurological complications related to etanercept were found. Clinical diagnosis was stroke or TIA in 9, demyelinating central nervous system disease in 3, cerebral venous thrombosis in 1, and other diagnoses in 3. Symptoms were deemed unrelated to antiTNF treatment in 5 cases (31%): 2 patients with stroke (atherothrombotic and cardioembolic stroke), 1 patient with psychogenic neurological symptoms and 2 patients with secondary headache (to calcium blockers and aseptic meningitis respectively). Neurological complaints prompted antiTNF discontinuation in 4 (30.7%)

Conclusion: In our experience, neurological complications of antiTNF therapies are rare, being infliximab the most commonly involved. Demyelinating disorders and venous thrombosis, previously described, are represented. A posible association with stroke of undetermined etiology should be assessed with prospective studies.

Disclosure: Nothing to disclose

EPR1131

Establishment of a high-throughput microELISA screen for naturally occurring human tau autoantibodies

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Background and aims: Currently, treatment strategies for tauopathies are scarce and there is a need for specific treatment options. A new approach striving towards the development of novel disease-modifying strategies for neurodegenerative diseases is the of use naturally occurring monoclonal antibodies as therapy. To interrogate the human immune repertoire, a high-throughput screen for naturally occurring tau antibodies will be performed to explore the potential value of tau antibodies as diagnostic biomarkers and therapeutics.

Methods: The Institute of Neuropathology has developed a high-throughput screening platform that allows for screening of 20,000 patients for naturally occurring antibodies against multiple antigens. Recombinant monomeric and aggregated tauK18 as well as full-length tau441 will be absorbed to 1536-well plates and heparin plasma samples will be serially diluted using acoustic dispensing technology. Tau autoantibodies will be detected using an indirect microELISA that runs in a fully-automated robotic platform.

Results: Preliminary data from an initial 953-patient screen showed distinctly reactive patients (negative logarithmic EC50 $\geq$ 2) for tauK18 monomers (corresponding to the 4-repeat sequence of the aggregation domain of tau). To confirm these, competitive ELISAs were performed.

Conclusion: The initial 953-patient screen served as proof-of-feasibility for the microELISA screen for naturally occurring human tau autoantibodies. We will continue to screen 20,000 patients and perform an epidemiological study of tau autoantibodies correlating patient reactivity with clinical data. This will enable us to explore the potential of tau autoantibodies as diagnostic biomarkers of tauopathies and elucidate on the current controversy about the occurrence of anti-tau autoantibodies in healthy vs. diseased subjects.

Disclosure: Nothing to disclose

EPR1132

Soluble factor profile in Natalizumab treated MS patients: increased Th1 promoting factors and sHLAg

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Background and aims: Natalizumab, a humanized monoclonal antibody targeting the cell adhesion molecule a4-integrin, is an effective treatment in multiple sclerosis (MS) preventing inflammatory blood cells from transmigration into the brain. The rare association of the development of progressive multifocal leukoencephalopathy (PML), due to reactivation of JCV polyomavirus, during natalizumab treatment limits its safety. The risk to develop Natalizumab associated PML is evaluated by the detection of JCV-Abs in serum, previous use of immunosuppressant and Natalizumab treatment for more than 24 months.

Methods: In the present study we analyzed serum soluble factors, cytokines and chemokines, soluble (s)HLA-G expression and its genotype (insertion/deletion 14base pairs, +3142 C>G), immunophenotype in order to understand if these factors are associated with PML risk. 19 RRMS were included and analyzed before therapy, 12 and 24 months after therapy.

Results: CXCL10 decreases between T0 and T24, while IL2, IL12p40, IL12p70, TNFa and IL23 increased. IFNg, GM-CSF, IL17, IL10, IL4, IL1, IL6 and CXCL13 do not vary. sHLA-G level divides the patient group into low (ins/ins; G/G), medium (ins/del; C/G) and high (del/del; C/C) producers depending on the HLA-G genotype and is stable in medium and low producers during therapy whereas increases in high producers.

Conclusion: In conclusion Natalizumab therapy seems to shape the inflammatory profile of patients increasing factors that promote Th1 differentiation and is increasing sHLAg production only in a sub group of patients. If this correlates with previous therapies, MS relapses after drug discontinuation or detection of PML risk factors is under investigation.

Disclosure: Nothing to disclose

EPR1133

Modulation of c-Jun N-terminal kinase as target in Multiple Sclerosis treatment

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Background and aims: Multiple Sclerosis (MS) is an inflammatory and degenerative pathology, thus far incurable, of the central nervous system. c-Jun N-terminal kinase (JNK), a mitogen activated kinase (MAPK), is involved in regulation of cytokine gene-expression, immunecell differentiation, neuronal-death-pathways and regulation of astrocyte inflammatory genes and might therefore influence pathomechanisms of MS. In an animal model of MS (experimental autoimmune encephalomyelitis, EAE), and in peripheral leukocytes of MS-patients upregulation of JNK was shown during active disease.
We aimed at investigating the influence of JNK-inhibition on the clinical EAE-course and its effect on T-cell viability in vitro.

Methods: Chronic EAE was induced by active immunization with MOG35-55 in female C57BL/6 wildtype mice. SP600125, a reversible ATP-competitive inhibitor of JNK 1-3, was given orally (30mg/kg, 15mg/kg or vehicle; n=6) on 9 successive days after individual disease onset (10 point scale EAE-Score $\geq$2).
Jurkat T-cell (T-ALL cell line) apoptosis in vitro by SP600125 (10μM) compared to control (DMSO) was analysed by FACS (AnnexinV/PI; 24h; n=5).

Results: In vivo treatment with 30mg/kg SP600125 significantly reduced disease-severity (p<0.0001) compared to controls (mean cumulative EAE-scores ±SD: control=3.5 ±0.8), 15mg/kg=2.9 ±0.5), 30mg/kg=2.2 ±0.4). SP600125-treated Jurkat T-cells exhibited increased apoptosis compared to control (mean±SD: 2.7-fold ±0.8; p<0.01).

Conclusion: Functional relevance of JNK-inhibition is indicated by a therapeutic effect on EAE-disease course. Upregulated apoptosis in an immortalized immune cell line in vitro could indicate potential mechanisms of action via depletion of T-cells. Detailed underlying mechanisms are currently under investigation.

EPR1134

Neuromyotonia in thymoma-associated myasthenia gravis: a clinico-serological study

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Background and aims: Acquired Neuromyotonia (NMT) is an autoimmune condition frequently associated with anti-contactin-associated-protein-like-2 (Caspr2) antibodies. NMT can occur as a paraneoplastic disorder in patients with thymoma, alone or in combination with Myasthenia Gravis (MG). Recently, antibodies against netrin-1-receptors (DCC and UNC5A) have been reported as predictors of thymoma in 6/9 patients with concomitant NMT and MG. We aimed to clinically characterize a large cohort of patients with thymoma-associated MG, and to explore serological correlation of NMT symptoms.

Methods: 268 consecutive patients with thymoma-associated MG were retrospectively collected. NMT was defined as muscle twitching/cramps in at least 2 skeletal districts. Patients with NMT(23) were screened for anti-neuronal antibodies by immunohistochemistry on rat brain and cell based assay.

Results: 23/268 patients developed NMT symptoms (muscle twitching, 3; cramps, 3, or both, 17). Overall, 33/268 patients with thymoma had a tumor recurrence, which was more frequent in those with (8/23) vs those without NMT (25/245, p=0.003). NMT onset preceded the tumor recurrence in 5/6 patients. In univariate analysis predictors of thymoma recurrence were younger age at thymectomy (odds ratio-OR:0.95, confidence interval-CI:0.93-0.97), Masaoka staging (OR:10.73, CI:2.38-48.36) and NMT (OR:4.69, CI:1.76-12.46). 6 patients with NMT had anti-neuronal antibodies (patient#1: Caspr2; patient#2: AMPAR; patient#3: DCC; patient#4: LGI1; patient#5: Caspr2+LGI1+DCC+UNC5A; patient#6: Caspr2+LGI1+DCC). Thymoma recurrence was found less frequently in negative (3/17) vs positive patients with NMT (4/6, #1, #2, #5 and #6; p=0.045).

Conclusion: The occurrence of NMT symptoms in patients with thymoma-associated MG can predict tumor recurrence, and warrants a closer oncologic follow-up. Anti-neuronal surface autoantibodies may be useful to further stratify the recurrence risk.

Disclosure: This work was funded by the 'Ricerca finalizzata ministeriale 2015-2017' provided by the Italian ministry of health

EPR1135

Prognostic impact of MOG antibodies titres in adults with an acquired demyelinating syndrome.

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Background and aims: Myelin oligodendrocyte glycoprotein antibodies (MOG-Ab) have been detected in adult patients with acquired demyelinating syndromes (ADS). Whether MOG-Ab titres predict relapse risk and disability is, currently, unknown.

We evaluate the usefulness of MOG-Ab titres to predict disease course and prognosis in adult patients with MOG-Ab-associated diseases.

Methods: Retrospective nationwide study including 62 MOG-Ab-positive patients aged ≥18, whose samples were obtained within 3 months after the first ADS. MOG-Ab were tested using a cell-based assay. MOG-Ab titres were categorized as low (≤1/1280), intermediate (1/2560-1/5120), and high (≥1/10240) levels. First, we studied association between clinical characteristics and MOG-Ab titres. Second, we investigated, with Cox regression models, the risk of relapse according to categorical MOG-Ab titres. Finally, we used a logistic regression model to investigate the association between disability (EDSS≥3.0 at last follow-up) and categorical MOG-Ab titres.

Results: Patients were mainly Caucasians (91.9%) with a median age at onset of 38.5 years and 54.8% were females. The only epidemiological/clinical features associated to MOG-Ab titers was ethnicity, and Caucasians had lower titers (median 5120) than other ethnicities (median 2560), p =0.030. No association was observed with clinical phenotype at onset or at last follow-up. Categorical MOG-Ab titers did not predict risk to a further relapse (figure1). Finally, categorical MOG-Ab titres were not related to further disability.
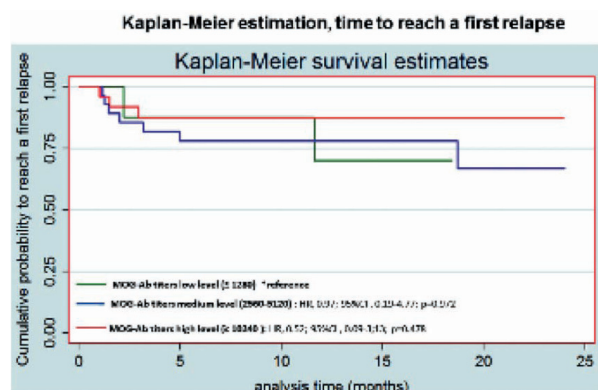
Figure 1.

Conclusion: In the present cohort of adults with MOG-Ab-associated diseases, MOG-Ab titres at onset of disease were not associated with a specific clinical phenotype, and do not predict neither disease course nor prognosis. Caucasians displayed higher MOG-Ab titres than other ethnicities.
Disclosure: Nothing to disclose

EPR1136

Proinflammatory MAIT (mucosal-associated invariant T-cells) cells react to gut flora yeasts and infiltrate multiple sclerosis CNS.

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Background and aims: The ability of intestinal microbiota to sustain an inappropriate immune reaction, such as in autoimmunity, at distant sites has been recently shown in animal models of disease. Similarly, the possibility to generate protective immune responses through the inoculation of selected commensal bacteria which induce regulatory cells has also been shown.
Methods: We have found that a distinct population of cells named MAIT (mucosal-associated invariant T) cells is expanded in individuals with Multiple Sclerosis (MS). These cells are IL-17 producers, they preferentially home to the intestine but can gain access to the brain. Here, we studied the gut microbiota in MS patients and in homozygotic twin pairs discordant for disease; we then studied the response of MAIT cells to yeast strains isolated from faecal samples from MS patients.
Results: We find that the frequency of MAIT cells is significantly increased in the peripheral blood of MS patients and that these cells are equipped with the array of molecules necessary for migration in the CNS. We show that in MS patients the gut mycobiota profiles are different compared to those of healthy volunteers. Furthermore, our immunological in vitro studies consistently show a higher reactivity to yeast extracts in cells of the innate arm of the immune system isolated form MS patients. CD8+ MAIT cells produce proinflammatory cytokines in response to yeast extracts obtained from MS patients.
Conclusion: In conclusion, we show for the first time that proinflammatory MAIT cells respond to yeasts that are more represented in the feces obtained from MS patients.
Disclosure: Nothing to disclose.

Neurological manifestations of systemic diseases

EPR1137

Progressive trigeminal neuropathy, limbic encephalitis and abdominal ganglionitis without primary cancer: an atypical case of anti-Hu auto-immune encephalitis

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Conclusion: Anti-Hu antibodies (Hu-Abs) are the most frequent onconeural antibodies associated with paraneoplastic neurologic syndromes (PNS). PNS include a variety of neurological syndromes, affecting less than 1/10,000 patients with cancer. In the majority of cases, PNS will occur before the malignancy is diagnosed. PNS can affect different levels of the central, peripheral en autonomous nervous systems. Multifocal involvement is common. Patients typically develop sensory neuropathy, cerebellar degeneration, limbic encephalitis and autonomic disfunction. The clinical course is monophasic and progressive with a poor prognosis. We present a case of 58-year-old man who developed a progressive trigeminal neuropathy over a period of 5 years, in combination with cerebellar degeneration, asymmetrical brainstem and limbic encephalitis. Serum showed repeatedly high positive anti-Hu antibodies. Repeated whole body FDG-PET-CTs could not demonstrate any primary malignancy. Patient was treated with corticosteroids and plasma exchange, without beneficial effect. Patient died after 5 years of the complications of an intestinal obstruction. Post-mortem autopsy revealed ganglionitis probably due to anti-Hu syndrome. Post-mortem autopsy revealed no primary malignancy. Brain autopsy showed gliotic changes in brain stem, hippocampus, amygdala and cingulate gyrus. Auto-immune anti-Hu encephalitis cases associated with SCLC or other primary neoplasms are described in literature, but this case is the first in which a progressive multifocal neurological syndrome occurs in the presence of positive anti-Hu antibodies, but without any primary neoplasm.
Disclosure: Nothing to disclose

EPR1138

Outcomes of Patients with Hereditary Transthyretin-Mediated Amyloidosis with Early Onset V30M versus all other Mutations in APOLLO, a Phase 3 Study of Patisiran

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Background and aims: Hereditary transthyretin-mediated (hATTR) amyloidosis is a multi-systemic, life-threatening, autosomal dominant disease caused by transthyretin gene mutations resulting in neuropathy and cardiomyopathy. Patisiran, an investigational RNAi therapeutic, resulted in statistically significant improvement in neuropathy (mNIS+7) and Norfolk Quality of Life for Diabetic Neuropathy (Norfolk QOL-DN) measures compared to placebo in hATTR amyloidosis patients and was generally well tolerated in the Phase 3 APOLLO study. We evaluated patisiran efficacy and safety in patients with early onset V30M versus all other mutations.
Methods: APOLLO was a multi-centre, international, randomized (2:1), double-blind study of patisiran 0.3mg/kg or placebo IV q3W in hATTR amyloidosis patients with polyneuropathy (NCT01960348). Primary endpoint was change from baseline at 18-months in mNIS+7 with multiple secondary endpoints including Norfolk QOL-DN. Pre-specified subgroup analyses were conducted to evaluate patients with early onset V30M (≤50 years of age at onset) and those with all other mutations including late onset V30M (>50 years of age at onset).
Results: APOLLO enrolled 225 patients with 39 different TTR mutations including 42.7% with V30M mutations with 10.2% considered to have early onset V30M disease. Similar to the overall patient population, patisiran demonstrated improvement in mNIS+7 and Norfolk QOL-DN compared to placebo in early onset V30M and as well as in all other mutations at 18-months (Tables 1, 2). Efficacy and safety data to be presented.

Disease characteristics	Placebo		Patisiran	
	N	LS Mean (SEM)	N	LS Mean (SEM)
mNIS+7				
Overall	77	74.6 (37.0)	148	80.9 (41.5)
Early onset V30M	10	68.9 (15.8)	13	81.1 (13.0)
All other mutations	66	75.5 (4.3)	135	80.9 (3.5)
Norfolk QOL-DN				
Overall	76	55.5 (24.3)	148	59.6 (28.2)
Early onset V30M	10	46.0 (7.6)	13	61.7 (9.9)
All other mutations	66	57.0 (3.0)	135	59.4 (2.4)

Table 1. mNIS+7 and Norfolk QOL-DN Baseline Values (Means)

Analysis	Disease Characteristics	Number of Patients (Placebo)	Number of Patients (Patisiran)	Treatment Difference (Patisiran-Placebo)	95% Confidence Interval
mNIS+7	Overall	77	148	-34.0	-39.9,-28.1
	Early Onset V30M	8	13	-22.3	-35,-9.5
	All Other Mutations	57	128	-36.1	-42.6,-29.6
Norfolk QOL-DN	Overall	77	148	-21.1	-27.5,-15.1
	Early Onset V30M	8	13	-21.1	-45.1,2.9
	All Other Mutations	57	128	-21.5	-28.2, 14.9

Table 2. mNIS+7 and Norfolk QOL-DN Results at 18-months

Conclusion: Patisiran, investigated in patients with early and late onset V30M as well as a wide range of non-V30M genotypes, demonstrated consistent benefit over placebo in mNIS+7 and Norfolk QOL-DN.

Disclosure: This research was supported by Alnylam Pharmaceuticals.

EPR1139

Population Pharmacokinetic (PK)/Pharmacodynamic (PD) Model of Serum Transthyretin (TTR) following Patisiran-LNP Administration in Healthy Volunteers and Patients with Hereditary TTR-Mediated (hATTR) Amyloidosis With Polyneuropathy

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Background and aims: hATTR amyloidosis is a rapidly progressive disease induced by deposition of TTR protein in multiple organs leading to morbidity and mortality. The PK/PD relationship between plasma ALN-18328 concentrations (siRNA) and serum TTR reduction following administration of patisiran-LNP was investigated.

Methods: Longitudinal PK and PD data were pooled from 5 clinical studies following single and multiple-dose administration of placebo and patisiran-LNP in healthy volunteers and patients over a wide dose range (0.01 to 0.5mg/kg). Non-linear mixed effects modelling was used to characterize the PK/PD relationship, quantify intra- and inter-individual variability, and evaluate covariate effects.

Results: PK and PD data from 283 subjects (84 placebo and 199 patisiran-LNP) were pooled. An indirect response model linking ALN-18328 plasma concentrations to inhibition of synthesis rate of TTR best described serum TTR reduction, with an IC50 of 9.45ng/mL. Average steady state ALN-18328 plasma concentrations from 0.3mg/kg q3w patisiran-LNP administration yields 80% to 90% reduction in serum TTR. Covariate analysis indicates similar TTR lowering across all subgroups including baseline age, body weight, sex, race (Caucasian/non-Caucasian), TTR genotype (V30M mutation/non-V30M mutation), mild hepatic impairment, and mild and moderate renal impairment. A 30mg dose for patients >or=100kg was predicted to have similar TTR lowering to 0.3mg/kg in patients up to 100kg.

Conclusion: Patisiran-LNP dose of 0.3 mg/kg q3w in patients up to 100 kg and 30 mg q3w in patients ≥100kg is supported by results from PK/PD modelling and simulation. No dose adjustment is required for any subgroups.

Disclosure: This research was supported by Alnylam Pharmaceuticals.

EPR1140
withdrawn

EPR1141

Long-term follow-up of patients with Neuro-Behçet's disease

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Background and aims: Neuro-Behçet's disease (NBD) is the most debilitating organ involvement of Behçet's disease. In this study, we present long-term follow-up of a large group of patients with Neuro-Behçet's disease.

Methods: We included all patients with NBD who had been followed up in our institution since 1973 in our study. We collected data including clinical and laboratory features, clinical course, and the effect of treatment. A new neurologic disability scale called the Neuro-Behçet's Disability Score (NBDS) devised for patients with NBD was employed to quantify patients' disabilities.

Results: We collected clinical data of 430 patients (291 males, 139 females). The mean follow-up period of patients was 5.2 ± 6.5 years. Patients with parenchymal NBD (p-NBD) had more relapses (41.4% vs. 13.5%; p<0.001), more frequent uveitis (60.3% vs. 46.1%; p=0.012), and a longer interval between the onset of NBD and BD (8.0 ± 7.8 vs. 6.2 ± 6.1; p=0.006). The most frequently involved region in p-NBD was mesencephalon (59.0%), followed by diencephalon (31.9%). Only the presence of uveitis and the time of onsets between BD and NBD predicted relapses in p-NBD.

Conclusion: Herein, we present an extensive series of patients with NBD. We employed a novel and quick assessment disability scale that fills a gap in this area. The presence of uveitis and the time between NBD and BD are prognostic factors for future relapses in p-NBD.

Disclosure: Nothing to disclose

EPR1142

The "face of the giant panda" sign on magnetic resonance imaging in adult onset of Leigh syndrome

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Background and aims: Mitochondrial diseases are a vast group of disorders with a broad of clinical expression related to the system or tissue affected. It presents primarily during infancy, but cases of adult onset have been described. The ''face of the giant panda'' sign on magnetic resonance imaging (MRI) is traditionally considered to be characteristic of Wilson disease. However it has also been reported in other metabolic and mitochondrial disorders.

Methods: Case Report

Results: A 25-year-old male presented with a four-month progressive vision loss and diplopia, associated with gastric pain. The neurological exam revealed bilateral internuclear ophthalmoplegia, upgaze palsy and abnormal vertical oculocephalic reflex. MRI revealed midbrain abnormalities, characteristic of the "face of the giant panda'' sign, with a hyperintensity caudal asymmetric extension of dorsal pons and medulla oblongata in T2. Systemic autoimmune diseases, serologies, metabolic and neoplastic investigation were negative in blood, urine and in CSF. Abdominal echography showed a hepatosplenomegaly. Genetic studies disclosed a homozygous mutation of SURF1 gene. Patient has started antioxidant medication. At a 6 month follow-up there was a clinical and neuroradiological improvement, with no other new symptoms.

Conclusion: Leigh syndrome is a progressive neurodegenerative mitochondrial disorder. It is a genetically heterogeneous disease characterised by a diverse spectrum of phenotypes with a variable neuroimaging findings and disease course. Although the survival rate in Leigh syndrome is generally poor, SURF1-deficient has been described as having a more favourable survival outcome. This patient is a rare case of Leigh syndrome, with limited clinical manifestations, misleading MRI findings and a clinical improvement with treatment.

Disclosure: Nothing to disclose

EPR1143

Partially reversible parkinsonism as an initial manifestation of brain vasculitis: an atypical case of polyarteritis nodosa with neurological involvement.

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Background and aims: Polyarteritis nodosa (PAN) is a rare inflammatory necrotizing vasculitis in which direct brain vascular damage is rare, occurs lately in the course of the disease and it usually presents as diffuse encephalopathy or multifocal deficits.

Methods: We describe an atypical form of brain vasculitis in a patient previously diagnosed with PAN. We then review current literature about brain involvement in PAN and related diseases.

Results: A 49-year-old woman with an established PAN diagnosis with skin complications and sensitive polyneuropathy presented at the emergency department with a rapid progressing akinetic-rigid syndrome consisting of hypokinesia, hypophonia, dysarthria, postural instability and gait disorder. Brain MRI showed multiple bilateral ischemic lesions affecting basal ganglia and subcortical white matter. Further studies discarded thrombophilia and other connective tissue diseases. Cerebrospinal fluid was normal except for mildly increased protein count. With the suspicion of brain vasculitis, we started high-dose methylprednisolone treatment observing a rapid improvement of the neurological symptoms.
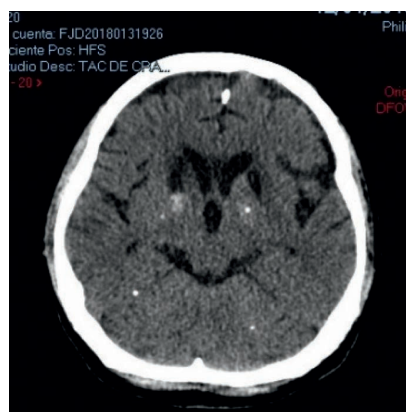
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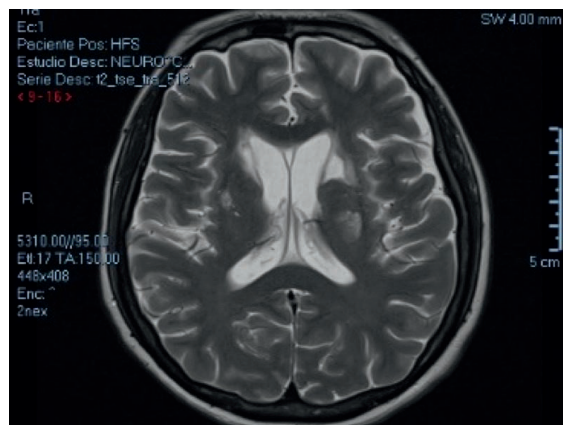
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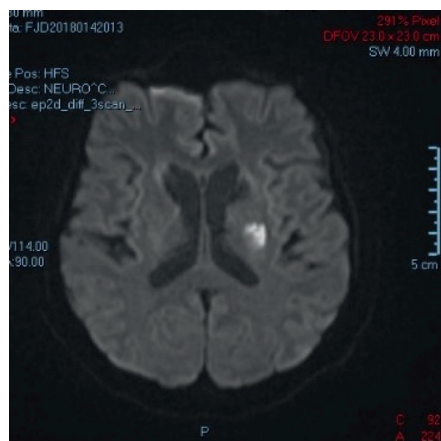
Diffusion

Conclusion: This case report constitutes an extremely atypical form of neurological involvement in PAN. While other atypical forms of CNS involvement have been associated with PAN, parkinsonism cases as the presenting form of PAN are scarce in literature. To our knowledge most parkinsonism syndromes associated with autoimmune diseases appear in the context of systemic lupus erythematosus and are also considered rare. Proposed pathophysiologic mechanism in SLE parkinsonism consists of multiple inmmune-mediated microinfarcts involving basal ganglia and subcortical white matter. As in the case we present here, usually there is a rapid and even complete response to steroid therapy.

Disclosure: Nothing to disclose

EPR2143

A difficult case of Immunoglobulin G4-Hypertrophic Pachymeningitis - Rituximab as part of the solution

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Background and aims: Immunoglobulin G4 (IgG4)-related disease is a recently recognized fibro-inflammatory condition. Its spectrum encompasses hypertrophic pachymeningitis (HP) which is often a challenging neurological manifestation.

Methods: n.a.

Results: A 70-year-old man developed progressive right ptosis and vision loss during the previous year, associated with frontal headache. Brain MRI depicted right frontal lobe hypersignal with homogeneous enhancement and meningeal thickening with dural enhancement along the falx and right frontal area; brain CT showed ethmoidal and frontal bone erosion.

An exhaustive serum and cerebrospinal fluid study for autoimmune, neoplastic and infectious causes was unremarkable. A cerebral biopsy was performed revealing a lymphoplasmacytic infiltrate, storiform fibrosis, and more than 10 IgG4-expressing plasma cells per field, consistent with IgG4-related HP.

The patient initiated oral corticotherapy which was tapered as the symptoms improved, but the patient started bilateral progressive deterioration of visual acuity with increased meningeal thickening on MRI. He received a 5-day course of intravenous methylprednisolone, followed by prednisolone, but there was no clinical improvement. Subsequently, he was treated with two infusions of rituximab with a slight improvement of visual acuity, but brain and orbits MRI remained unchanged and intrathecal rituximab administration was attempted.

Conclusion: Intravenous rituximab is emerging as a promising therapeutic strategy in patients with IgG4-related HP who respond poorly to steroids. Recent literature advocates intrathecal administration of rituximab in patients who fail to improve after its intravenous administration based on poor blood-brain barrier penetration of the drug.

Disclosure: Nothing to disclose

Neuro-ophthalmology/neuro-otology; Spinal cord and root disorders

EPR1144

Thalamic exotropia from paramedian thalamic infarction

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Background and aims: The supranuclear pathways for vergence eye movements are still not fully understood. It has been proposed that loss of vergence control can be caused by interruption of supranuclear pathways. Thalamic infarction might lead to such an interruption, as cortico-mesencephalic fibers traverse the paramedian thalamus. It is well established that unilateral lesions of the posterior thalamus may cause 'thalamic esotropia'(1). Likewise, convergence excess has been reported in a patient with bilateral paramedian thalamic-infarctions(2)and contralateral convergence paresis in unilateral thalamotectal haemorrhage(3). We here report a patient with thalamic exotropia from ipsilateral paramedian thalamic infarction.

Methods: Case presentation:
A 26-year-old female patient presented with horizontal diplopia and exotropia of the left eye in primary-gaze; upward-gaze was slowed bilaterally.
cMRI and neuro-ophthalmologic testing performed, inluding computer perimetry, test of skew and assessment of cyclorotation of the eyes and the subjective visual vertical. Detailed ocular motor and vestibular examination was performed by means of videooculography and rotational chair testing.

Results: Vergence testing revealed slowed convergence movement of the left eye, whithout other symptoms. Pupillary-light-reaction was normal.
cMRI disclosed unilateral left sided paramedian thalamic-infarction.

cMRI Flair

Gaze

Conclusion: The findings suggest that the syndrome of thalamic exotropia -not yet been described in the literature- is secondary to unilateral interruption of supranuclear fibers to midbrain vergence neurons, our findings support prior suggestions that descending cortical pathways pass the paramedian thalamus and exert an input to premotor vergence neurons in the midbrain. It is likely that this unilateral lesion has selectively interrupted projections to 'near-response-cells' to the medial rectus motoneurons on a supranuclear level(4).
Disclosure: Nothing to disclose

EPR1145

Pharmacological treatment of acquired pendular nystagmus: a case series

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Background and aims: Acquired pendular nystagmus (APN) is a rare but debilitating type of central nystagmus. Main causes include vascular lesions and multiple sclerosis. APN is attributed to brainstem and cerebellar dysfunction and almost always requires treatment due to severe oscillopsia. So far memantine and gabapentin have proven somewhat effective although often therapy efforts can be frustrating. In this study we evaluated the effect of acetyl-DL-leucin, a modified amino acid, on APN, as this drug has emerged in recent years as therapeutic option in cerebellar dysfunction, in comparison to standard therapies with gabapentin and memantine.

Methods: We evaluated nine patients with APN of different aetiology before and after therapy with memantine, gabapentin and acetylleucin. Eye movements were evaluated by performing a thorough neuro-opthalmological examination and videooculography, including testing of smooth pursuit, saccade, optokinetic nystagmus and gaze holding. The clinical examination was also documented with video recordings.

Results: Four out of nine patients responded to acetyl-DL-leucin 5g/d therapy. In those patients optimal results were achieved when acetyl-DL-leucin was combined with memantine 20-40mg/d. Other two patients responded partially to gabapentin monotherapy, whereas the remaining three patients did not respond to pharmacological treatment

Conclusion: Acetylleucin provides a new therapeutic alternative to APN therapy and should be tested individually on these patients, since its side effects are negligible.

Disclosure: Nothing to disclose

EPR1146

Response to eslicarbazepine in patients with vestibular paroxysmia

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Background and aims: Vestibular paroxysmia (VP) is a neurovascular compression syndrome characterized by recurrent spontaneous spells of dizziness/vertigo. Excellent response to carbamazepine has been referred and indeed, it has become a diagnostic criteria for this entity. Other antiepileptic drugs have been tried with different results. The aim of this studio was to describe safety and effectivenes of eslicarbazepine in a case series of patients from a tertiary hospital in Spain.

Methods: Descriptive retrospective study of a case series of 10 patients with VP treated with eslicarbazepine

Results: Nine out of ten patients were female, with a mean age of 54.5 years (range 38-84 years) an a mean age at onset of 49.8 years (range 36-64 years). All had paroxismal spells of dizziness/vertigo of less than 60 seconds. All patients had spontaneous spells and 62.5% had episodes triggered by cephalic movements. There was no evidence of other ear or neurological diseases that could explain the symptoms. MRI revealed a vascular compression of the estatoacoustic nerve in 55%. The response with eslicarbazepine was complete in 80% of patients and partial in the rest. Two patients had to withdraw treatment due to adverse effects (skin rash n=1, hyponatremia n=1). Other mild adverse side effects was reported by two patients.

Conclusion: Eslicarbacepine could be an effective therapeutic option in vestibular paroxysmia. Drug treatment is usually safe and well-tolerated.

Disclosure: Nothing to disclose

EPR1147

Intramedullary tuberculosis in the Neurology department at the University Hospital Center of Conakry

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Background and aims: The diagnostic certainty of the medullar tuberculosis without Pott disease is difficult to establish in the tropical environment with the large group of infectious, parasitic and systemic myelopathies.

We report 13 cases of tuberculous myelopathies without Pott disease for the purpose of a reevaluation of this pathology from the clinical, neuroradiological and evolutionary point of view.

Methods: We retrospectively analyzed the files of 186 patients hospitalized in the Department of Neurology and Neurosurgery of the University Hospital Center of Conakry between 2008 and 2016 for the management of non-compressive and compressive myelopathy. Biological evidence of tuberculous infection was demonstrated for 13 patients (6.9%).

Results: Infectious clinical picture prior to the installation of neurological signs was reported in 11 patients (84.6%). The neurological signs were summed up by the existence of a sensitivomotor semiology of progressive evolution (100% of cases) with sphincter disorders in 11 patients (84.6%) and a medullary compression symptomatology with a lesion and under lesion syndrome from the outset in 4 patients (30.8%). Medullary MRI revealed an extensive intramedullary hyper signal in 9 patients with non-compressive myelopathy and in 4 cases, the lesions appeared in T1 hyper signal and T2 isosignal localized.

Lumbar puncture revealed lymphocytic pleocytosis, hypoglucorrhage (0.3 to 0.5 g / l) and leukocytosis.

Conclusion: The avenue of Magnetic resonance imaging has revolutionized the diagnostic management of pathology. The biopsy remains the essential element to make the diagnosis, but the therapeutic response, is not left behind.

Disclosure: Nothing to disclose

EPR1148

Spinal-cord Stimulation in Pain Relief

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Background and aims: Patients with painful diabetic peripheral neuropathy of the lower extremities can reduce their pain with spinal-cord stimulation(SCS).

Methods: From an initial 136 painful diabetic peripheral neuropathy patients screened, 50 met the inclusion criteria and started trial stimulation. The results are the conclusion of a 4-year multicenter prospective study.

The mean age was 49.3, and 39% were female. The majority(90%) of patients had type 2 diabetes. They underwent test implantation with the SCS under local anesthesia. The patients had been experiencing pai for 4.5 years. The scor from numerical rating scale(NRS) for pain at baseline was 6.5.

Results: The results were evaluated after 1 year and every year until 4 years. Success of treatment defined as pain relief was >50% after 4 years. The NRS score during the day was 3.8 and during the night was 3.9 after 12 months. After 4 years, the mean day score was 4.3 and the mean night score was 4.6.

Of the patients, 85% had treatment success at 1 year, falling to 69% at 2 years, 75% at 3 years, and 55% at 4 years; 75% were still using their devices after 4 years.

Two patients had SCS device infection, eight needed battery replacement until the end of study period.

Conclusion: In conclusion, the SCS is reserved for patients with severe pain due to the high costs. Unfortunately, in our country the device is currently in the experimental stage.

Disclosure: Nothing to disclose

EPR1149

Electromyography in acute abdominal wall paresis

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Background and aims: Acute abdominal wall paresis caused by thoracic radiculopathy is very rare entity. The first clinical symptom is usually pain irradiating to the lower chest or abdomen. Patients are visiting general practitioner, internist or surgeon; however, final diagnosis is often determined with a long delay.

Methods: Needle electromyography (EMG) of obliguus abdominis and rectus abdominis muscles was performed in 8 subjects (4 females, 36 - 78 years), accompanied by conduction study on the lower limbs. Magnetic resonance imaging (MRI) of spinal cord was performed in all subjects. Routine blood tests and cerebrospinal fluid (CSF) assessment was obtained, too.

Results: In all subjects, spontaneous abnormal activity (fibrillation, positive sharp waves) was present in abdominal muscles. In two patients, diabetic mixed sensorimotor neuropathy was found. Four patients had acute neuroborreliosis proved by blood and CSF tests. MRI revealed disc protrusions at the level Th12/L1 in one patient, and foraminal herniation at Th10/11 in the other one.

Conclusion: Spontaneous deep abdominal pain manifested by unilateral or bilateral partial paresis of the abdominal wall is a rare condition. Except routine cerebrospinal fluid assessment and MRI of spinal cord we recommend to add needle EMG where findings of spontaneous activity confirmed an acute thoracic axonal root lesion. After final diagnosis, therapy according to main cause has to be performed (surgery, antibiotics, etc.).

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Disclosure: Nothing to disclose

EPR1150

Cervical Spinal Cord Gray Matter Atrophy in Post-Polio Syndrome

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Background and aims: Post-polio syndrome (PPS) is defined by progressive persistent new muscle weakness or fatigability occurring after a stable interval, decades after the initial viral infection of spinal cord (SC) motor neurons. The precise mechanisms underlying PPS are unknown. Recent advances in MR sequence development now allow for reliable quantitation of SC gray matter (GM) in vivo. The aim of this study was to quantitate SC GM in PPS patients.

Methods: 20 patients with PPS (mean age 66.5 years [SD 4.53], 12 men) and 20 age and sex-matched healthy controls (HC) were investigated at 3T by axial 2D-AMIRA imaging (in plane resolution 0.5x0.5mm) (Weigel & Bieri 2017) at the intervertebral disc levels C2/C3, C3/C4, C4/C5, C5/C6 and C6/C7. SC GM areas were segmented manually.

Results: Compared to HC, PPS patients showed significant SC GM atrophy at all levels (C2/C3 $p=0.0405$, C3/C4 $p=0.0002$, C4/C5 $p<0.0001$, C5/C6 $p=0.0006$, C6/C7 $p=0.0356$). In multivariable regression analysis GM area at C2/C3 (with age and sex as covariates) explained 56% of neck flexor strength variance.

Conclusion: AMIRA imaging is a sensitive method to quantitate SC GM atrophy in vivo. Cervical SC GM areas were reduced in PPS compared to HC, and correlated with muscle strength in the corresponding myotome in PPS. Longitudinal studies are necessary to investigate atrophy over time, its relation to symptom evolution and possible prognostic value. The methodology used here is promising for the development of novel imaging surrogates not only for PPS, but also for other neurodegenerative, genetic or autoimmune mediated diseases of the SC.

Disclosure: Nothing to disclose

EPR1151

Cervical musculoskeletal disorders: occupational and individual risk factors

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Background and aims: Cervical musculoskeletal disorders (CMSD) represent a common cause of morbidity, including absenteeism, as well as change/loss of employment. As the characterization of CMSD as occupational diseases remains debated. our objective was to evaluate the prevalence of CMSD in a cohort of employees, assessing potential personal and occupational risk factors.

Methods: The sample included a total of 473 employees from 31 private companies in the meat processing industry (2012-2013; Northern Italy). Participants were evaluated by two occupational physicians, who also personally analyzed the specific occupational risks. Working definition of CMSD is described. Associations between CMSD and current working conditions, as well as psychosocial factors were analyzed by means of Poisson regression models and calculation of corresponding proportional rate ratios (PRR).

Results: CMSD were identified in 49 out of 397 employees (12.3%) who completed the survey. Among the assessed occupational factors, only exposure to temperatures <17 ° C was actually associated with CMSD (PRR 2.510 95% CI 1.152-5.469). Among individual risk factors, a significant association was found for sedentary lifestyle (PRR 2.583 IC95% 1.173-5.687) and a personal history of low back pain (PRR 2.003 IC95% 1.006-3.986).

Conclusion: Workers from the meat processing industry are usually recognized as exposed to the highest levels of professional constraints. Although our study confirms a high prevalence (12.3%) of cervical pain, our data confirm the lack of a sound association between CMSD and occupational risk factors.

Disclosure: Nothing to disclose

Neurorehabilitation 1

EPR1152

Effect of treadmill training on challenging walking in people with Parkinson's Disease

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Background and aims: Impaired walking ability is one of the important motor symptoms in patients with Parkinson's Disease (PD). Walking ability under challenging conditions, such as dual-task walking, can predict the risk of falls. Treadmill training is commonly used in gait rehabilitation, but its effects on over-ground challenging walking in patients with PD are not clear. The purpose of this study is to investigate effect of treadmill training on walking ability under cognitive loads in patients with PD.

Methods: Eight individuals with PD received 8 weeks of treadmill training. Temporal spatial gait parameters were evaluated in single task over-ground walking with comfortable and fast speeds. The evaluations were also performed under challenging walking conditions which were dual task walking under cognitive loads of spatial memory, stroop, and calculation tasks. The evaluations were performed before training and after 4 and 8 weeks of training.

Results: The walking speed and step length increased (p=.012) after 4 weeks in single task comfortable speed walking but not in fast speed walking (p>.05). It took eight weeks for the walking speed and step length to improve in walking under cognitive loads of spatial memory and calculation tasks (p<.05). The cognitive performance did not change after training.

Conclusion: The effect of treadmill training can be translated to over-ground walking and walking under challenging conditions. Longer time of training is required for PD patients to obtain benefits of walking under challenging conditions.

Disclosure: Nothing to disclose

EPR1153

Computational Analysis of Movement for Evaluation of Motor Function Impairment after Stroke.

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Background and aims: Motion capture systems are used in neurological rehabilitation. We aimed to explore the usefulness of MCS to obtain an objective measurement of functional status after stroke.

Methods: Prospective observational case-control pilot study. Acute stroke patients and controls performed a battery of exercise in front of the camera Microsoft Kinect® and the movement were analyzed in the three-dimensional space with the software Akira®. The differences in performance before and after each exercise and between both sides of the body were compared between groups. The correlation between the NIHSS score and the mRS score were analyzed. The patients also were evaluated at 3 months.
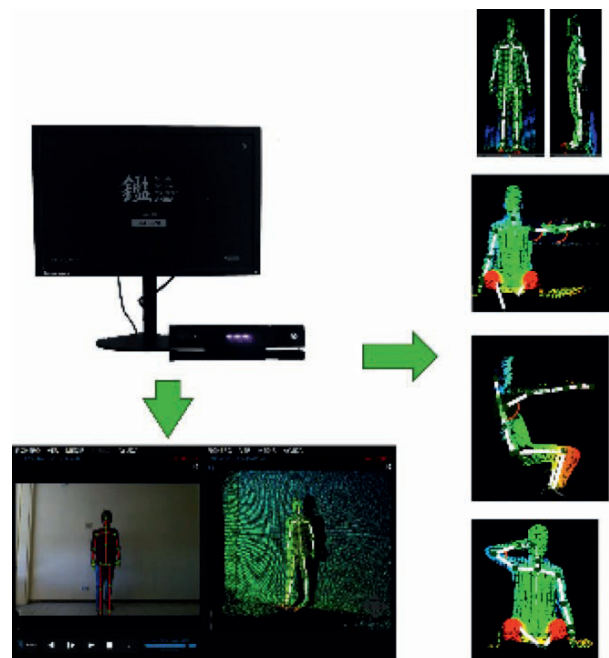
Microsoft Kinect with Software Akira. Exercises included in the study: balance, abduction of arm and flexion of shoulder and elbow.

Results: 72 controls and 37 patients were analyzed. The median NIHSS score was 2 (rank 0-12), and the median mRS was 0 (rank 0-4). The measurements that showed better discrimination capacity were those obtained from the

abduction of the arm: the shift of the joint angles was different between groups in the frontal plane of the elbow, shoulder, and forearm; all in pronation and supination (p<0.001). Those differences were independent of the NIHSS score, but were moderately correlated to the mRS score at the moment of the evaluation: elbow in supination (Rho=0.41, P=0.01); shoulder in pronation (Rho=0.45, P=0.006) and supination (Rho=0.64, P<0.001). There were no significant differences in those angles at 3 months.

Conclusion: Computational analysis of movement could be a useful tool for evaluation of upper limb function in stroke patients with slight deficit underestimated using current clinical scales, but correlated with outcome.

Disclosure: The research group of Cerebrovascular diseases of La Paz University Hospital has a collaboration agreement with System Friend Inc, an enterprise that provides the software and hardware used in the study.

EPR1154

Structural and Functional MRI Correlates of Motor Performance in Patients with Multiple Sclerosis

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Background and aims: Motor impairment affects a large proportion of multiple sclerosis (MS) patients. We applied voxel-wise methods and an independent component analysis in a large cohort of MS patients to evaluate correlations between abnormalities of brain gray matter (GM) volumes, white matter (WM) architecture and resting state functional connectivity (RS FC) and clinical and functional measures.

Methods: From 134 HC and 366 right-handed MS patients, brain 3D T1-weighted, diffusion tensor and functional MRI scans were acquired and used to perform an analysis of correlations with Expanded Disability Status Scale (EDSS), manual dexterity [9 Hole Peg Test (9HPT) and Finger Tapping (FT) test] and mobility [Timed 25 Foot Walk Test (T25FW)] tests.

Results: Compared with HC, MS patients showed a widespread pattern of GM atrophy. The analysis of WM architecture showed a distributed reduction of fractional anisotropy and an increased axial, radial and mean diffusivity in MS patients. RS FC was decreased in MS patients compared to HC, both in sensory-motor and cognitive networks. In MS patients, worse performance at 9HPT and higher EDSS correlated with atrophy of putamen, insula and cerebellum, whereas worse FT and T25FW performances correlated with atrophy in temporal areas. Several correlations between altered diffusion indexes and worse motor performances were found. Finally, correlations between lower RS FC and worse motor performances were found in all investigated networks.

Conclusion: Structural and functional abnormalities of cerebellum and deep GM structures contribute to explain motor dysfunction in MS patients.

Disclosure: Partially supported by Fondazione Italiana Sclerosi Multiple (FISM2013/S/1).

EPR1156

Methodology Matters: Comparing Approaches for Defining Persistent Post-Concussion Symptoms

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Background and aims: Post-concussive symptoms (PCS) such as headache, dizziness, fatigue, sleep disturbance, poor concentration, forgetfulness, irritability, and/or mood changes are common after mild traumatic brain injury (mTBI). The symptoms are not specific to mTBI, they are frequently experienced by other patient groups and healthy individuals. To complicate matters further, the tests used in research and clinical practice, and the definitions of persistent symptoms, vary considerably. The purpose of this study is to evaluate how the methodology used to define persistent PCS can influence the outcome of a study.

Methods: We included 221 patients who sustained mTBIs according to the WHO criteria, 64 age- and sex-matched trauma controls, and 74 community controls. The patients completed the Rivermead Post Concussion Symptoms Questionnaire (RPQ) and the British Columbia Postconcussion Symptom Inventory (BC-PSI) three months after injury. We compared and contrasted 11 methods for evaluating persistent PCS, including ICD-10 postconcussional syndrome diagnostic criteria as well as other commonly used criteria for defining persistent symptoms.

Results: The prevalence of persistent PCS ranged between 10% to 47% in the mTBI group, 2% to 34% in the trauma controls, and 0% to 32% in the community controls depending on the different classification methods used.

Conclusion: The methods used to define persistent PCS yield dramatically different results and are highly relevant for outcome research following mTBI. Researchers and clinicians should consider carefully which methods to use when evaluating persistent PCS.

EPR1157

Effects of two types of dual-task balance interventions on gait and cognitive performance under single- and dual-task conditions in patients with stroke

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Background and aims: Functional ambulation requires an ability to divide attention between concurrent tasks while walking. Interference between gait and cognition indicates that diminished dual-task abilities, which may impede functional mobility and community participation for stroke patients. The objective of this study is to investigate the effects of motor and cognitive dual-task training [MCDTT] and cognitive dual-task training [CDTT]) on gait and cognition under single- and dual-task conditions in patients with stroke.

Methods: Twelve subjects with stroke were randomly allocated to either MCDTT or CDTT group. Both groups received 12-session programs at progressively increasing task difficulty (5-min warm-up, 20-min standing balance, 10-min sitting-to-standing, 20-min treadmill walking, and 5-min cool-down). MCDTT group undertook balance and gait training while concurrently performing both motor and cognitive tasks. The CDTT group trained balance and gait while simultaneously performing cognitive tasks only (verbal fluency tasks, calculation tasks, and visual discrimination tasks). All participants were examined walking and cognition under single- and dual-tasking at pretreatment and posttreatment. Primary outcome measures of walking and cognition were gait speed and composite score of Stroop task under single- and dual-tasking. Cognitive-motor-interference was calculated.

Results: Both groups significantly improved gait speed under single- and dual-task walking after training. The MCDTT group was significantly less cognitive-motor-interference on cognition under dual-task fast walking at posttreatment. There was a trend that only MCDTT group improved cognitive costs under comfortable walking with Stroop at posttreatment.

Conclusion: The preliminary results showed a favorable trend toward motor and cognitive dual-task training with less cognitive-motor-interference and cost on cognition.

EPR1158

Simplified Evaluation of CONsciousness Disorders (SECONDs): A new tool to assess consciousness in severely brain-injured patients

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Background and aims: The Coma Recovery Scale-Revised (CRS-R) is currently the gold standard behavioural tool to assess patients with disorders of consciousness. However, the time needed to complete an assessment limits its use in intensive care and rehabilitation settings. Recent literature suggests that focusing on the five most frequent responses allows detecting 99% of conscious patients. We aim at developing a scale to assess consciousness within a short time-period, the SECONDs.

Methods: A group of experimenters (OB SW CA HC) assessed 12 patients with disorders of consciousness within two consecutive days. On day A, one CRS-R and one SECONDs were randomly administered one hour apart. On day B, two SECONDs were performed one hour apart. The order (A-B) was randomized. We compared the diagnoses based on the CRS-R vs. the SECONDs (same day), and the diagnoses based on the CRS-R vs. three SECONDs.

Results: Nine out of 12 patients had the same diagnosis with the CRS-R and the SECONDs performed on the same day. Globally, the three SECONDs gave the same diagnosis as the CRS-R in 10 patients. No diagnostic mismatch could be explained by the presence of a behavioural response not assessed by the SECONDs. Assessments using the SECONDs were faster than with the CRS-R [Z=-3.059, p=0.002218; median time (IQR) : 9 (6) vs. 22 (8.25) minutes].

Conclusion: Our preliminary results suggest that the SECONDs could be a useful, fast, alternative tool to detect consciousness in severely brain-injured patients when time is limited.

Disclosure: CA is research fellow, and SL research director, at the FRS-FNRS.

EPR1159

Perilesional Induction of Sleep Slow Waves improves Motor Recovery after Ischemic Stroke

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Background and aims: Clinical and experimental studies suggest a positive role for sleep in brain plasticity during stroke recovery. Here, we investigate the role of Slow Waves (SW) oscillations during sleep on motor recovery following ischemic stroke using optogenetic techniques and in vivo electrophysiology in mice.

Methods: Ischemic stroke was caused in wild type mice via middle cerebral artery occlusion (MCAO). Following injections of CamkII-ChR2-EYFP (ChR2), CamkII-ArchT-EYFP (ArchT) and CamkII-mCherry (control) adeno-associated viruses (AAV) within the peri-lesional primary somatosensory forelimb (S1FL) cortex, SW-like oscillations were induced by optical stimulations of transfected pyramidal neurons. Starting from post-stroke day 5, and consecutively every day until post-stroke day 15, animals underwent 2 h of stimulation session. Behavioural tests at post-stroke days 4, 7, 10 and 15 were used to assess the effect of optogenetically evoked SW on motor outcomes.

Results: MCAO induced an increased amount of NREM sleep and reduced wakefulness following ischemic stroke. Specifically, ipsilateral SWs showed longer duration compared to contralateral sleep slow waves. We showed that optogenetic activation (ChR2) and silencing (ArchT) of pyramidal neurons in the per-lesional S1FL cortex successfully induced SW sleep-like responses in both ipsilateral and contralateral EEG traces. Moreover, chronic optogenetic induction of SW-like, predominantly during NREM sleep, improved recovery of fine motor movements as compared to control mice.

Conclusion: Our results, in line with previous observations, suggest a positive role of sleep in motor recovery following ischemic stroke. Optogenetically-induced SW-like oscillations, targeting the activity of pyramidal neurons in the peri-lesional cortex, significantly promote functional outcomes after stroke.

Disclosure: Nothing to disclose

Peripheral nerve disorders 1

EPR1160

Carpal tunnel release follow-up: when do we perform instrumental tests?

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Background and aims: Electrodiagnostic studies (NCS) and high-resolution ultrasound can be used for follow-up after median nerve decompression at the carpal tunnel (CTS).

The study aims to find out the most relevant terms for follow-up tests in patients with idiopathic CTS after the complete ligament dissection.

Methods: 72 patients (or 108 affected hands), 11 men and 61 women, from 37 to 88 years (mean age 62.83 ± 11.74 years) with electromyographic evidence of carpal tunnel syndrome were recruited. The patients were examined before the nerve decompression, after 2 weeks, 1.5 and 6 months after the treatment. 25 healthy gender- and age-matched individuals were recruited as controls. The NCS (n. medianus – motor and sensory portions) was conducted with Dantec Keypoint Focus. The ultrasonography with an assessment of the median nerve cross-section area at the carpal tunnel was performed with Philips IU22. The results were processed in program Statistica 6.0 and Microsoft Excel.
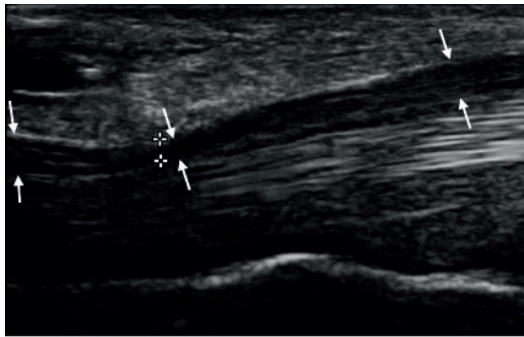
Median nerve entrapment at the carpal tunnel. Arrows - the borders of the nerve, markers - the nerve's narrowing.
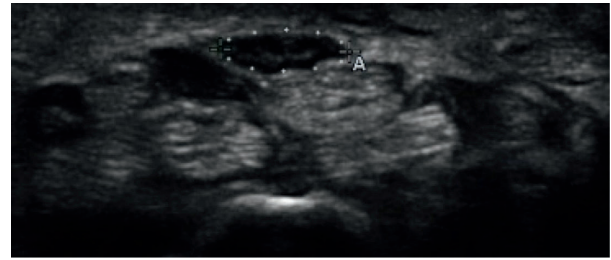
Cross-section area (CSA) measurement (markers) of the median nerve at the carpal tunnel. CSA=0,12cm2
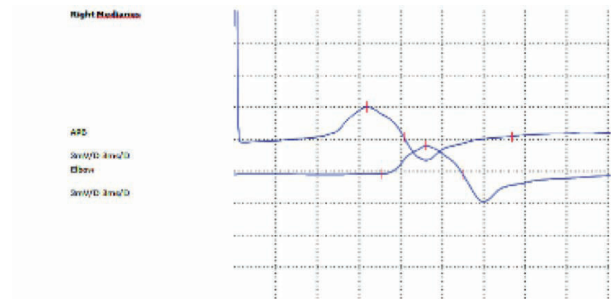
Right Medianus Motor			
	Lat	Amp	CV
	ms	mV	m/s
Wrist-APB	6.34	2.8	
Elbow-Wrist	10.7	2.6	57.3

Median nerve compound muscle action potentials (CMAPs) in a patient with CTS. Prolonged distal latency, decreased amplitude, normal conduction velocity at the forearm.

Results: In all cases the release was sufficient.

NCS showed sensory conduction velocity improvement in 2 weeks (p=0.027). Also motor and sensory distal latencies significantly improved in 1.5 months and 6 months accordingly. Such parameter as a nerve cross-section area did not change significantly over the whole period of observation.

Conclusion: The follow-up after the operation is important to assess the effectiveness of the procedure by confirming the complete carpal ligament dissection and visualizing the structures of the carpal tunnel in early post-operative period (2 weeks) already. NCS are already meaningful in 2 weeks after the nerve decompression.

Disclosure: Nothing to disclose

EPR1161

Chronic inflammatory demyelinating polyradiculoneuropathy is not a painless disease

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Background and aims: Recently, some newly recognized clinical features have been noticed in patients with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). We sought to gather new information about frequency, severity and features of neuropathic pain (NeP) in CIDP patients and to assess the association between NeP and other disease features.

Methods: We included 106 patients diagnosed with CIDP. PainDETECT questionnaire (PD-Q) was used to assess the presence of NeP. The Medical Research Council (MRC) Sum Score, INCAT disability and sensory scores, and Beck Depression Inventory were also used.

Results: NeP was present in 47 (44.3%) CIDP patients. Half of the patients with NeP had severe pain at testing. The most common neuropathic symptoms were sensations of sudden attacks of electric shocks, slight pressure triggering pain, and allodynia. Slowly-progressive course of the disease was more frequent in patients with NeP (86.4% vs 59.6, $p < 0.05$). Patients with NeP had worse INCAT sensory score ($p < 0.001$), INCAT disability score ($p < 0.01$) and MRC sum score ($p < 0.001$) at time of testing. Depression was more common in patients with NeP (45.5% vs 25.9%, $p < 0.01$). More severe weakness (lower MRC score) and higher INCAT sensory score appeared as significant independent predictors of higher score on PD-Q in patients with CIDP.

Conclusion: NeP was very common and often severe in our cohort of CIDP patients. It was associated with worse functional disability, sensory deficit, and depression. Special attention should be paid to these patients since they request additional symptomatic therapy.

Disclosure: Nothing to disclose

EPR1162

Obinutuzumab, a new anti-CD20 antibody, is active and effective in anti-MAG antibody polyneuropathy.

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Background and aims: Rituximab, a chimeric anti-CD20 monoclonal antibody (mAb), has been used in polyneuropathy associated with anti-myelin-associated-glycoprotein (MAG) antibodies with controversial results. Obinutuzumab, a new glycoengineered humanized anti-CD20 mAb, in combination with chemotherapy, induces longer progression-free survival in B-cell lymphomas, as compared with rituximab.

Methods: A 82-yr-old man presented with severe demyelinating sensory-motor neuropathy. At our first evaluation, he used wheelchair to travel outdoors, was incapable of standing and walked few steps only with bilateral support. He had distal weakness at lower limbs (2/5 MRC), tactile hypoestesia and loss of vibration up to knees, areflexia. He had a clonal B lymphocytosis CD5+ CD23+, compatible with chronic lymphocytic leukemia (CLL), IgM lambda paraprotein and anti-MAG titre was >70,000BTU. The presence of favorable CLL prognostic markers (mutated IGHV gene and absent of TP53 deletions or mutations) prompt us to use chlorambucil+obinutuzumab (obinutuzumab iv at 1000mg on day 1, 8 and 15 of cycle 1 and day 1 of cycles 2-6; chlorambucil os at 0.5mg/kg on day 1 and 15 of cycles 1-6).

Results: At cycle 6 the patient was able to stand, gait was possible with monolateral support, tactile hypoestesia was limited to feet, distal strength and vibration improved. M-protein decreased from 15.8g/L to 11.61 at cycle 6. Similarly, IgM level (14.8 vs 8.7g/L), lambda free-light chain (145 vs 59mg/L) and lymphocytes (6,340 vs 900/μl) decreased.

Conclusion: CLL might have had a role in the response to therapy, but a possible role of chlorambucil+obinutuzumab in anti-MAG polyneuropathy, regardless of the associated hematological condition, should be considered in future trials.

Disclosure: Nothing to disclose

EPR1163

Influence of diabetes mellitus on chronic inflammatory demyelinating polyradiculoneuropathy

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Background and aims: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a treatable disease characterized by progressive weakness and sensory abnormalities. Diabetes mellitus (DM) is one of the most frequently reported comorbidities in CIDP. We aimed to analyze association of DM with clinical, paraclinical features and outcome of CIDP.

Methods: Study comprised 194 CIDP patients examined between 2007-2016 in medical centers of Serbia, Bosnia and Herzegovina and Montenegro. Patients were divided in groups with and without diabetes. The degree of disability was assessed by Inflammatory Neuropathy Cause and Treatment score (INCAT) and Medical Research Council (MRC) sum score.

Results: At the time of CIDP diagnosis 21.6% of patients had DM, increasing to 26.3% after 8±6 years follow-up. Those patients had later onset of CIDP (p<0.01), more extensive sensory disturbances (p<0.05) with worse sensory INCAT score in lower extremities (p<0.01). INCAT disability and MRC sum score did not differ between groups. DM patients more frequently had ataxia (48.8% vs. 29.9%, p<0.05) and facial nerve palsy (12.5% vs. 4.1%, p=0.05). They also less frequently fullfiled definitive electrophysiological criteria (68% vs. 92%, p<0.01), while cerebrospinal fluid parameters were similar between groups. Slowly progressive course was present more often in DM patients (97.5% vs. 68.3%, p<0.01). No difference in the response to CIDP therapy was noticed between groups (p>0.05). However, death occured more frequently in DM group (p<0.05).

Conclusion: CIDP patients with DM had specific clinical presentation with more sensory symptoms and ataxia. Response to therapy was similar, but lethal outcome was more frequent in DM positive group.

Disclosure: Nothing to disclose

EPR1164

Benefit-Risk Profile of Intravenous Immunoglobulin (IVIG) and Subcutaneous Immunoglobulin (SCIG) in Chronic Inflammatory Demyelinating Polyneuropathy (CIDP): the PATH Study

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Background and aims: PATH investigated efficacy and safety of SCIG (IgPro20, Hizentra®, CSL Behring) as maintenance therapy for CIDP. Before randomisation to IgPro20 or placebo, subjects underwent IVIG withdrawal and, upon clinical deterioration, were re-stabilised with IVIG (IgPro10, Privigen®, CSL Behring). IgPro10 and IgPro20 have the same manufacturing process with the only differences between products being the final immunoglobulin concentration and administration route. The benefit-risk profiles of IgPro10 IVIG and IgPro20 SCIG are evaluated here.

Methods: IVIG re-stabilisation comprised an initial dose of 2g/kg followed by 3–4 doses of 1g/kg at 3 week intervals. Subjects were then randomised to weekly SCIG maintenance therapy (0.2 or 0.4 g/kg) or placebo for 24 weeks. The adverse event (AE) profile and relapse (change in adjusted Inflammatory Neuropathy Cause and Treatment [INCAT] score) were analysed for both products.

Results: A total of 207 subjects received 1894 IVIG infusions and 115 of these subjects subsequently received 4225 SCIG infusions. The most frequent AEs were headache (IVIG) and local reactions (SCIG). The majority of headaches (65%) and local reactions (95%) were mild. With IVIG, 9 haemolysis AEs occurred (all non serious and resolved without transfusion); none occurred with SCIG. No thromboembolic events, renal failures or deaths were reported. A total of 83% of subjects re-stabilised on IVIG; subsequently, 81% of subjects did not relapse on SCIG 0.4 g/kg (0.2 g/kg: 67%; placebo: 44%).

Conclusion: Both IVIG and SCIG had the expected effectiveness reported in literature, while rates of systemic AEs were lower with both SCIG doses.

Disclosure: This study was sponsored by CSL Behring

EPR1165

Focal neurological episodes in Familial Amyloid Polyneuropathy patients – clinical and laboratory features

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Background and aims: Liver transplantation in Familial Amyloid Polyneuropathy (FAP) slows disease progression by replacing the variant TTR by wild-type TTR. However, mutant TTR production in the choroid plexus and in the retina continues. Focal neurological episodes (FNEs) have been described in FAP patients with over 10 years of disease duration. Similarly to amyloid spells, FNEs were divided in negative phenomena (TIA-like and aura-like) and positive phenomena (aura-like and epileptic seizures).
Methods: Descriptive analysis of clinical and paraclinical data of 5 FAP patients with FNEs.
Results: 5 male patients, aged between 42 and 53 years-old, presented with FNEs at a median of 15 (10.19-19.8) years post liver transplant. We describe a total of 12 events, 8 AIT-like, 4 epileptic seizures of which 2 were followed by prolonged focal neurological deficits. The events tended to maintain the same clinical presentation for each patient. 3 patients underwent CSF analysis, which showed elevated protein without pleocytosis. EEG was performed in all patients in the acute phase at least once: findings were variable, ranging from normal (3) to non-convulsive status epilepticus (1).
Conclusion: Our demographic and clinical data are consistent with what has been previously reported by Maia et al., The frequency of abnormalities in the EEG argue in favor of the existence of cortical dysfunction, and elevated protein in CSF could implicate disruption of the blood brain barrier, supporting that amyloid deposition in leptomeningeal vessels is the most likely etiology
Disclosure: Nothing to disclose

EPR1166

A new variant in the WNK1 gene causing Hereditary Sensory and Autonomic Neuropathy type 2

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Background and aims: Hereditary Sensory and Autonomic Neuropathies (HSAN) are a group of rare genetic disorders affecting specifically the sensory and autonomic peripheral nerve fibers. Its classification, created before genetic testing was available, proposes four clinical subtypes. We present a case of HSAN type 2 whose genetic evaluation revealed a novel disease-causing variant in the WNK1 gene.
Results: A 30-year-old African woman born to normal consanguineous parents presented at nine years of age with a painless wound in her left foot, complicated with osteomyelitis and amputation of the fifth toe. The family reported repeated painless injuries, burns and loss of sensation in her distal limbs since three years of age. Neurological examination revealed loss of deep tendon reflexes, sensory ataxia and loss of all sensory modalities in all four limbs. A sural nerve biopsy revealed complete absence of myelinated nerve fibres without onion bulbs. The diagnosis of HSAN type 2 was established. In light of recently reported variants associated with HSAN, a next-generation sequencing panel of 15 genes was ordered. It revealed a novel homozygous variant at the WNK1 gene resulting in a truncated protein [c.2920C>T;p.(Gln974*)].
Conclusion: Variants in WNK1, RETREG1, KIF1A and SCN9A have been associated with HSAN type 2. Our patient presents an unreported variant resulting in a truncated WNK1 protein, a serine/threonine protein kinase, expressed in sensory ganglia neurons, whose exact function in the nervous system is unknown. This work contributes to enlarge the still limited knowledge about the clinical, pathological and genetic features of this group of rare diseases.
Disclosure: Nothing to disclose

EPR1167

A novel Alanyl-tRNA synthetase gene mutation identified in three Charcot-Marie-Tooth families

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Background and aims: Hereditary neuropathy is caused by a large number of genes involved in different cellular mechanisms. Charcot-Marie-Tooth (CMT) disease is the most prevalent inherited neuropathy. Next-generation sequencing (NGS) has proven to be efficient in the diagnostics of disorders where multiple genes can be involved. Alanyl-tRNA synthetase (AARS) catalyzes the attachment of the respective amino acid to the appropriate tRNA. Heterozygous mutations in the AARS gene cause axonal CMT while homozygous mutations cause early infantile epileptic encephalopathy.

Methods: Neuropathy patients from different families have been investigated with a NGS-based targeted gene panel of 99 genes, mostly CMT genes.

Results: We have identified three unrelated CMT families with a shared, novel AARS gene mutation. Mutations in other neuropathy genes better explaining the phenotype in the affected were not found.

Conclusion: The identification of a unique AARS sequence variant in neuropathy patients from three unrelated families makes it plausible that this variant is causative for CMT in these three families. In addition, the NGS analysis of the other hereditary neuropathy genes did not reveal other sequence variants better explaining the phenotype of the affected in these families.

Disclosure: Nothing to disclose

EPR1168

Age-dependent cognitive dysfunction in untreated and liver transplanted ATTRV30M patients

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Background and aims: Central nervous system (CNS) involvement, including cognitive dysfunction, has been recently described in hereditary transthyretin (TTR) amyloidosis. This study aims to explore the effects of age on cognitive dysfunction in TTRVal30Met mutation carriers.

Methods: A series of 547 carriers of the TTRVal30Met mutation (160 asymptomatic, 180 untreated symptomatic, and 207 treated with liver transplant - LT) underwent a neuropsychological assessment, which included the Dementia Rating Scale-2 (DRS-2), Auditory Verbal Learning Test, Semantic Fluency, Phonemic Fluency, and Trail Making Test. Cognitive deficits were identified at the individual level, after adjusting the neuropsychological test scores for demographic characteristics (sex, age, and education), based on large national normative data. The presence of cognitive dysfunction was determined by deficit ($\leq$5th percentile) in DRS-2 and/or multiple cognitive domains (i.e., learning/memory, language, and attention/executive functions). Chi-square (or Fisher's Exact) and Mann-Whitney test were applied for group comparisons.

Results: The frequency of cognitive dysfunction was higher in untreated symptomatic (9%) than in asymptomatic carriers (2%, p=0.003), but similar to patients treated with LT (9%, p=0.798). Cognitive dysfunction in untreated symptomatic participants was associated with older age ($\geq$50 years) at disease onset (p<0.001) and at assessment (p<0.001), and with longer disease duration (p=0.001). Cognitive dysfunction in treated patients with LT was associated with older age at disease onset (p=0.009), but not with older age at assessment (p=0.332) or disease duration (p=0.830).

Conclusion: This cross-sectional study shows that cognitive dysfunction is associated with late onset of ATTRV30M amyloidosis.

Disclosure: Nothing to disclose

Peripheral nerve disorders 2

EPR1170

A Multicenter, Double-Blind, Placebo-Controlled, Pivotal Phase III Study (PLEO-CMT) of a Fixed Combination of Baclofen, Naltrexone and Sorbitol (PXT3003) for Charcot-Marie-Tooth Disease Type 1A (CMT1A)

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Background and aims: Disability and impairment associated with CMT1A improved after 12 months of treatment with PXT3003 in a randomized, placebo-controlled, double-blind explorative phase II study (Attarian, 2014). In December 2015, the PLEO-CMT phase III study (ClinicalTrials.gov: NCT02579759) was initiated, to assess the efficacy and safety of 2 doses of PXT3003 compared to placebo in mildly to moderately affected adult CMT1A patients.

Methods: The primary objective is to assess the effect on disability as measured by the mean change from baseline Overall Neurology Limitations Scale (ONLS) score after 15 month of treatment with PXT3003. Furthermore, efficacy on the proportion of responders (i.e. improvement of ONLS), impairment (CMTNS-V2), functional tests (10-MWT, QMT, 9-HPT), electrophysiological parameters (CMAP, SNAP and NCV) and quality of life are secondary endpoints. Pursuant this study, patients will be eligible for a 9-month extension study, allowing all patients to receive PXT3003.

Results: Randomization of patients was completed (n=323) in December 2016. The screen failure rate was 26%, as expected (437 patients were screened). The independent DSMB recommended to continue the study as planned following a safety analysis on all available data in September 2017. A blind variability analysis and blind futility analysis concluded that the study can continue as planned in November 2017. To date, 34 patients (10.5%) withdrew from the study, 8 (2.5%) due to adverse events possibly related to study treatment. The baseline patient characteristics and demographics, and study status will be presented.

Conclusion: This pivotal study of PXT3003 is expected to be completed in December 2018.

Disclosure: Study is sponsored by Pharnext SA Julie Foucquier: employee Pharnext SA René Goedkoop: employee Pharnext SA

EPR1171

Diabetes-related risk factors for the painful diabetic neuropathy

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Background and aims: Unsatisfactory diabetes control and other factors associated with diabetes have repeatedly shown significant association with the development of diabetic distal symmetrical sensory-motor polyneuropathy (DSPN), while association of these factors with pain related to DSPN is discussed contradictory. We aimed to identify the diabetes-related factors significantly associated with neuropathic pain in a large cohort of well-defined DSPN subjects.

Methods: In this observational cross-sectional cohort study of 400 subjects with non-painful (n=215) and painful (n=185) DSPN associated with diabetes mellitus of type 1 and 2 (median age 62 years, range 21-87 years; 236 men), factors related to diabetes (type, duration, control expressed as HbA1C level, presence of dyslipidaemia and nefropathy, BMI) were analyzed with regard to the presence of neuropathic pain.

Results: In painful DSPN subgroup, significantly higher number of patients showed abnormally increased serum creatinine levels and abnormally decreased estimated glomerular filtration rate as markers of possible diabetic nephropathy in comparison with non-painful DSPN patients. We were not able to confirm an association of painful neuropathy with any other of the diabetes-related parameters. Diabetes control expressed as HbA1c levels showed only unsignificant trend towards better control in non-painful DSPN.

Conclusion: The only diabetes-related factor, confirmed by our study as being significantly associated with the presence of pain in DSPN, was diabetic nefropathy, as another microvascular complication of diabetes. Other metabolic factors, relevant for the presence or severity of polyneuropathy, did not showed any significant difference between painful and painless patients.

Disclosure: Nothing to disclose

EPR1172

Feasibility of Switching from Intravenous to Subcutaneous Immunoglobulin Therapy in Chronic Inflammatory Demyelinating Polyneuropathy (CIDP): Comparison of PATH Trial Results with Clinical Experience

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Background and aims: In chronic inflammatory demyelinating polyneuropathy (CIDP), immunoglobulin (Ig) therapy is typically administered intravenously (IVIG). Subcutaneous Ig administration (SCIG) enables independence from hospitals and increased convenience. The phase 3 PATH study showed efficacy of SCIG in CIDP. Here we evaluate the feasibility of switching from IVIG to SCIG in CIDP patients by comparing PATH data with clinical experience.

Methods: In PATH, subjects with CIDP were switched to SCIG (0.2 or 0.4 g/kg/week) or placebo after IVIG induction. Adverse events (AEs), quality of life (QoL; EuroQol - 5 Dimension questionnaire) and patient preference were assessed. Observational studies of switching from IVIG to SCIG in CIDP and multifocal motor neuropathy (MMN), with assessment of safety, QoL (Life Quality Index [LQI] questionnaire) and patient preference are detailed.

Results: The percentage of PATH subjects who experienced ≥ 1 AE with IVIG was 48% (rate: 0.175/infusion). Corresponding percentages for SCIG-0.2 and SCIG-0.4 were 58% and 52% (0.08 and 0.05/infusion). The most common AE was headache for IVIG (16%, 0.033/infusion), and local infusion site reactions for SCIG (19% [0.03/infusion] for SCIG-0.2; 29% [0.02/infusion] for SCIG-0.4). Most subjects (88%) felt SCIG was easier to use versus IVIG. Significantly more subjects (P-values <0.005) improved/maintained QoL health status with SCIG versus placebo. In observational studies, switching from IVIG to SCIG was associated with increased QoL and reduced systemic AEs.

Conclusion: The randomised PATH study and observational studies comprising large cohorts of subjects have documented the feasibility, safety and efficacy of SCIG therapy in CIDP.

Disclosure: This study is sponsored by CSL Behring

EPR1173

Clinical and Magnetic Resonance Imaging features of a series of 11 Spanish patients who carry mutations in the BICD2 gene

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Background and aims: Mutations in the BICD2 gene are a cause of dominant spinal muscular atrophy. We report 11 Spanish patients (five families) carriers of mutations in the BICD2 gene.

Methods: Patients underwent neurological examination and electrophysiological studies with standard techniques. Muscle magnetic resonance imaging (MRI) of lower limbs (LL), including pelvis and feet, was performed in seven patients. Genetic diagnosed was reached using a gene panel for genetic testing of inherited neuropathies. Punch skin biopsy for the study of Epidermal Nerve Fiber Density (ENFD) was performed in two patients.

Results: Three novel mutations (p.Val485Gly; p.Tyr557His and p.Ser681Leu) and the already described p.Ser107Leu mutation were identified. The most frequent clinical phenotype consisted in mild weakness in proximal muscles of LL combined with foot deformities. In one patient, nerve conduction studies (NCS) showed reduced sensory and motor nerve action potentials. In the rest of patients, NCS were normal and electromyography showed chronic denervation predominantly in LL. In muscle MRI the most affected muscles were rectus femoris, vastus lateralis, medial gastrocnemius, gluteus medius and gluteus minimus. There was fatty infiltration in intrinsic muscles of feet in two patients. There was a reduction of ENFD in one patient with normal NCS.

Conclusion: We report three new pathogenic mutations in the BICD2 gene. In our study we include MRI findings at the level of pelvis and feet, which allow us to better define the pattern of muscle involvement related with this gene. Our results also raise the subject of a possible sensory involvement in the disease.

Disclosure: Study funding: grants IIS La Fe 2015/0085, ISCIII (PI12/00946), PI Fundación Grupo ERESA 2013.

EPR1174

Effects of alpha lipoic acid on loss of myelin sheath of sciatic nerve in experimentally induced diabetic rats

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Background and aims: Diabetic neuropathy is the most frequent chronic complication of diabetes. It may attack to sensory, motor or autonomous fibers. Varied mechanisms account for the development of diabetic neuropathy such as metabolic disorders, microvascular damages, neurotrophic support deficit, alternation in neuro-immune interactions, neural and glial cell apoptosis, and inflammation. Alpha lipoic acid (ALA) is a potent lipophilic antioxidant in vitro and in vivo conditions, which plays a main role as cofactor in many mitochondrial reactions, easily absorbed from gastrointestinal tract and can easily cross the blood brain barrier (BBB). Apoptosis is an important mechanism of degenerative diseases, which is induced by some factors like hyperglycemia toxicity. In vivo and in vitro studies showed that hyperglycemia affected the cell survival and induced apoptotic changes in dorsal root ganglion neurons and Schwann cells.

Methods: In this experiment we used a total of 28 rats. 14 rats were given 180mg/kg streptozotocin (STZ) dissolved by single intraperitoneally (i.p.) injection. Rats are divided into 4 groups; Control (group I), DM (group II), ALA (group III) and DM+ALA (group IV). Myelin sheaths of sciatic nerves were examined histologically for each group.

Results: In the results of the histological examination, showed that loss of myelin sheath in sciatic nerves of rats while the group treated with ALA showed less myelin loss.
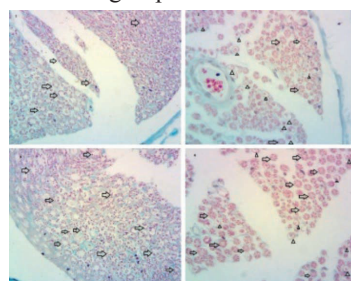
Figure 1.1 shows sciatic nerve control group, figure 1.2 is sciatic nerve DM group, figure 1.3 is sciatic nerve ALA group, figure 1.4 is sciatic nerve DM+ALA group. Tissue was stained with hematoxylin-eosin. Arrows show normal myelin sheath, arrowheads show myelin obliteration in histological imaging of sciatic horizontal section of groups.

Conclusion: This study might be suggested that ALA has a protective effect on peripheral neuronal cell damage generated with Diabetes mellitus (DM).

Disclosure: This study was supported by a grant from Firat University.

EPR1175

Baseline characteristics of patients with hereditary transthyretin (hATTR) amyloidosis with polyneuropathy enrolled in the phase 3 study NEURO-TTR demonstrate significant disease burden

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Background and aims: hATTR is a rare, progressive, and fatal disease, caused by systemic accumulation of transthyretin (TTR) protein that significantly impacts patient quality of life (QOL). We evaluated QOL at baseline in patients with hATTR with polyneuropathy (hATTR-PN) in the NEURO-TTR study (NCT01737398).

Methods: Adults (n=172) with hATTR-PN (stage 1 or 2) were randomized (2:1) and received 300-mg weekly subcutaneous inotersen, an antisense oligonucleotide inhibitor of TTR protein production, or placebo. At baseline, neuropathy was assessed using the modified Neuropathy Impairment Score+7 (mNIS+7), and QOL was assessed using the patient-reported questionnaires Norfolk Quality of Life–Diabetic Neuropathy (Norfolk QOL-DN) and the SF-36v2 Health Survey (SF-36v2). For these analyses, baseline QOL scores from patients in this study were reported relative to healthy controls.

Results: At baseline, 69% of patients were male; 67.4% stage 1 and 32.6% stage 2 disease; and 63% of patients had cardiomyopathy. Mean baseline QOL scores were significantly worse for patients with hATTR than healthy controls. The baseline mean (standard deviation [SD]) scores in QOL measures for patients with hATTR vs healthy controls was 48.4 (27.2) vs 2.6 (5.0) for Norfolk QOL-DN total score (higher scores reflect worse QOL) and 36.3 (9.1) vs 50.0 for SF-36v2 Physical Component Summary score (lower scores reflect worse QOL). The mNIS+7 and Norfolk QOL-DN total score showed strong correlation with each other and with disease severity.

Conclusion: The significantly impaired QOL observed in patients with hATTR compared with healthy controls confirms the unmet medical need for effective treatments that can reduce disease burden.

Disclosure: This study was sponsored by Ionis Pharmaceuticals (Carlsbad, CA, USA).

EPR1176

Inotersen improves quality of life and neuropathy in patients with hereditary transthyretin (hATTR) amyloidosis with polyneuropathy: results of the phase 3 study NEURO-TTR

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Background and aims: hATTR is a rare, progressive, fatal disease caused by systemic accumulation of transthyretin (TTR) amyloid, causing significant morbidity and progressive decline in quality of life (QOL). We report safety and efficacy of inotersen, an antisense oligonucleotide inhibitor of TTR protein production, in patients with hATTR with polyneuropathy (hATTR-PN).

Methods: NEURO-TTR (NCT01737398) is a global, randomised, double-blind, placebo-controlled phase 3 study. Adults (n=172) with hATTR-PN (stage 1 or 2) were randomised (2:1) and received 300-mg weekly subcutaneous inotersen or placebo for 15 months. Primary endpoints were change from baseline to week 66 in the Norfolk Quality of Life–Diabetic Neuropathy (Norfolk QOL-DN) total score and modified Neuropathy Impairment Score+7 (mNIS+7).

Results: At baseline, 69% of patients were male; mean age was 59 years. Compared with placebo, inotersen treatment resulted in significant improvement in primary endpoints based on the difference in mean change from baseline to week 66 [95% CI] in mNIS+7 (−19.73 [−26.43, −13.03], P<0.0001) and Norfolk QOL-DN (−11.68 [−18.29, −5.06], P=0.0006) total score. 50.0% and 36.5% of inotersen-treated patients improved from baseline to week 66 in Norfolk QOL-DN total score and mNIS+7, respectively. Most adverse events were mild or moderate. Key safety findings of thrombocytopenia and renal events were easily managed and monitored with routine testing. 80% of patients completed the 15-month treatment period, and >95% of patients who completed treatment entered the open-label extension study.

Conclusion: Inotersen demonstrated highly significant benefits in QOL and prevention of neurological disease progression in patients with hATTR-PN.

EPR1177

Changes of nerve conduction velocity and ultrasound characteristics in cidp over time. a three-year prospective study in seventeen patients

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Background and aims: About 50% of nerve segments in CIDP patients shows quantitative and qualitative ultrasound (US) changes, which correlate with neurophysiological findings, disease duration, MRC sum-score and INCAT score.

Methods: During a three-year F-U, we evaluated changes of clinical, neurophysiological (EDX), and US characteristics in 17 CIDP patients. The nerve cross sectional area (NCSA) in 236 nerve segments was evaluated with US by the same examiner, while EDX study was performed in 136 nerve segments by another examiner, at baseline and FU-end. The EDX data in each segment were stratified in normal, axonopathic and myelinopathic.

Results: Both at baseline and FU-end, MCV, NCSA, MRC-80 and INCAT score were all significantly correlated each other (p=0.001). Mean MCV was 43.04+13.73 m/s at baseline and 42.29+13.68 at FU end (p=0.34). At baseline EDX was normal in 34% of segments, axonopathic in 22% and myelinopathic in 44%; at FU-end it was normal in 22%, axonopathic in 46% and myelinopathic in 32% (p<0.0001). US was abnormal in 104/235 (44.5%) at baseline and in 116/235 (48.7%) segments at FU-end. In 102/235 (43%) segments US was normal at baseline and didn't change during FU. NCSA decreased significantly in 97 (41%) segments and increased in 104 (44%) (paired data t-test. p<0.0001) during the FU; it remained unchanged in 34 (14%) segments. MCV decreased (p=0.024) in segments with increased NCSA.

Conclusion: This prospective study confirms the correlation between clinical, electrophysiological and US characteristics in CIDP both at baseline and at FU-end. US could be a useful tool to follow nerve morphological changes over time.

Disclosure: Nothing to disclose

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Ageing and dementia 2

EPR2001

Physical activity as a moderator of AD pathology: a systematic review of observational studies

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Background and aims: Physical exercise has been shown to reduce Alzheimer's disease (AD) pathology in animal models, and is associated with reduced risk of cognitive decline in humans. The objective was to carry out a systematic review of observational studies on the possible association between physical activity (PA)/physical fitness (PF) and AD pathology.

Methods: The systematic review was carried out according to the PRISMA guideline. Observational studies of physical activity or physical fitness with AD biomarkers as outcome measures (Beta-amyloid, total-tau, phosphorylated-tau in cerebrospinal fluid (CSF); 18F-FDG-PET, Amyloid-PET, hippocampal atrophy on MRI) in healthy subjects, patients with mild cognitive impairment and patients with AD, were included.

Results: A total of 55,114 studies were identified and screened. Fifty studies were included. Nine studies reported results on amyloid PET, 5 on CSF, 4 on 18F-FDG-PET and 32 on hippocampal volume. Three studies were longitudinal. Twelve studies reported a significant association between hippocampal volume and either PA or PF, 2 studies reported a significant association between total-tau and phosphorylated tau and PF/PA and 1 study for beta-amyloid, in a favourable direction, whereas 2 studies found an association between amyloid tracer uptake and PF/PA, in a similar direction. Lastly, 2 studies reported increased metabolism in parietal and temporal areas to be correlated with PF/PA.

Conclusion: The findings do not support a physically active lifestyle being associated with less detrimental AD related biomarkers. However, the number of studies was limited apart from studies utilising MRI in healthy subjects, thus limiting a final conclusion. Further studies are needed.

Disclosure: Nothing to disclose

EPR2002

Rapidly progressive Alzheimer's disease and sporadic Creutzfeldt-Jakob disease: comparison of clinical and neuropathological features

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Background and aims: Rapidly progressive forms of Alzheimer's disease (rAD) with a rapid cognitive decline and an early occurrence of focal neurological symptoms, mimicking prion diseases, appear to exist.

Methods: We performed immunohistochemical analysis of brain autopsy tissue samples and compared clinical characteristics of 8 patients with rAD and 8 matched patients with sporadic Creutzfeldt-Jakob disease (sCJD). Survival time did not differ significantly between two groups. In all patients, sCJD was clinically suspected and included in the differential diagnosis at the time of death.

Results: All patients experienced a progressive cognitive deterioration as a main clinical symptom. Magnetic resonance imaging (MRI) lesions characteristic for sCJD could be observed in five sCJD patients, but in none of rAD patients. sCJD typical electroencephalographic (EEG) findings could be seen in two cases with sCJD; none of rAD patients displayed those changes. Cerebrospinal fluid proteins 14-3-3 were positive in seven sCJD cases; four of rAD cases were also positive.

Immunohistochemical stainings with markers that do not discriminate between resident microglia and monocyte-derived macrophages (MDM) (HLA-DP, -DQ, -DR antibody and CD68 antibody), and with the astrogliosis marker (GFAP antibody), did not reveal any significant differences in immunopositivity. TMEM119 (a marker unique to brain resident microglia) immunopositivity was significantly increased in rAD patients in comparison with sCJD patients.
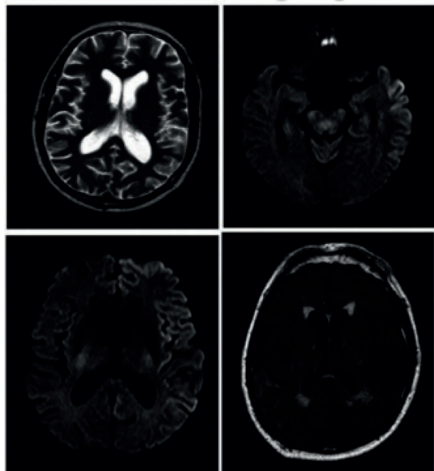
Typical MRI lesion patterns in rAD and sCJD patients
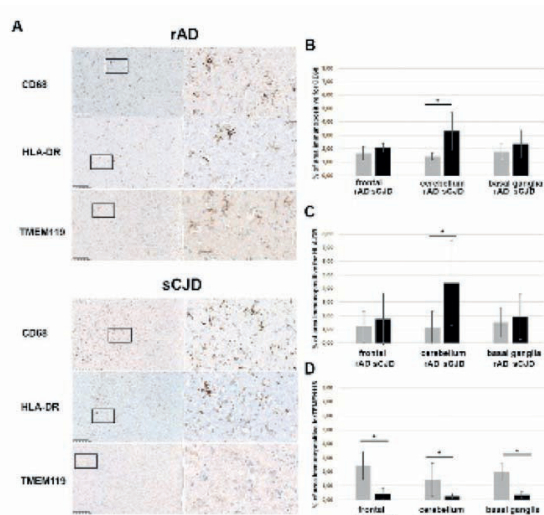
Immunohistochemical stainings with HLA-DP, DR, DQ, CD68 and TMEM119

Conclusion: rAD should be considered in the differential diagnosis in patients presenting with a rapidly progressive multifocal neurological syndrome. Future studies of microglial activation may provide new insight into the pathogenesis of AD in general and a possibility to modulate disease progression.

Disclosure: Nothing to disclose

EPR2003

Association between Tau haplotype and Frontotemporal Lobar Degeneration

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Background and aims: Frontotemporal lobar degeneration (FTLD) have been associated with the microtubule-associated tau protein since tau gene mutations have been demonstrated to be the cause of FTLD and parkinsonism linked to chromosome 17. The objective of this study was to determine whether genetic variability in tau gene is associated with the development or modulation of FTLD.

Methods: Retrospective study from different Tissue Banks and pathological diagnosis of FTLD. Molecular data: H1/H2 MAPT gene polymorphism. Clinical data: Age of onset and death, average time of disease, personal history and cardiovascular risk factors, clinical diagnosis, first clinical symptom and evolution of the disease. Pathological data: FLTD diagnosis – PiD, PSP, CBD, FTLD-Tau, TDP and FUS. Other - TDP43 inclusions, Braak stage, CERAD and vascular pathology.

Results: Fifty-one cases were analyzed. The most frequent haplotype for the MAPT gene was H1/H1 (48.6%). Regarding neuropathological diagnosis, H1/H1 was related to PSP cases and H1/H2 to TDP-43 cases. Supranuclear gaze palsy (64.7%; p=0.037), parkinsonism (59.5%; p=0.005) and gait disturbance (58.1%; p=0.065) was related to H1/H1 cases (75%) and behavioral disturbances to H1/H2 (38:9%) as the most frequent initial symptom. There were no statistically significant differences in age of onset / death and time of disease. No mutation was found in MAPT gene.

Conclusion: Phenotypic clinical characteristics were different in H1/H2 haplotype in MAPT gene and they were related to specific FTLD diagnosis. These findings support a role of tau protein in modulating disease phenotype in these FTLD cases.

Disclosure: Nothing to disclose

EPR2004

Prion protein codon 129 polymorphism modifies progression but not age at onset in Alzheimer's disease

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Background and aims: Recent studies have proposed a role for cellular prion protein (PrPc) in neuronal death induced by amyloid-β (Aβ) oligomers. Therefore, PrPc appears to be closely linked to the pathogenic process in Alzheimer's disease (AD). Our goal is to determine whether the PRNP codon 129 polymorphism (M129V) could influence the occurrence of AD and/or modify age at onset or progression of the disease in a sample of Spanish subjects.

Methods: In this case-control study, we compared the genotype frequencies of the PRNP M129V polymorphism in 200 sporadic AD patients (median age 79.7±6.7 years, 66.5% women) and 201 healthy controls older than 75 years (median age 71.0±4.9 years, 51.7% women). The PRNP M129V polymorphism (rs1799990) was analyzed using qQRT-PCR technique. We also determined age at onset and rate of cognitive decline in AD patients (rapid progression, MMSE decay/follow-up time [years]>4.5).

Results: Subjects carrying the M129V genotype were not significantly more susceptible to AD [MV vs MM: OR=1.50; CI95%=0.95-2.35; p=0.081]. However, a direct association between AD and M129V genotype was present in APOE ε4 non-carriers [OR=1.93; CI95%=1.16–3.20; p=0.011]. Moreover, the M129V genotype displayed consistent effects on disease progression (25.0% MV vs 11% MM and 9.1% VV rapid progression, p=0.027), but not on age at onset (p=0.413).

Conclusion: Our data show that the PRNP M129V genotype increases the speed of progression in AD. Further research is needed about the potential role of APOE4 for the oligomers of PrPc and PrPsc in the development of the disease.

Disclosure: Nothing to disclose

EPR2005

Impairment of basal forebrain projections contributes to hippocampal atrophy in subjects at risk of Alzheimer's disease

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Background and aims: Basal forebrain (BF) degenerates early in Alzheimer's disease(AD) and is a major source of acetelcholine in brain cortical areas including hippocampus. The aim of this study was to assess, if impairment of basal forebrain projections to hippocampus contributes to hippocampal atrophy in cognitively normal elderly(CN) subjects with subjective memory complaints(SMC) or mild cognitive impairment(MCI).

Methods: 85 subjects from ADNI2 cohort were selected - CN(n=30), SMC(n=32) and MCI(n=23). The diffusion and structural images were obtained from ADNI website. Fornical projections from basal forebrain (BF) to hippocampus were reconstructed using probabilistic tractography and diffusion tensor-based tract integrity measures were derived (mean diffusivity(MD), fractional anisotropy(FA), radial diffusivity(RD), axial diffusivity(AxD)). Pearson correlation coefficient was used to assess correlation of BF and hippocampal volumes. Causal mediation analysis was performed in 2 directions (1.BF to hippocampus, 2. hippocampus to BF) to evaluate the mediation effect of tract integrity measures while controlling for intracranial volume, sex, age, education and APOE status.

Results: We found significant correlations between hippocampal and BF volume (r2=0.251, p=0.02), BF volume and MD, RD, AxD (r2=(-0.37)-(-0.41), p=0.001-0.005), FA(r2=0.26, p=0.013) and hippocampal volume and MD, RD, AxD(r2=(-0.40)-(-0.50), p<0.0001), FA (r2=0.45, p<0.0001). We found significant mediation effect (ME) and total effect (TE) in first direction in MD, RD and AxD (ME.p=0.006-0.03, TE.p=0.042-0.049). There was no significant TE in second direction.

Conclusion: Track integrity of BF projections to hippocampus mediates association of BF and hippocampal volumes, but only in BF to hippocampus direction. This supports the hypothesis that atrophy of BF contributes to hippocampal atrophy.

Disclosure: Nothing to disclose

EPR2006

Serum BDNF levels in patients with vascular cognitive impairment (VCI): association with MoCA

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Background and aims: The association between the levels of brain derived neurotrophic factor (BDNF) and Mini Mental State Examination (MMSE) scores has been previously documented in Alzheimer's disease and aging, however there is a lack of studies on BDNF as a biomarker in VCI, where MoCA is the more suitable instrument for evaluation of cognitive function.

Methods: 104 patients with VCI (mean age 66.7±8.4 years, 65 women) were assessed using the Hachinski ischemic scale, MMSE and Montreal Cognitive Assessment (MoCA). Serum BDNF was measured using Quantikine ELISA kits (RnD Systems). BDNF data in VCI patients was compared with values from 20 healthy controls without significant cognitive impairment.

Results: In VCI patients (MoCA 22.2±2.5) serum BDNF levels were lower compared to controls (24.1±7.1 ng/ml vs. 27.5±7.4 ng/ml; p=0.03; Mann–Whitney U test). When we tested the association of MMSE and MoCA with age, gender and BDNF using multiple linear regression, the impact of age (beta= -0.32, p= 0.0009) and BDNF (beta=0.31, p=0.002) on MMSE, as well as the association between MoCA and BDNF (beta=0.31, p=0.00047) were revealed.

Conclusion: Our study demonstrated an association between MoCA scores and BDNF levels that opens new avenues in the studies of VCI.

Disclosure: Nothing to disclose

EPR2007

Cerebrospinal fluid neurofilament light chain illustrates that semantic dementia is a distinctive neurodegenerative disease

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Background and aims: Semantic dementia (SD) is a homogeneous neurodegenerative disorder characterized by progressive language problems that falls within the

frontotemporal dementia (FTD) spectrum. Its relative homogeneity facilitates the development of disease-modifying agents, wherefore robust biomarkers are required. We aimed to investigate the utility of cerebrospinal fluid (CSF) neurofilament light chain (NfL) as a biomarker in SD.

Methods: This large retrospective multicenter study compared CSF NfL levels of 162 SD patients with 44 controls. CSF NfL levels of patients were correlated to clinical parameters (including survival), neuropsychological test scores, and regional gray matter atrophy.

Results: CSF NfL levels were significantly higher in SD patients (median: 2326 pg/mL, interquartile range: 1628-3535 pg/mL) than in controls (989 [682-1362]). Higher CSF NfL levels associated with more severe language impairment, as measured by the Boston Naming Test, and with smaller gray matter volume of the parahippocampal gyri. However, CSF NfL levels did not associate with progression of gray matter atrophy, and were not able to predict survival. In addition, age at onset influenced total survival after onset, but we did not identify different factors influencing survival.
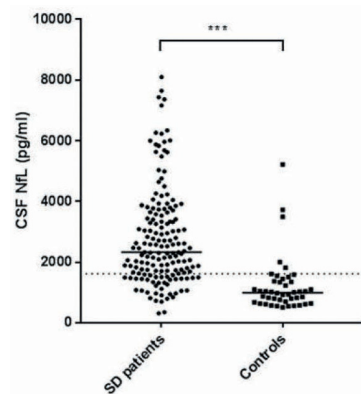
Figure 1. CSF NfL concentrations in SD patients and controls.
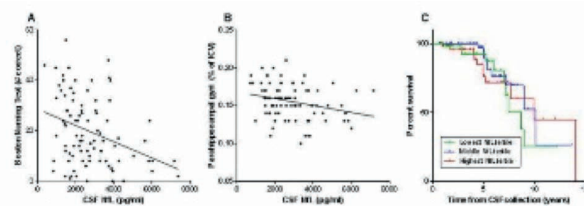
Figure 2. Relationship of CSF NfL to language impairment, parahippocampal atrophy, and survival in SD patients.

Conclusion: These results suggest that CSF NfL has the potential to serve as a biomarker for disease staging and monitoring of disease severity. However, unlike other FTD subtypes, NfL does not predict progression of atrophy or survival in SD, which illustrates the distinctiveness of SD within the FTD spectrum.

Disclosure: Nothing to disclose

EPR2008

Comparison of sulcal opening in posterior cortical atrophy and typical Alzheimer's disease

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Background and aims: Calculate the discriminating power of sulcal opening in the differentiation between Posterior Cortical Atrophy (PCA) and typical Alzheimer disease (tAD).

Methods: MRI of twelve PCA patients were compared to 27 tAD patients and to 14 matched controls. All patients fulfilled the current clinical criteria: Cruth 2017 for PCA, Dubois 2014 for tAD. For each subject, 6 cortical areas (olfactory sulcus, temporal pole, medial temporal, posterior cingulate sulcus, precuneus, parieto-occipital sulcus, both sides) were analysed using Brainvisa software. Moreover visual rating scales for each area were scored by two raters. Results were compared among PCA, tAD and controls using Mann-Whitney U-test. Pearson correlation was calculated between the two methods.

Results: Using Brainvisa, PCA compared to controls showed more atrophy in right olfactory, right temporal pole, right precuneus, medial temporal and parieto-occipital both sides, while compared to tAD showed more atrophy in medial temporal both sides and right parieto-occipital. Likewise, visual rating scales showed more sulcal opening in right olfactory, temporal pole, medial temporal and parieto-occipital both sides in PCA compared to controls, while only right parieto-occipital sulcus was wider than tAD. The correlation between the two methods was significant for all the areas.

Both methods have demonstrated the utility of sulcal opening in the differentiation between PCA, tAD and controls, showing that atrophy particularly affects the right hemisphere in PCA, especially around the parieto-occipital sulcus. The results obtained in visual rating have been validated using Brainvisa.

Conclusion: Opening of right parieto-occipital sulcus can differentiate between Posterior cortical atrophy and typical Alzheimer disease.

Disclosure: Nothing to disclose

Autonomic nervous system; Sleep disorders

EPR2011

Vagomimetic Fingolimod effects are compensated by central up-regulation of cardiovagal withdrawal upon rapid blood pressure decrease

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Background and aims: Fingolimod, an oral disease modifying drug used in relapsing-remitting multiple sclerosis (RRMS) has vagomimetic cardiac effects which might compromise the ability to quickly withdraw cardiovagal-activity which might impose the risk of syncope. We aimed at assessing whether Fingolimod-initiation alters the ability to withdraw cardiovagal-activity in patients with RRMS.

Methods: We tested 26 RRMS patients (mean age 33.5±1.8 years, 13 women) before and 0.5, 1, 2, 3, 4, 5, 6 hours after Fingolimod-initiation. We recorded heart rate (HR), RR-intervals (RRIs) and systolic blood pressure (BPsys) at rest to monitor HR slowing and during Valsalva maneuver (VM) to assess rapid cardiovagal-withdrawal as the baroreflex cardiovagal-gain (BRG) which is calculated from the slope of the regression between RRIs and BPsys during early VM phase II. Parameters were compared by ANOVA for repeated measurements and post-hoc paired t-tests (significance: p<0.05).

Results: In 15/26 patients, HR decreased while BRG increased (3.9±2.02 ms/mmHg vs. 5.4±3.5ms/mmHg; p=0.03) until 5 hours after Fingolimod-initiation, and then HR re-increased and BRG decreased at the 6th hour (3.92±2.023 ms/mmHg vs 3.90±4.53 ms/mmHg; p=0.98). In 11/26 patients, HR decrease beyond 5 hours while BRG showed a tendency to increase till the 6th hour (3.3±1.2 ms/mmHg vs 5.9±1.1 ms/mmHg; p=0.05).

Conclusion: As long as Fingolimod slows HR, central autonomic regulation compensates the vagomimetic effects during situation associated with a rapid BP-decrease requiring swift cardiovagal-withdrawal and assures higher BRG as long as HR-slowing prevails. This central compensation prevents cardiovascular instability with the risk of syncope.

Disclosure: Nothing to disclose

EPR2012

Comparison of polysomnographic parameters of RLS patients with and without augmentation

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Background and aims: Augmentation can frequently occur in restless legs syndrome (RLS) patients treated with dopaminergic agents. Video-polysomnographic (PSG) data from augmented RLS patients are scant. The aim of this study was to evaluate PSG findings in augmented RLS patients and compare them with those of non-augmented RLS patients.

Methods: Valid PSG data from 99 augmented and 84 non-augmented insufficiently treated RLS inpatients with severe RLS who underwent one-night PSG were analysed and compared.

Results: Both patient groups showed a high subjective burden of RLS symptoms. The mean scores on the IRLS in the group with augmentation were 31.75±4.66, higher than in the group without augmentation (29.63±7.57, p=0.02). The PLM index (PLMI) was increased in both groups (54.09±43.09 vs 53.86±51.97, p=0.973), mostly on the account of the PLM in wakefulness (PLMW: augmentation 93.11±60.07 vs non-augmentation 78.75±58.92). Both groups presented a reduced sleep efficiency (70.60±14.55 vs 72.27±13.22) and an increased sleep latency (28.45±33.83 vs 29.21±28.93). The Levo-dopa equivalent dose (LED) was significantly higher in the augmented group (74.24±165.83mg vs 29.46±44.42mg, p< 0.0001).

Conclusion: Our study confirms that RLS patients with augmentation have subjectively and objectively disturbed sleep with a high amount of PLM and sleep fragmentation. Overall, however, polysomnographic characteristics were not different between insufficiently treated RLS and severely augmented RLS patients, implying that augmentation could represent a severe form of RLS in the night and not a distinctive sleep pattern.

Disclosure: The statistical analysis was supported from a grant from UCB Pharma

EPR2013

REM sleep behavior disorder in the diagnosis of neurodegenerative diseases: Retrospective analysis of polysomnographic records at Hospital Egas Moniz between 2012-2017

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Background and aims: REM sleep behavior disorder (RBD) is prevalent in the early stages of alpha-synucleinopathies. Video-polysomnography (V-PSG) assessment may be relevant in the differential diagnosis of neurodegenerative diseases. We aim to describe the impact of RBD detection on V-PSG in the diagnosis and therapeutic approach of neurodegenerative syndromes

Methods: Retrospective analysis of clinical and polysomnographic records of all patients submitted to V-PSG at the Egas Moniz Hospital Neurology Department between July 2012 and March 2017. We selected cases of neurodegenerative syndromes without a defined clinical diagnosis and recorded whether the result of V-PSG was useful 1) to define the diagnosis (Lewy Body Dementia); 2) as a diagnostic clue in cases clinically confirmed as alpha-synucleinopathy (Multiple System Atrophy and Parkinson's Disease; 3) in the therapeutic decision

Results: 325 patients were submitted to V-PSG. 61 exams were requested for neurodegenerative syndromes without definitive clinical diagnosis: 60.6% were cases of dementia, 31.3% of parkinsonism and 8.1% of ataxia. The detection of RBD generated definitive criteria for LBD in 13 patients (72.2%), modifying therapy in 61.5%. Of the 7 patients in whom this diagnosis would be possible without V-PSG, the mean time for diagnosis without and with V-PSG would be 24.7 and 14.3 months, respectively. In the study of parkinsonian/ataxic syndromes, V-PSG served as a diagnostic clue in 14 patients (60.9%), changing therapy in 35.7%

Conclusion: RBD detection by V-PSG is an important diagnostic aid in alpha-synucleinopathies, with potencial impact on therapeutic approach and diagnostic time reduction

Disclosure: Nothing to disclose

EPR2014

Effect of CPAP therapy on neurographic features in male OSA patients with and without sensomotor polyneuropathy

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Background and aims: So far, the effect of CPAP therapy on neurographic features of peripheral nerves in OSA patients has not been sufficiently investigated.

Objectives: The aim of this study was to determine the effect of CPAP therapy on neurographic features of peripheral nerves in male OSA patients with (n=5) and without (n=5) peripheral polyneuropathy.

Methods: We conducted a cohort study on 10 male OSA patients confirmed by the whole - night polysomnography (PSG).

All subjects underwent neurological examination and standardised electroneurographic testing of peroneal and sural nerves, before and one year after CPAP therapy. For statistical analysis a paired t-test test was used. Level of significance was set at P<0.05

Results: The one-year application of CPAP therapy resulted in the improvement of neurographic features in terms of a significant increase in CMAP and SNAP amplitude values, but also of sensory conduction velocities.

Averaged peroneal nerve CMAP amplitudes were 4.64±2.53 mV before and 6.56±1.65 mV after therapy, p=0.001.

Averaged SNAP amplitudes were 9.96±5.78 µV at baseline and 15.6±7.28 µV after therapy, p=0.0015.

Sensory conduction velocities were 43,36±3,90 m/s at baseline and 45.99±5.44 m/s after therapy, p=0.0048.

Conclusion: These results confirmed that CPAP therapy is effective in OSA patients with and without peripheral polyneuropathy in terms of an increase in CMAP and SNAP amplitude values and sensory conduction velocities.

Disclosure: Nothing to disclose

EPR2015

Biomarkers of alphasynucleinopathies in REM sleep behavior disorder: a pilot cross-sectional study

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Background and aims: REM sleep behavior disorder (RBD) is a parasomnia related to loss of muscle atonia during REM sleep phase manifesting with abnormal behavior. It has been shown that great majority of patients with RBD develop alphasynucleinopathies. Among these Parkinson's disease (PD) is most common. We wanted to evaluate the occurrence of various biomarkers of prodromal alphasynucleinopathies in idiopathic RBD.

Methods: In this pilot cross-sectional study we evaluated six patients (age 66.7±11.3, three female) with polysomnographically confirmed RBD. They underwent neurological and cognitive examination, University of Pennsylvania Smell Identification Test (UPSIT), Beck Depression Inventory (BDI), MRI, dopamine transporter imaging (DaTSCAN) and 18F-FDG-PET. PD related metabolic and cognitive patterns (PDRP, PDCP) expressions were calculated and compared to 20 PD patients and 20 normal controls (NC). Alpha-synuclein (αS) in cerebrospinal fluid (CSF) was measured for three of them.

Results: Neurological examination and DaTSCAN were normal in all cases. MoCA score for RBD patients was 25.7±1.6, UPSIT (20.3±2.1/40) confirmed hyposmia (anosmia in one patient), five were depressed and one constipated. PDRP and PDCP expressions in RDB patients were above the average of NC, but below the PD average. In two cases expressions were in the range of PD patients. CSF αS was higher in RBD patients compared to PD, LBD and MSA patients.

Conclusion: All RDB patients had multiple signs of prodromal alphasynucleinopathy including changes in brain metabolism, similar to those in PD, although presynaptic dopaminergic integrity was still normal. Metabolic brain changes may develop earlier in the course of alphasynucleinopathies then presynaptic dopaminergic dysfunction.

Disclosure: Nothing to disclose

EPR2016

Validation of Wearable Sleep Monitoring Device Based on Cardiopulmonary Coupling and Accelerometer with Comparison to Polysomnography in Adults

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Background and aims: Long-term monitoring of sleep with wearable devices is getting increasingly popular, but the accuracy of most devices tracking movements with accelerometers is poor. New products combining actimeters and autonomic markers like heart rate variability are being developed. We compare the accuracy of a novel smart watch classifying sleep and wakefulness based on cardiopulmonary coupling (CPC) and actimetry with video-polysomnography (PSG).

Methods: 59 PSGs from 32 volunteers (f: 20; age: 18-54; no self-reported sleep disorder) were collected while wearing a smart watch (Huawei FIT, Huawei Device (Dongguan) Co., Ltd, China). Four males had sleep apnea syndrome and one female (measured twice) had bruxism, so 53 out of 59 PSGs were from healthy population. The PSGs were manually scored by experienced somnologists. The wearable data were analyzed by the company blinded to the PSG results.

Results: Epoch-by-epoch (1-min) comparison with all PSGs revealed that Huawei FIT showed sleep detection sensitivity, specificity, accuracy and Cohen's kappa of 96.3%, 73%, 93.5% and 0.7, respectively. Values from the 53 healthy PSGs were 96.8%, 76.4%, 94.2% and 0.74, respectively. In the 59 PSGs the sleep duration highly correlated to the one measured by the watch, and Bland–Altman analysis suggested good agreement in measuring sleep length and efficiency using PSG and Huawei FIT.

Conclusion: Wearable devices measuring CPC and actimetry are promising tools for sleep detection at home. They may be valuable for studying sleep related epidemiology and its impact on public health. Whether they can assess sleep architecture needs to be further studied.

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Cerebrovascular diseases 3

EPR2018

Cervical Artery Dissection : Risk Factors, Clinical Features and MRA Manifestations

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Background and aims: In cervical artery dissections(CAD), which are the most common etiologic cause of young stroke group, clinical suspicion and appropriate radiologic examination increase the accuracy of diagnosis and reduce morbidity and mortality. Our aim in this study is to retrospectively evaluate the clinical and radiological findings of the patients who were diagnosed with dissection.
Methods: Demographic and referral clinical characteristics of patients were recorded. Parenchymal and vascular views were analyzed in the application. Localization of dissection, risk factors and clinical evaluation were noted. Patients were treated with anticoagulation/antiplatelet therapy. Vascular imaging was used to confirm the diagnosis of CAD. Angiographic findings of the dissection include a string sign (Figure 1), stenosis, occlusion (Figure 2b), intimal flap, dissecting aneurysm (Figure 2a), pseudo/double lumen.
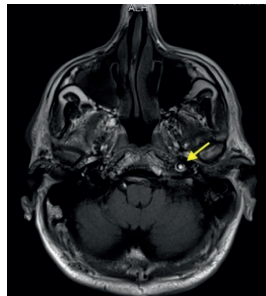
Figure 1. Fat-SE T1 axial cranial MRI, Subacute dissection appearance of the left ICA with 'crescent sing' intramural hematoma (yellow arrow)
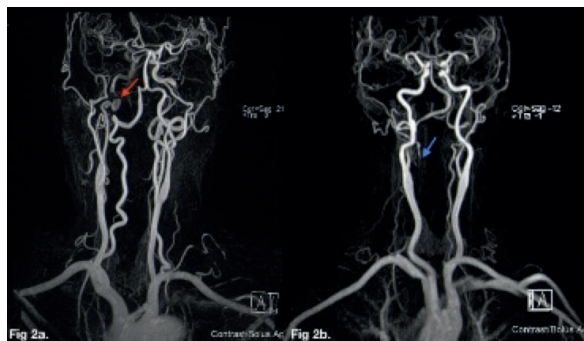
Figure 2a. MRA oblique projection   right ICA dissection, pseudoaneurysm (red arrow) Figure 2b. MRA coranal projection, right VA V1 segment occlusion (blue arrow)

Results: A total of 45 patients (28 male, 17 female) with a mean age of 44.17 (± 13.8) with the diagnosis of CAD were enrolled. Hypertension (24.4%) is the most common risk factor in the history (Table 1). In the etiology 40% of cases had minor/major trauma. The most common cause of minor trauma was drop/crash (38.9%) (Table 2). The most common clinical presentation was stroke (46.7%). Headache/neck pain (42.3%) is the most common local symptom. The most common vascular findings on angiographic imaging were intaramural hematoma (31.3%).
Conclusion: Multimodal CT or MRI assessment is crucial for defining vessel wall abnormalities. Recognition of CAD are highly important in the presence of localized symptoms, TİA/stroke, especially in the young adults with clinical suspicion.
Disclosure: Nothing to disclose

EPR2019

Would intravitreal bevacizumab injection increase risk of cerebral infarction?

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Background and aims: Although studies have evaluated the relationship between intravitreal bevacizumab (IVB) injection and cerebral infarction(CI), the effects of IVB on CI are still not clear. The aim of this study was therefore to investigate the effects of IVB injection on CI patients with age-related macular degeneration (AMD).
Methods: We retrospectively reviewed patients with AMD who received IVB injections for 1 year and determined the incidence of CI within 60 days after IVB injection to analyze the possible association between IVB and CI.
Results: Over a 12-month period, 263 patients were enrolled. Six patients (2.28%) were diagnosed with CI within 2 months after receiving an IVB injection. The incidence of CI in patients 75–84 years of age was 6.38%. These results showed a higher incidence of patients with IVB injections than the results of previous epidemiological studies (0.13% for all age groups, 1.68% for patients 75–84 years of age). All CI occurred 21–53 days after the IVB injection (mean: 39.33±14.65 days). Logistic regression analyses showed that age and a history of previous CI were factors associated with CVA. However, the total number of IVB injections and the number of IVB injections over 1 year were not associated with CI.
Conclusion: Treatment with IVB might be an independent risk factor for CI. These results are useful for planning treatment strategies for patients with AMD and for prevention of CI.
Disclosure: This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science and ICT (grant number: 2017R1E1A1A01074324)

EPR2020

Free fatty acid and pro-BNP as predictors of atrial fibrillation in acute ischemic stroke patients

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Background and aims: Atrial fibrillation (AF) is a common arrhythmia and a major risk factors for stroke. A recent study has shownthat AF relate to some biomarkers such as free fatty acid (FFA) and pro-brain natriuretic peptide (pro-BNP) have been reported. The purpose of this study is to investigate the useful blood biomarkers to predict AF in acute ischemic stroke.
Methods: Total 195 consecutive patients (mean age, 66.7±12.4 years; 39.5% women; 16.9% AF group) with acuteischemic stroke within 72 hours of onset were retrospectively enrolled. We analyzed the biomarkers such as hs-CRP, FFA, pro-BNP, D-dimer, myoglobin and eGFR between stroke with and without AF.
Results: Age, heart rate, FFA, pro-BNP, D-dimer, myoglobin and the frequency of woman were significantly higher in AF group (p <0.05). eGFR was significantly lower in AF group (p<0.05). hs-CRP was no significant difference. The respective cut-off value of FFA, pro-BNP and D-dimer level for prediction of the AF were 1235.5 µEq/ml, 287.5pg/ml and 1.105 µg/ml (sensitivity 58%, specificity 91%, AUC 0.80 for FFA; 88%, 83%, 0.93 for pro-BNP;39%, 82%, 0.73 for D-dimer). The combination of FFA, pro-BNP or D-dimer for the prediction of the AF had a sensitivity of 94% and and a specificity of 66%. Multivariate logistic regression analysis demonstrated that female gender, FFA and pro-BNP were independently associated with the presence of AF.
Conclusion: The combination of FFA or pro-BNP can be a strong biochemical marker for the prediction of AF on admission in patients with acute ischemic stroke.
Disclosure: Nothing to disclose

EPR2021

Diagnostic workup and aetiologic diagnosis of ischemic stroke in young adults: a two-centre comparison

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Background and aims: Identifying the aetiology of ischemic stroke in young adults is often a difficult task. Strategies for diagnostic assessment vary between a comprehensive approach, a staged workup emphasizing local prevalence of potential causes and a clinical hints-based approach.

This study attempts to compare the workup strategy of ischemic stroke in young adults between two stroke units in Europe, ultimately aiming to investigate the influence of workup variations in aetiologic classification.

Methods: This study included patients aged 18 to 55 years admitted for ischemic stroke or transient ischemic attack to the stroke units of Santa Maria Hospital in Lisbon, Portugal, and Innsbruck State Hospital in Innsbruck, Austria, between 2014 and 2016. Aetiology and diagnostic procedures were compared between centres.

Results: This study enrolled 156 patients from Innsbruck State Hospital and 110 patients from Santa Maria Hospital. CT (computed tomography) and MR (magnetic resonance) angiography (p<0.01), transoesophageal echocardiography (p<0.05) and ophthalmologic and dermatologic evaluation (p<0.01) were more commonly performed in Innsbruck, whereas patients in Lisbon were more frequently submitted to transcranial Doppler (p<0.01) and screening for thrombophilia (p<0.05), autoimmune disorders (p<0.01) and other causes. No significant differences in aetiology were found.

Conclusion: The variations in the diagnostic workup between both centres did not influence aetiologic diagnosis. Extensive laboratory testing not guided by clinical hints does not seem to influence diagnosis of stroke of other determined cause, thereby emphasizing the importance of a clinically-oriented diagnostic approach.

Disclosure: Nothing to disclose

EPR2022

Predictors for timely arrival in hospital and effect on clinical outcome in patients with acute stroke in Germany

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Background and aims: Even though effect of recanalization therapies for acute stroke has been proved to be highly effective, most of stroke patients still reaches hospitals outside the time window.

We aimed at identifying factors decisive for timely arrival at the hospital of patients with acute stroke within the therapeutic time window.

Methods: In two regional stroke units in North-Rhine-Westfalia, Germany 895 consecutive patients with ischaemic stroke or TIA were surveyed after admission to hospital and 3 months later.

Results: Only 44.9% of subjects reached the hospital within 4 hours and 54% within 6 hours, respectively. 12.3% received rTPA, 3.1% thrombectomy. Patients who notified emergency service were more likely to arrive in due time (OR 2.3 95% CI [1.1-4.9]). Knowledge of stroke symptoms (OR=1.2 95% CI [1.1-1.4]) and private health insurance (OR=3.9 95% CI [1.1-13.9]) were associated with a timely arrival.

At discharge 46.8% of timely arrived patients were symptom free compared to 30.9% of those who arrived late (Chi-Quadrat= 27.8, df =6, p=0.001). Three months later, clinical outcome of timely arrived patients still was better (Chi-Quadrat= 3.66, df=6,p= 0.72).

Conclusion: Despite free access to medical care the acute treatment of stroke in Germany is still insufficient. More than a half of stroke victims arrive too late and do not receive adequate treatment. The results call for public awareness campaign in order to increase the number of timely arriving stroke patients.

Disclosure: Nothing to disclose

EPR2023

Dexamethasone Therapy versus Surgery for Chronic Subdural Haematoma, a clinical randomised controlled trial (DECSA - trial)

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Background and aims: Chronic subdural haematoma (CSDH) is a common neurological disease with rapidly rising incidence due to increasing age and widespread anticoagulant use. Current treatment for symptomatic patients is mostly surgical intervention by burr hole craniostomy (BHC). However, dexamethasone (DXM) therapy is used increasingly as a non-surgical alternative. Randomised controlled trials comparing both therapies are lacking, leaving beneficial effects of DXM unsettled.
Objective: To compare the effect of primary DXM therapy versus BHC on functional outcome in symptomatic patients with CSDH in a multicentre randomised controlled trial.
Methods: CSDH patients with Markwalder Grading Scale (MGS) grade 1-3 are randomised to either BHC or DXM-treatment. The latter contains 16 mg DXM per day on day 1 to 4, after which the dose is halved every three days and stopped on day 20. Primary outcome is functional outcome assessed with the modified Rankin Scale (mRS) at three months. Secondary outcomes include mRS and MGS at discharge, two weeks and six months, Extended Glasgow Outcome Scale score at three months, quality of life and haematoma recurrence at six months, haematoma thickness on follow–up CT at two weeks, complications and mortality. Assuming a treatment effect of 80% in the BHC treatment arm compared to 60% for DXM, 170 patients are required to test our hypothesis of BHC superiority over DXM.
Results: Results are expected in 2019.
Conclusion: This study aims to demonstrate whether BHC is superior to DXM on functional outcome in symptomatic patients with CSDH. Ultimately it will provide a basis for future guidelines on CSDH management.
Disclosure: Nothing to disclose

EPR2024

Clinical characteristics of ischemic stroke in patients treated previously with direct oral anticoagulants

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Background and aims: Clinical guidelines recommend direct oral anticoagulants (DOACs) for secondary prevention of ischemic stroke (IS) in atrial fibrillation (AF). Optimal management of recurrent IS on DOAC therapy is controversial.
Methods: Prospective registry (2010-2015) of patients with AF treated with DOACs in secondary prevention of IS. Demographic, clinical variables, IS recurrence and its management were analyzed.
Results: We included 425 patients, 53.4% women, with a mean age of 77.1±10.2 years, mean CHA2DS2VASc 5± and HASBLED 2±, treated with dabigatran (57.7%), rivaroxaban (24.7%), and apixaban (17.6%), with a mean follow-up of 20±18.1 months. Thirty-four incidental IS (7.95%) were registered in a median time of 7 months from treatment onset (1-52); 14 (41.2%) were transient ischemic attacks. Annual rate of IS was 0.05 cases/person-years. All recurrent IS patients were receiving the correct dose of DOACs according to the label, and mean glomerular filtration rate in the event was similar to baseline (61.8±31ml/min). Reperfusion therapies were performed in 5 patients (4 intravenous thrombolysis and 1 mechanical thrombectomy). Twenty patients (58.8%) were independent (mRS ≤2) at three months, while one patient died (2.9%). For further IS prevention, 21 patients retained the same DOAC, 7 were switched to a different DOAC, and 1 to acenocoumarol. Two patients underwent left appendage closure in addition to DOAC therapy.
Conclusion: In our experience with patients treated with DOACs in secondary IS prevention, rate and clinical features of recurrent IS was similar to the pivotal trials. Clinical decisions following recurrent IS were individualized, in the absence of formal guidelines.
Disclosure: Nothing to disclose

EPR2025

Inhibiting aquaporin 4 modulates the perivascular drainage of amyloid Aβ peptide in the brain.

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Background and aims: The absence of aquaporin 4 (AQP4) in mice with APP/PS1 overexpression has a negative effect on Aβ paravascular drainage, leading to its deposition especially as cerebral amyloid angiopathy. In this pilot study, we aimed to assess the influence of direct AQP4 inhibition on the diffusion and paravascular drainage of Aβ.

Methods: We have injected 1µl of fluorescently Aβ40 peptide into the cortex of TgN(hGFAP-mRFP1) mice exhibiting endogenous fluorescent astrocytes, under a two-photon microscope, and visualizing in the same time the blood vessels (fluorescently labelled Dextran). We imaged the lesion site continuous for 90 min after the injection. We utilized non-injected animals (N=6), Aβ40 injected animals (N=6), and animals injected with Aβ40 after a single intraperitoneal administration of the AQP4 inhibitor TGN-020 (100mg/kg) (N=6). Image datasets were interpreted in order to measure the diffusion of Aβ40.

Results: Our data confirmed first that, after slow injection, Aβ40 diffuses around the site of injection in the parenchyma and slowly clears around small and medium-sized blood vessels, dissecting between the blood vessels lumina and the astrocytes end-feets. Next we showed for the first time that after AQP4 temporal inhibition, Aβ40 diffuses in the parenchyma at comparable speeds as without AQP4 inhibition, but it tends to remain located in the perivascular perimeter longer than in animals without TGN-020 treatment.

Conclusion: Altogether, these findings support the hypothesis that functional AQP4 deficiency that appears with age-related vascular changes (hyalinization of the basement membranes, increased rigidity, etc.) favors Aβ accumulation in these patients.

Cerebrovascular diseases 4

EPR2026

Risk of recurrent ischemic stroke in young patients with a cryptogenic cause

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Background and aims: The cause of ischemic stroke (IS) remains often cryptogenic, despite of an extensive diagnostic setting and especially in younger patients. Thus secondary preventive treatment does not have to be adequate. Our aim was to assess the risk of recurrent IS (RIS) in young cryptogenic IS (CIS) patients.

Methods: The study set consisted of young acute IS patients<50 years enrolled in the prospective HISTORY (Heart and Ischemic STrOke Relationship studY) study registered on ClinicalTrials.gov (NCT01541163). In all patients, the brain ischemia was confirmed on CT or MRI. Admission ECG, serum specific cardiac and thrombophilia markers, neurosonology, TEE, 24-hour and 3-week ECG-Holter were performed in all patients to assess CIS according to the ASCOD classification.

Results: Of 220 enrolled young IS patients<50 years, 161 (74%) patients were identified as cryptogenic (90 males, mean age 41.3±7.4 years). All patients were on antiplatelet therapy during the follow-up (FUP) with a median of 35 months. Six (4%, 2 males, mean age 46.8±1.2 years) CIS patients suffered RIS during FUP with a median of 13 months after first IS (median of admission NIHSS was 4 points). Median of 3-month clinical outcome was 1 point in modified Rankin Scale. One-year risk of RIS was calculated as 0.021 (95% CI: 0-0.044) using Kaplan-Meier analysis.

Conclusion: The risk of RIS in young CIS patients seems to be very low and with good outcome despite unclear cause.

Disclosure: Supported by the grant of Ministry of Health of Czech Republic nr. 17-30101A, and by the grant IGA LF UP_018_2018.

EPR2027

Predictors of readmission after acute ischemic stroke in a tertiary care center

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Background and aims: Stroke is one of the leading causes of disability both in developing as well as developed nations. Among those who survive the acute period, there remains a risk of recurrent vascular events or other stroke related non vascular complications leading to re-hospitalizations and increasing economic and health care related burden, especially in a country with limited availability of health insurance schemes.

Methods: We performed the study to evaluate the frequency and factors affecting readmission within one month of discharge among patients with acute ischemic stroke who were admitted to the stroke unit of the Aga Khan University Hospital, Pakistan, from January to December 2016. Retrospective review of data was performed on 1109 patients who fulfilled the inclusion criteria. Logistic regression was performed to evaluate for factors associated with readmission.

Results: Of the 1109 patients discharged after acute stroke, 115 (10.3%) were readmitted within one month. The most frequent causes for readmission were found to be recurrent strokes, infections particularly chest and urinary tract, seizures, electrolyte imbalances and cardiovascular events. Older age, higher MRS score at discharge and multiple underlying stroke risk factors were independent predictors of readmission.

Conclusion: Survivors of acute stroke are a vulnerable population with a higher likelihood of requiring readmission from certain stroke or non stroke related complications. Recognition of these factors and cautious monitoring may help develop strategies for quality of care improvement in these patients.

Disclosure: Nothing to disclose

EPR2028

Comparison of short longitudinal and transverse skin incision for carotid endarterectomy

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Background and aims: Nerve injuries, wound complications and poor cosmetic results still have an important impact on patient's outcome after carotid endarterectomy (CEA). The study aimed to compare 30-day morbidity and cosmetic outcome between patients undergoing CEA using short longitudinal incision (SLI) and transverse skin incision (TSI).

Methods: All consecutive patients with ICA stenosis >70% indicated for CEA were screened in this monocenter prospective study and randomly allocated to SLI or TSI group. Physical and neurological examinations were performed 30 and 90 days after surgery. Cosmetic results were evaluated using the Patient and Observer Scar Assessment Scale (POSAS) 90 days after surgery.

Results: Out of 189 enrolled patients, SLI was used in 102 patients (71 males; mean age 64.0±7.1 years) and TSI in 87 patients (58 males; mean age 66.4±7.2 years). Stroke or transient ischemic attack occurred during 30 days in 4 (3.9%) patients in SLI group and in 2 (2.3%) patients in TSI group (P=0.689). The scar quality assessed using POSAS was higher in TSI than in SLI patients (12.4 vs. 16.6 points; P<0.01). Patients in TSI group evaluated better than SLI patients the scar pigmentation, thickness, relief, pliability and surface area (P<0.01 in all cases). No significant differences were found in the occurrence of local complications (8.0% in TSI and 8.8% in SLI group; P=1.00).

Conclusion: Better cosmetic results were observed in patients after CEA using TSI than SLI. No differences in morbidity and in the occurrence of local complications were observed.

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EPR2029

Illicit substance use as a cause of stroke in young adults: a case control study

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Background and aims: Illicit drug use is a potential cause of stroke in young adults. The concomitant role of conventional cardiovascular risk factors and other co-morbidities in young adult stroke associated with illicit drug use is unclear.

Methods: We retrieved from the Stroke registry of an acute stroke unit (SU) of a tertiary care hospital all young adult patients admitted between 2005 and 2016 with a history of illicit drug use (cases). Controls (3:1) were consecutive stroke patients admitted to the SU during the same period, matched by age and gender. We compared cardiovascular risk factors, co-morbidities, type of stroke and outcome.

Results: We identified 42 stroke patients with illicit drug use (opioids-48%, cocaine-43%, cannabinoids-38%, LSD-7%, multiple drugs-43%). Smoking and other comorbidities (viral hepatitis, HIV and chronic renal disease) were statistically significant more frequent among drug users (X2=9.20, p=0.002; X2=7.8, p=0.005, respectively). All drug users had at least a cardiovascular risk factor or comorbidities potentially predisposing to stroke, while 8.5% of stroke in controls were not associated to other conditions (X2=2.49, p=0.115).

Both groups had comparable rates of ischemic vs hemorrhagic stroke. The anterior circulation territory was the most often affected in both groups (69.2% and 68.4%). The posterior circulation territory was frequently involved in cannabis users (42.9%).

The clinical outcome at hospital discharge was similar in both groups.

Conclusion: Stroke type and outcome were similar between drug users and non-users. Illicit drug users had cardiovascular risk factors and other comorbidities, which may have a synergistic effect with illicit drug use in causing stroke.

Disclosure: Nothing to disclose

EPR2030

Comparison of transcranial Doppler and echocardiogram for patent foramen ovale diagnosis

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Background and aims: Patent foramen ovale (PFO) is an interatrial septum defect present in about 25% of adults, and a possible cause of cryptogenic stroke. Recent studies suggest the benefit of its closure in embolic strokes of undetermined origin. Therefore, PFO presence is frequently searched, especially in young adults with stroke, either by echocardiography or transcranial Doppler (TCD) with IV gaseous contrast for left-right shunt detection. TCD results are interpreted according to the number of detected microembolic signals (MES), with and without Valsalva maneuver (VM): 0-negative; 1-10; >10 without curtain; curtain (not individualized MES).

Our objective is to compare the results of TCD and echocardiogram for PFO detection.

Methods: Analysis of TCD exams for left-right shunt detection at our center in the last 2 years, and comparison with echocardiogram results.

Results: Fifty-seven PFO studies were performed, 34 early positive. One acute stroke patient, unable to perform Valsalva manouver, had negative TCD, while a later transesophageal echocardiogram (TEE) was positive. Of the patients with PFO on TCD, 9 were confirmed by TTE (transthoracic echocardiogram) and 16 by TEE. Three positive TCD were not confirmed by echocardiogram; of these, one was positive only with VM (7 MES), another had 3 MES without VM and >10 with VM, and another had >10 MES without VM. Six positive DTC had negative TTE and wait for TEE. Regarding the echocardiogram, TCD had 96% sensitivity, 87% specificity, 89% PPV and 95% NPV.

Conclusion: In our series, TCD showed great accuracy compared to echocardiogram, currently considered the gold standard for PFO diagnosis.

Disclosure: Nothing to disclose

EPR2031

Intravenous trombolysis for ischemic stroke in pregnancy and puerperium – case series

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Background and aims: Pregnancy and puerperium have been reported to be associated with an increased risk of ischemic stroke with higher risk in puerperium. Reported incidence is from 11 to 34 per 100 000 pregnancies. Standard recanalization therapy with intravenous thrombolysis (IVT) in pregnant women is not verified by large clinical trials. Although there are number of reported cases showing safety of thrombolysis in pregnant women and postpartum period, there are still doubts for use of IVT in common practice.

Methods: Case series of 5 ischemic stroke patients from Motol comprehensive stroke centre treated in 2014 -2017 when pregnant or postpartum.

Results: Three patients were pregnant (1st and 2nd trimester), two were in puerperium. Mean age was 34 (29-38 years), mean NIHSS at admission was 7.4 (5-15). Affected territory was twice middle cerebral artery, twice posterior cerebral artery and in one patient vertebral and basilar artery. We have not seen any bleeding complications – intra or extracranial. One patient was complicated with infratentorial decompressive craniectomy for cerebellar ischemia with oedema. Modified Rankin scale at 3 months was good in all patients (0-1 points). Outcome of pregnancies was also good, 2 women delivered healthy child, 1 is still pregnant with no complications. 1 from 2 at puerperium had another safe pregnancy after the stroke.

Conclusion: Thrombolysis during pregnancy and the puerperium in our experience is safe and has good efficacy and should be considered in therapy of stroke in pregnant women.

Disclosure: Nothing to disclose

EPR2032

Emergent carotid artery stenting in internal carotid artery atherosclerotic disease with tandem intracranial occlusion

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Background and aims: Several randomized trials have proven the safety and efficacy of mechanical thrombectomy (MT) in large vessel occlusions; nonetheless, there is still no consensus concerning hyperacute management of tandem occlusions. Recent studies have proposed emergent carotid artery stenting (eCAS), along with MT, as an effective and safe treatment option.

Aims: To characterize safety and short-term outcome of patients treated with eCAS during endovascular treatment of acute ischaemic stroke.

Methods: Review of the prospective patient registry submitted to MT for anterior circulation acute ischaemic stroke in a single referral centre and selection of patients treated with eCAS for atherosclerotic occlusion/near-occlusion of cervical internal carotid artery between January/2015 and July/2017. Clinical data was collected and assessment of procedure safety and 3-month-outcome were performed.

Results: Among 252 patients submitted to MT, 24 patients (9.5%) underwent eCAS. Most patients were male (23/24), median age was 65.2 years (IQR=57.3-73.8), median admission NIHSS was 14 (IQR=11-17) and 14/24 patients had been submitted to intravenous thrombolysis. Successful recanalization was obtained in 95.8% of patients. Two patients (8,3%) experienced symptomatic intracranial haemorrhage, one patient experienced early intra-stent thrombosis and one patient developed cerebral hyperperfusion syndrome. At 3-month follow-up, 17 patients were independent (70.8%) and 1 patient died (4,2%).

Conclusion: Overall, positive results were obtained using emergent carotid stenting (eCAS). Although an optimal intervention for this type of occlusions has not yet been formally established, eCAS has been surging has a feasible and safe treatment option.

Disclosure: Nothing to disclose

EPR2033

Early transcranial color-coded Doppler in the prediction of cerebral edema post-thrombectomy

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Background and aims: Recanalization of a large vessel occlusion (LVO) has a dramatic impact on patients' outcome, however it also increases the risk of reperfusion injury and devastating clinical consequences, such as cerebral edema and hemorrhagic transformation. We aimed to assess the accuracy of the hemodynamic status post-thrombectomy, evaluated by transcranial color-coded Doppler (TCCD), in the prediction of cerebral edema.

Methods: Cohort study of acute stroke patients with LVO in the anterior circulation, who achieved effective arterial recanalization (TICI 2b/3 post-thrombectomy) and were evaluated by TCCD in first 24 hours. We analyzed the mean velocity in the M1 segment of the symptomatic and asymptomatic middle cerebral arteries (MCAs), and the symptomatic/asymptomatic MCAs ratio (MCAsRa). Cerebral edema was classified in the 24 hours CT scan by blinded-Neurorradiologist. Statistical analysis included univariate analysis and logistic regression adjusted for age, initial NIHSS and previous arterial hypertension.

Results: One-hundred patients were enrolled, mean age 67.69 (±13.86) years, 59 males (59.0%). The mean velocity in the symptomatic MCA was not statistical different in patients with (60.55±22.31cm/sec) vs. without cerebral edema (54.55±17.09cm/sec),p=0.173; MCAsRa were also similar between groups (1.04±0.359 vs. 1.00±0.32;p=0.608). Neither mean velocity or MCAsRa were predictors of cerebral edema: OR 1.020 (0.996-1.045,p=0.105) and OR 1.594 (0.431-5.895,p=0.484).

Conclusion: Cerebral reperfusion injury has a complex mechanism with multiple pathologic processes and cerebral edema is frequent. Nevertheless, early TCCD does not seem to identify predictors of cerebral edema post-thrombectomy.

Disclosure: Nothing to disclose

Child neurology/developmental neurology

EPR2034

Basal Ganglionic Lesions in Egyptian Children: Radiological Findings in Correlation with Etiology and Clinical Manifestations

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Background and aims: In childhood, the metabolic activity of the basal ganglia is greater and they are particularly prone to injury, that causes problems controlling movement, muscle tone and cognition.

Aim of work: to determine the etiology of basal ganglionic disorders in a sample of Egyptian children.

Methods: A cross-sectional observational study was utilized on 34 patients attended at the Pediatric Neuro Outpatient Unit of Neurology department at f Al-Azhar University Hospitals during a period of one year from November 2014 to November 2015. A specialized pediatric neurological sheet, Cognitive assessment using Stanford-Binet Intelligence Scale and Laboratory investigations were performed. The included patients were classified according to MRI into two groups; ganglionic (included patients with isolated basal ganglionic lesions) (n=23) and para-ganglionic (included patients with combined ganglionic and para-ganglionic lesions) (n=11).

Results: Frequency of male was higher than female patients in both groups without significant difference (13 (56.5%) versus 6 (43.5%) and 10 (54.5%) versus 5 (45.5%), in ganglionic and para-ganglionic groups, respectively). acute ischemic stroke was the most frequent cause, which was found in 12 (35.3%) cases, followed by 10 (29.4%) had metabolic and infectious causes, and lastly 2 (5.9%) had toxic causes. The incidence of toxic causes (CO poisoning) was higher among ganglionic group compared to para-ganglionic group (2(8.7%) versus 0(0.0%), respectively).

Conclusion: Acute ischemic stroke was the most frequent cause of basal ganglionic lesion in a sample of Egyptian children.

Disclosure: Nothing to disclose

EPR2035

The concentration of Doublecortin in the cerebrospinal fluid from human infants is developmentally regulated

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Background and aims: Doublecortin (DCX) is specifically expressed in neuronal precursor cells and migrating neurons. DCX is neurodevelopmentally regulated, and its concentration in the rodent cerebrospinal fluid (CSF) and in rodent and human brain declines during early postnatal stages. In this study, we analyzed the concentration of DCX in the CSF (DCX-CSF) from human infants.

Methods: CSF was collected from pediatric patients requiring neurosurgical treatment. DCX concentration was measured with the Mesoscale platform. Clinical data was retrospectively collected from individual patient charts. Chronological age was adjusted for premature birth.

Results: A total of 52 CSF samples from 35 patients (18 females) were collected between February 2013 and June 2016. The patients' age was from 0.3 years before due date to 18 years (median 2.9; interquartile range 0.3-7.3). DCX-CSF could be quantified in 21 samples from 12 patients ranging from 13 to 21,568 pg/ml (1065; 150-3,495). All 11 patients younger than 4 months had detectable DCX-CSF that decreased with age. Only one 5-year-old with a grade III astrocytoma also had detectable DCX-CSF (331 pg/ml).

Conclusion: Our results show an age-dependent downregulation of DCX-CSF from humans until 4 months of age, similar to that observed in rodent neonates. This time window for the detection of DCX in human CSF strikingly coincides with the recently described migration of DCX+ cells to the frontal lobe in the human brain that persists for 5 months after birth. Further investigations are warranted to understand the clinical significance of DCX-CSF in humans.

Disclosure: Nothing to disclose

EPR2036

The role of monoamine oxidase A mutation in a boy with neurodevelopmental and behavioural problems – a new family with Brunner Syndrome?

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Background and aims: Monoamine oxidase A (MAOA) gene polymorphisms have been associated with various behavioural and psychiatric phenotypes. Brunner Syndrome was first described in 1993 as a recessive X-linked disorder characterized by altered behaviour with impulsive aggressiveness and mild mental retardation associated with MAOA deficiency. Only more recently, after two decades since the first Brunner Syndrome description, three more families have been identified, indicating that this entity should be more frequently suspected.

Methods: Case report.

Results: We present a case of a 9-year-old boy followed in neurology consultation since 2 years of age due to epilepsy, behaviour problems, sleep disturbance with night terrors, attention deficit and hyperactivity symptoms and a borderline intellectual disability with important language delay. He had a history of impulsivity, frustration intolerance and heteroaggressiveness with anger outbursts. Due to the complexity of the clinical picture, together with a family history of male individuals (two brothers and one nephew) with similar neurodevelopmental and behavioural problems, the suspicion of a recessive X-linked disorder was raised. Accordingly, a disease-focused exome sequencing was performed and a MAOA mutation c.617G>A(p.Arg206Gln) was identified in hemizigoty in the clinical proband.

Conclusion: We describe a new genetic MAOA variant, associated with a severe behavioural phenotype, in a family with several male elements affected with psychiatric symptoms, suggesting an X-linked pattern of disease inheritance. Further biochemical and genetic studies are now being performed. If confirmed, this corresponds to the fifth family identified with this syndrome worldwide.

Disclosure: Nothing to disclose

EPR2037

Imaging of the Mechanisms of Thalamic Damage in Pediatric Multiple Sclerosis

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Background and aims: Thalamic damage occurs in pediatric multiple sclerosis (MS) patients. Thalamus location exposes this structure to different pathobiological processes: Wallerian degeneration for its extensive cortical and subcortical white matter (WM) connections and neuroinflammation due to cerebrospinal fluid (CSF) mediated immune-cytotoxic factors. This study is aimed at characterizing thalamic volumetric abnormalities according to their distance from CSF and their correlation with WM lesions in pediatric MS patients.

Methods: Dual-echo and 3DT1-weighted images were acquired from 70 pediatric MS and 26 age and sex-matched healthy controls (HC). To assess thalamic shape differences a vertex-analysis was performed using the FMRIB Integrated Registration and Segmentation Tool. Cortical surface reconstruction and mean cortical thickness measurement were performed using FreeSurfer. Correlations with clinical and conventional MRI variables were also explored.

Results: Global thalamic volume did not differ between HC and pediatric MS patients (p=0.06). The vertex analysis revealed significant differences in thalamic shape with a prominent inwards displacement of thalamic ependymal surface and a relative sparing of ventrolateral thalamic surface (p<0.05). No correlation was found between thalamic surface inwards displacement and T2 and T1 lesion volume, cortical thickness, disease duration and clinical disability.

Conclusion: In pediatric MS, the absence of correlations between thalamic volumetric abnormalities, focal WM lesions and clinical variables supports the hypothesis of an early damage, linked to acute inflammatory processes occurring close to disease onset rather than to Wallerian degeneration. Thalamic inward surface displacement could represent an early neurodegenerative process, potential target for monitoring disease progression from the earliest stages of disease.

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EPR2038

Headaches in preschoolers: are "red flags" predictive of positive neuroimaging in Emergency Department? Preliminary data.

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Background and aims: Headache at preschool age can frequently be secondary. An emerging problem is to establish the role of neuroimaging in children suffering headaches, but to date in literature we do not have clear evidence concerning when neuroimaging study is necessary, mostly in this age group, rather than clinical follow-up to limit repeated visits to Emergency Department (ED). Aim of this study is to explore and verify the relationship between the presence of red flags and neuroimaging abnormalities in a preschool population.

Methods: We collected clinical data of children aged from 1 to 7 years old admitted in ED from October 2015 to September 2016. We used a predetermined list of red flags (acute onset, associated symptoms, abnormal neurologic examination and others) and we evaluate the number of children underwent computed tomography (CT).

Results: We found that 128/400 (32%) children admitted in ED are preschoolers, 58 males and 70 females. Seventy-nine of these (61.7%) showing one or more red flags at the access, 57/79 (72.15%) were investigated with CT. Thirty-eight of them showed positive TC for incidental benign abnormalities, while just one patient, with more than one red flags (acute onset, occipital localization and paresis) at the access, showed altered TC for dangerous anomalies.

Conclusion: These is the first study on a selected preschool population with headache. Preliminary results confirm literature data about the poor specificity of undifferentiated red flags in identifying which patients need neuroimaging, underlying that in the setting of a normal neurologic examination neuroimaging can be deferred in most pediatric patients.

Disclosure: Nothing to disclose

EPR2039

ELAC2 mutation and phenotypic spectrum, a case report

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Background and aims: ElaC Ribonuclease Z 2 (ELAC2) encodes the long form of RNase Z, an endonuclease responsible for the removal of the 3-prime extensions from tRNA precursors, which is an essential step in tRNA biogenesis both in nucleus and mitochondria. Primarily the ELAC2 gene was regarded as a heritable prostate cancer susceptibility factor.However, ELAC2 mutations also cause a mitochondrial RNA processing defect associated with hypertrophic cardiomyopathy and combined oxidative phosphorylation deficiency. In some instances symptomatology such as encephalopathy, microcephaly, muscular hypotonia, seizures and growth retardation as well as early death have been reported. Next-generation sequencing (NGS) has proven to be efficient in the diagnostics of disorders where multiple genes can be involved. NGS-based exome trio analysis of proband and parents detects recessive, X-linked and de novo genetic disorders.

Methods: A twelve year old girl with ataxia, deafness and scoliosis was primarily referred for NGS ataxia testing. However, due to growth retardation and mixed developmental disorder NGS exome was performed.

Results: A homozygous sequence variant in ELAC2 was identified. The identified sequence variant probably explains her symptomatology.

Conclusion: NGS is versatile tool when investigating probable genetic causes of undiagnosed child neurology or developmental delay cases. Due to the ELAC2 finding an echocardiogram was performed. The ELAC2 symptomatology is probably more diverse than originally suspected.

Disclosure: Nothing to disclose

EPR2040

Visual cortical excitability in pediatric migraine: a study with sound-induced flash illusions

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Background and aims: Sound-induced flash illusions (SIFI) are related with the level of visual cortex(V1) excitability(1). In adults migraineurs, in response to SIFI, V1 is hyperexcitable(2). Susceptibility to SIFI in children is increased because during childhood acoustic dominance switch to a visual(3). We evaluate by SIFI the V1 excitability in children with migraine to assessing also age-related differences in audio-visual perception. Twenty-six migraine children (examined interictally), fifteen children and twenty-four adult healthy with no familiarity for migraine were tested.

Methods: Visual(flash) and sound(beep) stimuli are presented with different combinations: multiple flashes with a single beep causes perception of less flashes (fusion illusion) while multiple beeps and single flash, induce perception of more flashes (fission illusion). Each combination was randomly presented and the subject had to indicate the number of the flashes seen.
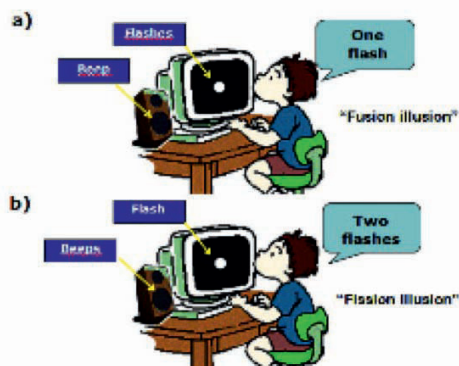
Results: Children see more illusions than adults. Children with migraine do not differ from age matched control in the illusory percept, but they perceive more flashes in multiple flash trials.
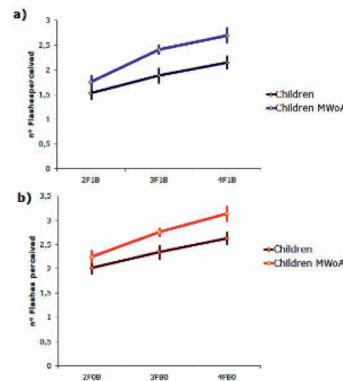
Flash seen with (a) and without beep (b).

Conclusion: Children see a greater number of SIFI than adults, this is due to the higher propensity of visual stimulation to be driven by auditory stimulus. Even if no difference in the illusory percept between controls and patients emerge, the migraine children have an increased ability to perceive flashes, even outside migraine attack, that reveal a hyper-functional visual cortex in migraine also in pediatric age. The SIFI can be used in pediatric migraine for testing the responsivity of V1.

Disclosure: Nothing to disclose

Clinical neurophysiology

EPR2041

Effects of 10- and 20-Hz transcranial alternating current stimulation (tACS) over motor cortex on blink reflex excitability. A blink reflex recruitment curve study

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Background and aims: Brain oscillations play a pivotal role in motor function. Pathological increase of beta-band oscillations has been associated with motor dysfunction in Parkinson's disease. Transcranial alternating current stimulation (tACS) may modulate brain oscillations in a non-invasive fashion. As a way to understand the role of brain oscillations is to study their effects on reflex circuits, we wished to explore the result of 20-Hz and 10-Hz tACS sessions over M1 on blink reflex excitability.

Methods: Fifteen healthy volunteers (age:27.4±2.7;11F) underwent 10-minutes tACS sessions (active/reference:C4/Pz; intensity: 1 mA; three conditions: 1) 20-Hz tACS; 2) 10-Hz tACS and 3) sham tACS). Blink reflex recruitment curves were obtained for interstimulus intervals (ISI) of 100, 150, 200, 300, 400, 500 and 750 milliseconds before (T0), at the end of each stimulation (T1) and 30 minutes from onset of each tACS session (T2).

Results: Repeated measures of ANOVA showed a significant effect of ISI ($F=62.610$, $p=0.0000$) and type of stimulation ($F=3.5917$, $p=0.01627$). R2 responses were significantly increased at T2 after 20-Hz stimulation whether compared to baseline ($F=7.8102$, $p=0.00927$) and sham sessions ($F=5.4862$, $p=0.02651$). 10-Hz tACS didn't differ from baseline and sham sessions.

Conclusion: This is the first study exploring a modulatory effect of tACS on trigemino-facial reflex circuits. In our study, 20-Hz tACS determines a late increase of blink reflex excitability. At beta-band frequency, tACS was able to determine a larger effect than at alpha-band frequency, supporting a driving role of beta band- oscillations of motor cortex on exciting subcortical structures such as basal ganglia and brainstem circuits.

Disclosure: Nothing to disclose

EPR2042

PCI & Auditory ERPs for the diagnosis of disorders of consciousness: an EEG-based methods comparison study.

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Background and aims: Diagnosing the level of consciousness in patients suffering from severe brain lesions is still a major challenge. EEG-based systems can help discriminate conscious from unconscious patients. This study aims to confront the results from two of the most reliable methods: the Perturbational Complexity Index (PCI) which is based on Transcranial Magnetic Stimulation (TMS-EEG), and a recent machine learning approach using EEG-extracted markers from a standardized oddball auditory stimulation paradigm (EEG-ERP).

Methods: Patients presenting either an unresponsive wakefulness syndrome (UWS), a minimally conscious state (MCS) or an emergence of MCS (EMCS) underwent both TMS-EEG and EEG-ERP. We computed PCI value by compressing the spatiotemporal pattern of cortical responses to the perturbation of the cortex with TMS. For EEG-ERP, we extracted 60 markers corresponding to quantification of power spectrum and complexity in individual EEG sensors and information sharing between them. Using machine-learning, we predicted the individual probability of being (minimally) conscious.

Results: PCI and EEG markers, when considered categorically (i.e. UWS vs MCS), were consistent for all UWS and EMCS patients, whereas the results for MCS patients showed less consistency. Nevertheless, we found a significant correlation between PCI values and the probability of being conscious with the multivariate classifier.

Conclusion: PCI correlated positively with the combination of EEG markers in severely brain-injured patients. These findings imply that EEG signatures of consciousness can be reliably extracted from different contexts and combined into coherent predictive models, encouraging future efforts in large-scale data-driven clinical neuroscience.

Disclosure: Nothing to disclose

EPR2043

Relationship between EEG and psychophysical responses to perception of contact heat stimuli

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Background and aims: Only a few indirect methods allow for the assessment of sensory processing and conscious perception of nociceptive inputs in humans.

Methods: In 12 healthy subjects, we obtained contact-heat evoked potentials (CHEPs) to thermoalgesic stimuli of two intensities (lowT-42ºC and highT-52ºC) while subjects assessed stimulus perception time through the Libet's clock (AW). In test trials, they were requested to do the same but also hitting a switch at stimulus perception (React). We compared the timing of CHEPs, React and AW in the two stimulus intensities.

Results: Stimulus intensity was more effective to modulate CHEPs (472ms±40ms for highT and 748ms±47ms for lowT) than RT (486±74 vs 649±72) but it did not show a significant effect on AW (337±83 vs 384±83). At both stimulus intensities, task complexity did not affect CHEPs but prolonged RT and AW. Temporal profiles induced by changing stimulus intensity and task complexity were non-linear for CHEPs, React and AW.

Conclusion: Our findings support the dissociation between CHEPs, React and AW in the assessment of nociceptive stimulus processing. AW brings valuable information on conscious perception of painful stimuli.

Disclosure: Grant ESPY-112/18 from Instituto de Salud Carlos III to J. M. Castellote

EPR2044

Early Transient Dysphagia in Acute Pontin Infarctus

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Background and aims: Early transient dysphagia in stroke patients with pontin infarctus has not been studied by electromyographical methods. This study aims to evaluate the presence of swallowing abnormalities and some pathophysiology of dysphagia in the patients with acute pontine infarctus using electrophysiological methods.

Methods: A prospective study of 30 patients with pontin infarctus within 9 days after the onset of stroke and 20 age-matched healthy adults were investigated. Electrophysiological methods included dysphagia limit (DL) and sequential water swallowing (SWS) tests.

Results: 58% of the patients who are not suffering from dysphagia clinically have been found to be pathological in terms of both DL and SWS tests. Among pathological patients with DL; 77.8% of them were also pathologic in SWS test. Among non-pathological patients with DL; 35.3% of them were pathological in SWS test.

Conclusion: The electrophysiological methods presented here are non-invasive, easy to apply, and very simple to complete. They can be used in patients with neurogenic dysphagia of any kind, including the acute stroke patients. We recommend electrophysiologic methods to detect oropharyngeal dysphagia in stroke patients even if they have no overt swallowing complaint.

Disclosure: Nothing to disclose

EPR2045
withdrawn

EPR2046

Cognitive impairment in MRI-negative epilepsy: Relationship between neurophysiological and neuropsychological assessments.

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Background and aims: Epileptic patients frequently develop cognitive impairment due to seizures and antiepileptic drugs. The aim of the current study is to evaluate the cognitive status of epilepsy patients using neurophysiological and neuropsychological measures and seek for possible correlations.

Methods: The study sample consisted of twenty MRI-negative epilepsy patients (mean age±SD: 30.3±12.56 years; average disease duration: 13.95 years) and ten age-matched controls. Auditory ERPs were elicited and latencies and amplitudes of the major late ERP waves (N200, P300 and Slow Wave) were determined. EpiTrack, a brief screening tool for measuring cognitive impairment was administered to all patients.

Results: Latencies of P300 and Slow wave were prolonged in patients compared to controls ($p<0.05$). Moreover statistical significant difference was evident in the subtests Trail-Making A,B of the EpiTrack test. Significant negative correlations were observed between P300 latency and all Epitrack subtests (all p's<0.05) AED load and the performance of the patients' in the maze subtest were the most significant predictors of P300 latency

Conclusion: A decline in the memory, attention and speed of mental processing of MRI-negative epileptic patients compared to age matched controls which is also corroborated by P300 latency and the Epitrack scores was observed and seems to be mostly due to antiepileptic drug load.

Disclosure: Nothing to disclose

EPR2047

Peripersonal space in Autism Spectrum Disorder: an electrophysiological study

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Background and aims: People with Autism Spectrum Disorder (ASD), characterized by impaired social functioning, fail to adjust a normal peripersonal space (PPS) with others, either keeping the distance too far or disturbingly close.

The features of PPS in healthy subjects has been delineated by using hand-blink reflex (HBR). Our aim was to assess its spatial and electrophysiological properties in people with ASD compared to controls.

Methods: A total number of 16 patients diagnosed with ASD and 12 healthy volunteers, (14-30 years) were included in the study. The blink reflex responses elicited by stimulating the median nerve was recorded in three positions of the stimulated hand: far, medium and near (Table1). The data were entered into SPSS 20 programme and statistical significance was analysed with t-test, chi-square and Friedman tests.

Table 1: Three positions of the stimulated hand in hand blink reflex; far, medium and near (from left to right)

Results: HBR responses resembled in latency between the two groups, but the amplitudes were 1.5-4 times higher in the ASD group in all positions. Though the near position elicited the highest amplitude in controls, it was still lower than the minimum response in ASD group (Table2). While the HBR responses are expected to intensify as the hand approaches to face, ASD patients showed a decrease in amplitude in the medium position; and the near-far responses did not show a significant difference (Table3).
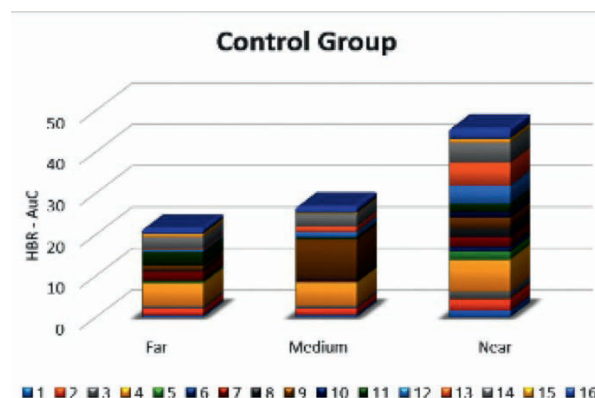
Table 2: This table shows the cumulative hand-blink reflex responses of the control group, seperated by the far, medium and near positions of the stimulated hand. HBR: Hand blink reflex, AuC: Area under the curve
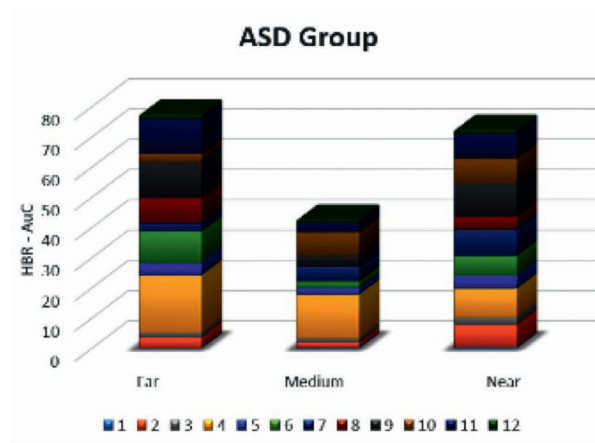
Table 3: This table shows the cumulative hand-blink reflex responses of the ASD group, seperated by the far, medium and near positions of the stimulated hand. HBR: Hand blink reflex, AuC: Area under the curve ASD: Autism spectrum disorder

Conclusion: This is the first study to investigate the electrophysiological and spatial properties of PPS in ASD, which revealed a marked qualitative and quantitative difference in patients compared to controls, in correlation with odd choices of personal space use in people with autism.

Disclosure: Nothing to disclose

EPR2048

Gender differences in Parkinson's disease: transcranial magnetic stimulation study of newly diagnosed and drug-naive PD patients

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Background and aims: Demographic studies of Parkinson's disease (PD) found that women are almost twice less affected than men, implying protective effect of female sex. It is not known, once the symptoms develop, if disease course differs between genders, which would suggest differences in pathophysiology. In early PD, functional changes may be detected in primary motor cortex (M1) using transcranial magnetic stimulation (TMS). We hypothesised that, if pathophysiology differ between genders in PD, this will be reflected in differences of M1 TMS measurements.

Methods: Thirty-nine newly diagnosed and untreated PD patients (23 males, 16 females) were assessed using UPDRS. Motor thresholds, input/ output curve (IO), short interval intracortical inhibition (SICI), cortical silent period (CSP) and intracortical facilitation (ICF) were measured over both hemispheres, corresponding to less and more affected side, using TMS. Plasticity was probed using paired associative stimulation (PAS) protocol. Twenty-three healthy controls were studied for comparison.

Results: There were no gender differences in UPDRS. Female patients had less steep IO curve on the less affected side. Females also had more preserved SICI and trend toward better response to PAS protocol in both hemispheres, compared to male PD patients, while there were no differences in motor thresholds, ICF and CSP. Healthy controls showed no gender differences in any of the TMS parameters.

Conclusion: Less steep IO curve, preserved SICI and tendency toward preserved cortical plasticity in female compared to male patients with early PD suggest gender differences in disease pathophysiology. We provide first neurophysiological evidence that sex is an important factor in heterogeneity of PD.

Disclosure: Nothing to disclose

EPR2049

A comparison of the P300 and PET in patients with disorders of consciousness in absence of response to command

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Background and aims: Diagnosis of patients with disorders of consciousness (DOC) has become more accurate by using standardized behavioral assessment and objective measures of consciousness derived from neuroimaging. Another major challenge is the assessment of covert response to command in patients who do not present overt response to command, in order to ultimately find a means of communication.

Methods: We assess the passive (auditory and tactile) and active (tactile) P300 ERP in twelve patients without behavioral command following to test its sensitivity for the detection of residual consciousness and confront it to cerebral metabolism as measured with glucose PET, the most sensitive objective diagnostic tool.

Results: For the passive paradigms we have found that the accuracy of the discrimination of the standard and deviant stimuli in the auditory paradigm is higher for UWS than for MCS patients, while for the tactile paradigm the accuracy is slightly higher for MCS than UWS patients. There was no correlation between percentage of glucose metabolism reduction and P300 accuracy. One patient reached a high accuracy during the active tactile paradigm, suggestive of covert command following, even if behavioral command following was absent, and no discernable difference between the PET of this and other patients could be observed.

Conclusion: Our results suggest that the passive P300 is not a good marker for consciousness or overall brain metabolism. On the other hand, the active P300 might probe covert command following in patients without behavioral response to command and therefore could be a valuable addition in the clinical assessment of DOC patients.

Disclosure: The authors declare that the hard- and software was made available by Gtec.

Epilepsy 2

EPR2050

Parkinson's disease and the risk of epileptic seizures

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Background and aims: To assess the association between incident Parkinson's disease (PD) and subsequent incident epileptic seizures.

Methods: Retrospective cohort study with nested case-control analysis using data from the UK Clinical Practice Research Datalink. We identified patients aged $\geq$40 years with an incident diagnosis of PD between 1995 and 2016 and a matched comparison group of PD-free individuals. We calculated crude incidence rates (IRs) with 95% confidence intervals (CIs) of epileptic seizures in PD patients and the PD-free comparison group, and corresponding crude incidence rate ratios (IRRs). In the nested case-control analysis, we calculated adjusted odds ratios (adj. ORs) of incident PD among cases with incident epileptic seizures and seizure-free controls overall and stratified by various, seizure-provoking comorbidities.

Results: Among 23,086 incident PD patients and 92,343 PD-free individuals, we identified 898 patients with incident epileptic seizures. The crude IR of epileptic seizures in PD patients was 266.7/100,000 person years (95% CI 235.6-297.7), and in PD-free individuals 112.4/100,000 person years (95% CI 103.5-121.3) [IRR: 2.37, 95% CI 2.06-2.37]. The adj. OR of epileptic seizures was 1.68 [95% CI 1.43-1.98]) in PD patients compared with PD-free individuals. PD patients with comorbid brain disorders (adj. OR 12.36 [95% CI 8.74-17.48]) or with >1 seizure-provoking comorbidity (adj. OR 13.24 [95% CI 10.15-17.25]) were at the highest risk of epileptic seizures compared with PD-free individuals with no seizure-provoking comorbidities.

Conclusion: This study suggests that incident PD is associated with an increased risk of incident epileptic seizures.

Disclosure: Nothing to disclose

EPR2051

Abnormal visual connectivity in Eyelid Myoclonia with Absences: evidences from Electrocortical Connectivity and Non-linear Quantitative Analysis of EEG Signal

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Background and aims: Eyelid myoclonia with absences (EMA) is an epileptic syndrome characterized by eyelid myoclonia with or without absences, eye-closure sensitivity and photosensitivity. The objective of our study was to analyze the electrocortical networks of visual sensitivity in EMA.

Methods: Data of 10 EMA patients and 10 controls were analyzed. EEG networks were computed using independent components analysis LORETA. Moreover, the power law exponent β was obtained. β values ~ 1 imply self-similarity, property of fractal phenomena.

Results: A reduction of alpha activity over the occipital lobe and of beta activity over the frontal lobe during the resting state and an increase of beta activity over the frontal lobe after eyes-closure was found in patients. A significant increase of the beta index over the frontal regions was found in patients (F3: 2.89±0.28, vs 2.61±0.24, p=0.03; F4: 2.88±0.26 vs 2.62±0.28, p=0.05; F7: 2.64±0.33 vs 2.28±0.31, p=0.02) and, among patients, significant differences were found between the resting state and the eyes-closed task with an increase of beta index over the parieto-occipital regions after eyes-closure (P3: 2.86±0.35 vs 3.01±0.37, p=0.03; P4: 2.86±0.37 vs 3.02±0.38, p<0.01; O1: 2.76±0.42 vs 2.98±0.43, p<0.01; O2: 2.81 ±0.37 vs 3.01±0.36, p<0.01).

Conclusion: The findings of our study confirm the role of an intrinsic abnormality of the occipital cortex with an altered occipital-frontal network in determining the visual sensitivity in EMA.

Disclosure: Nothing to disclose

EPR2052

Influence of "epilepsy school" on the quality of life of patients with epilepsy

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Background and aims: To study the effect of "epilepsy school" on the quality of life of patients using QOLIE-31 questionnaire.

Methods: 100 patients with epilepsy were divided into 2 groups randomly. The main group consisted of 50 patients who later visited "epilepsy school" combined with optimized pharmacotherapy to improve their compliance. "Epilepsy school" was held once in a month during 6 month. The comparison group included 50 patients with epilepsy, only with optimized pharmacotherapy. Both groups were comparable (p˂0.05). Quality of life was checked twice by using QOLIE-31 questionnaire at the beginning and after 1 year.

Results: In the comparison group (without attending "epilepsy school") after 12-month follow-up, most (58%) patients had rare seizures, 2% - achieved clinical remission, and 40% had high-frequency seizures. During analysing QOLIE-31 subscales after 12 month (2nd visit) the highest scores were obtained for the subscales "Overall Quality of Life" (59.2±6.56), "Emotional Well-Being" (53.36±9.23), "Medication Effects" (46.98±7.98).

In the main group after attending "epilepsy school" half of patients (50%) had rare seizures, only 14% had high-frequency seizures, and 36% of patients achieved control over seizures. When analyzing the QOLIE-31 subscales, after 12 months, most of QOLIE-31 subscales were increased. The highest scores were obtained for the subscales "Overall Quality of Life" (72.76±12.20), "Emotional Well-Being" (64.51±10.12), "Social Functioning" (62.34±11.46).

Conclusion: Thus, optimized pharmacotherapy in combination with the school of epilepsy can reduce the incidence of side effects, improve the effectiveness of treatment and improve the emotional, social and physical state of patients with epilepsy.

Disclosure: Nothing to disclose

EPR2055

Autonomic Cardiovascular Dysfunction in Patients with Temporal Lobe Epilepsy (TLE)

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Background and aims: Impaired autonomic function is considered to be one of the possible mechanisms of sudden unexplained death in epilepsy. The aim of the study was to evaluate the level of autonomic cardiovascular regulation in patients with TLE.

Methods: Twelve adult patients (mean age 36.83 ± SD 7.33 years, 6 males) with TLE and twelve gender- and age-matched healthy controls were included in the study. We performed the time and frequency domain analysis of heart rate variability (HRV) and systolic blood pressure variability (sBPV) was investigated. The following parameters were recorded: standard deviation of normal-to-normal RR intervals (SDNN), root mean square of successive differences (RMSSD), total power (TP) of HRV and sBPV, the range of high frequency (HF) of HRV, the range of low frequency (LF) of HRV and sBPV. We also estimated the sensitivity of spontaneous arterial baroreflex (BRS) and parasympathetic reactivity (RRmax/RRmin). Data are presented as median [interquartile range].

Results: People with epilepsy (PWE) had decreased level of cardiovascular autonomic modulation as revealed by significantly lower SDNN (17 [15;22] vs 53 [39;58] msec [p=0.001]) and TP of HRV (331 [228;490] vs 2448 [976;3275] msec^2 [p=0.001]) compared to healthy controls. Significant difference between PWE and controls was revealed for RMSSD and HF of HRV, reflecting decreased parasympathetic activity and for LF of HRV and sBPV, indicating lower sympathetic activity. BRS and parasympathetic reactivity were also reduced in patients with epilepsy.

Conclusion: Patients with TLE have impaired autonomic cardiovascular function, especially in the domain of parasympathetic regulation.

Disclosure: Nothing to disclose

EPR2056

Morphology of noninvasive ictal electroencephalographic recordings in patients with intractable focal epilepsy

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Background and aims: Morphology of noninvasive electroencephalographic (EEG) recordings is influenced by connections, size, location and orientation of the epileptogenic zone and epilepsy etiology. The aim of this investigation was determining the morphology of ictal EEG recordings in patients with intractable focal epilepsy and a magnetic resonance imaging (MRI) evident remporal (TL) or extratemporal (ETL) lesion.

Methods: We retrospectively analyzed 125 consecutive patients at The Neurology Clinic, Clinical Center of Serbia with intractable focal epilepsy who were evaluated for epilepsy surgery between 2014. and 2016. and who had at least one seizure registered and a MRI evident EL confound to either the temporal (TL) or extratemporal (ETL) region (82 and 43 patients respectively). Morphology of ictal EEG recordings was classified as 1. Attenuation (A) of amplitude of baseline activity $\geq 50\%$; 2. Rhythmic activity (RA) comprised of waves of uniform frequency, 3. Irregular activity (IRA) comprised of waves of mixed frequency, 4. Paroxysmal fast activity (PFA) frequency $\geq 13Hz$, and 5. Repetitive epileptiform activity (REA) comprised of 3 or more successive epileptiform discharges. Seizures with no ictal EEG changes or obscured ictal patterns were not analyzed. Statistical difference was determined using $\chi 2$-test.

Results: Seizures that initiated with A (41.5% vs. 16.5%, p<0.001), RA (38.5% vs. 14.9%, p<0.001) i IARA (15.8% vs. 8.0%, p=0.008) were statistically more frequent in patients with TL, while PBA (0.0% vs. 33,0%, p<0.001) i REA (4.2% vs. 27.7%, p<0.001) were statistically less frequent in patients with TL.

Conclusion: Morphology of ictal EEG recordings is significantly different in patients with TL and ETL.

Disclosure: Nothing to disclose

EPR2057

Physician Adherence to EEG Guidelines and Prognostic Factors for Obtaining EEG in Patients Admitted to Intensive Care Unit for Intracranial Hemorrhage

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Background and aims: Electroencephalography (EEG) aids seizure detection in intracerebral hemorrhage (ICH). However, physician adherence to EEG guidelines for assessing electrographic seizures in ICH patients is uncertain. We sought to determine physician adherence to EEG guidelines and assess potential clinical confounders that impact guideline adherence.

Methods: Retrospective analysis of 330 patients with ICH (49% women, 42% lobar hemorrhage) admitted to a neurological intensive care unit at a single tertiary care academic center between 01/2013-12/2015. Multivariable logistic regression models were constructed to determine clinical confounders for physician adherence to guidelines for obtaining EEG. Model fit was compared using C-statistics (area under the curve [AUC]).

Results: Overall, 83 (25.2%) underwent EEG. 190 (57.6%) of included patients fulfilled criteria for obtaining EEG per existing guidelines, 78 (41.1%) of whom underwent EEG (sensitivity 94.0%). Of 140 patients not fulfilling criteria, 135 (96.4%) did not have an EEG (specificity 54.7%). The C-statistics of guideline adherence to predict EEG in unadjusted analyses was 0.74 (95%-CI 0.69-0.80). After adjustment for age, admission Glasgow coma scale score, and presence of a clinical seizure during hospitalization the C-statistics of guideline adherence to predict EEG was 0.85 (95%-CI 0.81-0.90). Model performance was similar when forcing withdrawal of care / in-hospital death into the model.

Conclusion: Our data suggest that physicians based their decision to obtain EEG in patients with ICH on clinical criteria beyond those recommended for the routine EEG criteria. Ongoing analyses are aimed at understanding the impact of physician non-adherence to EEG guidelines on patient care.

Disclosure: Nothing to disclose

Headache and pain 2

EPR2059

Interictal mismatch between neuronal activation and resting metabolism in the visual cortex of migraine patients: a study comparing FDG-PET and visual evoked potentials

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Background and aims: Migraine attacks might be triggered by a disruption of cerebral homeostasis. Between attacks, migraine patients are characterized by abnormal sensory information processing, but this functional abnormality may not be sufficient to disrupt cortical equilibrium unless it is accompanied by a reduction in energy reserve.

The aim of this study was to compare resting cerebral metabolism using 18fluorodeoxyglucose-positron emission tomography (18FDG-PET) and visual cortex activation using visual evoked potentials (VEP) between interictal migraineurs and healthy volunteers.

Methods: Twenty episodic migraine without aura patients and twenty healthy volunteers were studied. 18FDG-PET and VEP recordings were performed on separate days. PET scans were compared between groups using area under the VEP as regressor. For case-wise analysis, eigenvalues from the cluster exhibiting significantly different FDG-uptake in the visual cortex were extracted. Standardized metabolism and VEP values from each subject were coupled and compared between groups.

Results: The mean area under the curve (AUC) of VEP was greater in migraine patients than in healthy controls. In patients, cortical metabolism in relation to VEP's AUC was significantly reduced in a cluster extending through Brodmann's areas 7, 19, and 18. A visual Z-score exceeding the metabolic Z-score was found in 90% of migraine patients, but in only 15% of healthy volunteers.

Conclusion: Comparing FDG-PET and visual evoked potentials, our study identifies an area of mismatch between neuronal activation and glucose uptake in the visual cortex of migraine patients between attacks. This observation supports the concept that activity-induced rupture of cerebral metabolic homeostasis may be a cornerstone in migraine pathophysiology.

Disclosure: Nothing to disclose

EPR2060

Are there clinical differences in episodic and chronic cluster headache patients? Results from the Danish Cluster Headache Survey

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Background and aims: Episodic (eCH) and chronic (cCH) cluster headache are defined by the duration of the symptom-free interval between the bouts. However, it remains unclear whether there are other differences between the two phenotypes. Therefore, we aimed to describe differences in the clinical presentation of eCH and cCH in a large and well-characterized CH population.

Methods: CH patients from the Danish Headache Center, aged 18–65 years, diagnosed with CH according to International Classification of Headache Disorders-II completed questionnaires followed by a semi-structured interview. The clinical presentation in eCH and cCH was compared. Pain intensity was rated on a Likert scale from 0-4.

Results: A total of 400 patients participated (cCH: 154 eCH: 246) with a higher prevalence of women with cCH than with eCH (41% vs. 28%, p<0.05). Age of CH onset was comparable (32.7 vs. 30.6 years, p=0.16). cCH patients reported more attacks/day (4.07 vs. 3.33, p<0.01) and longer treated attack duration (47 vs. 34 minutes, p<0.05), however untreated attack duration (106 vs. 103 minutes, p=0.72) and pain intensity were comparable (3.51 vs. 3.59, p=0.21) between eCH and cCH. Accompanying symptoms as ptosis, eyelid edema, feeling uneasy and flushing were more frequently reported in cCH than in eCH.

Conclusion: cCH patients were more severely affected than eCH patients in relation to attack frequency and treated attack duration, which indicate a significant need for more awareness and more effective acute and preventive treatment of this highly disabling neurological disease.

Disclosure: Nothing to disclose

EPR2061

A Multicenter, Prospective, Randomized, Open-Label Study to Compare the Efficacy, Safety, and Tolerability of OnabotulinumtoxinA and Topiramate for Headache Prevention in Adults with Chronic Migraine: The FORWARD Study

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Background and aims: To compare effectiveness and tolerability of onabotulinumtoxinA and topiramate for chronic migraine (CM).
Methods: The FORWARD Study (ClinicalTrials.gov, NCT02191579) is a multicenter, randomized, parallel-group, open-label prospective study. Adults with CM were randomized to receive either 155U of onabotulinumtoxinA for 3 treatment cycles or 50-100 mg/day of topiramate administered daily up to week 36. Patients who discontinued topiramate could cross-over to onabotulinumtoxinA no earlier than 12 weeks. The primary efficacy outcome was the 50% headache day responder rate weeks 29-32. Analyses were performed on the ITT dataset using logistic regression with baseline carried forward to impute missing data. Adverse events (AEs) were monitored.
Results: 282 patients were enrolled (onabotulinumtoxinA, n=140; topiramate, n=142); mean(SD) baseline headache days (onabotulinumtoxinA, 22.1[4.6]; topiramate, 21.8[4.8]) were similar. 148 patients completed treatment as randomized (onabotulinumtoxinA, 85.7%; topiramate, 19.7%). Primary reasons for withdrawal were ineffective treatment (onabotulinumtoxinA, 5.0%; topiramate, 19.0%) and AEs (onabotulinumtoxinA, 3.6%; topiramate, 50.7%). 80 topiramate patients crossed-over to onabotulinumtoxinA. OnabotulinumtoxinA demonstrated significantly higher proportion of patients with ≥50% reduction in headache frequency compared to baseline vs topiramate (40.0% vs 12.0%, respectively; adjusted OR, 4.9 [95% CI, 2.7-9.1]; P<0.001). All secondary endpoints were met including: change in headache day frequency, HIT-6 scores, and ≥70% responder rate (P<0.001). Treatment-related AEs were reported by 17.3% of onabotulinumtoxinA-treated patients and 69.7% of topiramate-treated patients.
Conclusion: OnabotulinumtoxinA had a more favorable tolerability profile versus topiramate based on treatment-related AEs and overall discontinuations. When using imputation methods accounting for discontinuation differences, onabotulinumtoxinA was more effective than topiramate.
Disclosure: The funding source for this study is Allergan plc (Dublin, Ireland)

EPR2062

Safety of Erenumab among Patients with Migraine using Triptans or With Cardiovascular Risk Factors

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Background and aims: Erenumab is a fully human anti-CGRP receptor antibody in development for migraine prevention. As CGRP can mediate vasodilation, inhibiting the CGRP pathway may carry a theoretical cardiovascular risk. Here, we assess the safety of erenumab in patients with cardiovascular risk factors and in those using triptans/ergotamines.
Methods: A 12-week, integrated safety analysis of patients in phase 2/3 studies (NCT02066415, NCT01952574, NCT02456740 and NCT02483585) who received ≥1 dose of placebo or erenumab (7, 21, 70 or 140 mg).
Results: Overall, 66.2% (n=690/1043) of placebo-treated and 65.5% (n=1056/1613) of erenumab-treated patients used migraine medications (primarily triptans [>99%]). AE incidence in placebo- and erenumab-treated patients was 49.6% and 47.4% among triptan/ergotamine users and 47.9% and 47.2% among non-users, respectively. Serious AE (SAE) incidence in placebo- and erenumab-treated patients was 1.9% and 1.7% among triptan/ergotamine users and 0.8% and 0.5% among non-users, respectively. At baseline, 29.7%, 40.6% and 29.7% of placebo-treated and 28.2%, 41.7% and 30.1% of erenumab-treated patients had 0, 1 or ≥2 cardiovascular risk factors, respectively. AE incidence for 0, 1 or ≥2 cardiovascular risk factors was similar between placebo-treated (47.4%, 46.3% and 54.2%, respectively) and erenumab-treated patients (44.8%, 46.4% and 51.1%, respectively). Cardiac (<2.0%) or vascular AE incidence (≤2.3%) was similar among the cardiovascular risk subgroups and the treatment groups, as was SAE incidence (<2.0%). No dose relationship was observed with triptans/ergotamines or cardiovascular risk factors.
Conclusion: AEs, including cardiovascular AEs, were similar between erenumab and placebo in triptan/ergotamine users and in those with cardiovascular risk factors.
Disclosure: This study was supported by Amgen Inc., USA

EPR2063

Patient–Reported Outcomes in Chronic Migraine Patients with Prior Prophylactic Treatment Failure Receiving Placebo or Erenumab: Subgroup Analysis of a Pivotal Randomised Study

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Background and aims: Erenumab, a fully human monoclonal antibody, selectively targets the CGRP receptor. A pivotal 12-week randomised, double-blind study demonstrated efficacy and safety of erenumab (70mg and 140mg monthly) in patients with chronic migraine (CM). We report here the patient–reported outcomes (PROs) in subgroup of patients with prior prophylactic treatment failure (TF) (≥1 and ≥2 medication-categories) due to lack of efficacy and/or poor tolerability.

Methods: 667 adults with CM were randomised (3:2:2) to receive monthly subcutaneous placebo or erenumab 70mg or 140mg. Exploratory-endpoints included: headache impact measured by the Headache Impact Test (HIT–6), migraine–related disability measured by the Migraine Disability Assessment Test (MIDAS), and person-centred evaluations of physical, mental, and social health measured monthly by the Patient-Reported Outcome Measurement Information System (PROMIS). No formal hypothesis was tested; p–values (erenumab dose-groups vs placebo) are descriptive.

Results: For both subgroups with ≥1 and ≥2-TF, treatment with erenumab (both doses) resulted in greater reduction (improvement) in HIT-6 total-scores, MIDAS total-score, absenteeism and presenteeism-scores as compared with placebo at Week 12. For both TF-subgroups, erenumab (both-doses) resulted in greater reduction (improvement) in PROMIS scores as compared with placebo at Weeks 4, 8 and 12–except for erenumab 70mg at Week 4. Week 12 results are shown below. Treatment-corrected differences exceeded established minimal-intergroup differences where applicable (eg. for HIT-6 of -2.3 points).

Conclusion: Erenumab–treated-CM patients with prior-TF experienced consistent and clinically meaningful improvements in PROs as compared with placebo starting from first month of treatment. Improvement was particularly visible among patients with ≥2 TF, hard-to-treat population.

Disclosure: This study was supported by Amgen Inc., Thousand Oaks, California, USA and Novartis Pharma AG, Basel, Switzerland.

EPR2064

Effect of Erenumab on Patient-Reported Outcomes in Episodic Migraine Patients with Prior Prophylactic Treatment Failure: Results from a Post-Hoc Analysis of the STRIVE study

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Background and aims: There is a high unmet need for new prophylactic treatments for migraine, especially for patients who have failed existing migraine therapies or have contraindications. In the STRIVE study (NCT02456740), erenumab 70 mg and 140 mg QM led to significant improvement of patient-reported outcomes (PROs) in patients with episodic migraine. We report results from a subgroup analysis assessing the effect of erenumab (70 mg and 140 mg) on PROs in patients with ≥1 prior prophylactic treatment failure(s) due to lack of efficacy and/or poor tolerability.

Methods: PRO endpoints were change from baseline in mean monthly scores over months 4–6 for modified monthly Migraine Disability Assessment Questionnaire (MIDAS; total score, absenteeism, and presenteeism), the Headache Impact Test (HIT–6TM) and the Migraine–Specific Quality of Life Questionnaire (MSQ; -role function restrictive, -role function preventive, and -emotional function), based on eDiary calculations. P-values comparing erenumab vs placebo are nominal without multiplicity adjustment.

Results: At baseline, mean values for all measures were similar between groups. Clinically meaningful improvements were observed in the total MIDAS (greater reduction), HIT-6TM (greater reduction) and MSQ scores (greater increase) in patients treated with erenumab (70 mg and 140 mg) vs placebo.

Conclusion: Erenumab 70 mg and 140 mg showed robust treatment effects on migraine-related disability, functional impact and quality of life in episodic migraine patients with ≥1 prior prophylactic treatment failure(s) showing the benefit of treatment with erenumab in this subgroup of patients. Numerically better or equal scores were observed for the 140 mg dose compared with 70 mg for all PROs.

Disclosure: This study was supported by Amgen Inc., Thousand Oaks, California, USA and Novartis Pharma AG, Basel, Switzerland.

Infectious diseases

EPR2066

Prolonged upregulation of C5a is associated with unfavorable outcome in bacterial meningitis

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Background and aims: The uncontrolled inflammatory response in patients with bacterial meningitis is associated with complications and unfavorable outcome. Complement component 5a (C5a), an anaphylatoxin critical in upregulating the inflammatory response, emerges as a promising treatment target in bacterial meningitis. We aim to assess the concentration of C5a in the acute phase of bacterial meningitis and the associated clinical outcome.

Methods: Patients (≥ 16 years old) with suspected community-acquired bacterial meningitis and typical findings in the cerebrospinal fluid, who present at one of the 12 participating hospitals in the Netherlands, undergo serial blood sampling at day 0, 1, 2, 7 and 3 months of presentation. Patients are also included in a prospective nationwide clinical cohort study. We performed C5a ELISAs (BD) of all serially-collected EDTA samples which were handled and stored according to manufacturer's protocol.

Results: A total of 155 samples of 39 patients (17 male, median age 57 years, 12 unfavorable outcome (Glasgow Outcome Scale score 1-4), 3 death) were analysed. C5a concentration during bacterial meningitis was significantly elevated compared to controls and patients with a history of bacterial meningitis, even at 3 months (median 47 (IQR 15) vs. 30ng/ml (IQR 12), $p<0.001$, Figure 1). Median C5a concentration was highest at day 1 (median 68ng/ml, IQR 26). Increase of C5a after day 1 was significantly associated with an unfavorable outcome (44% vs 8%, $p=0.05$, Figure 2).
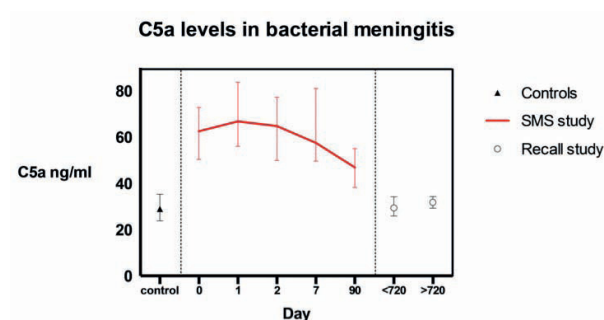
Figure 1
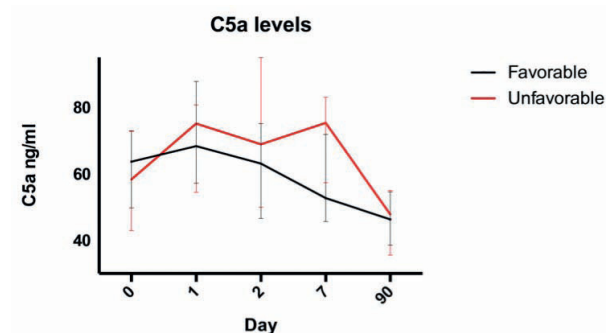
Figure 2

Conclusion: C5a is significantly upregulated during bacterial meningitis and a prolonged upregulation is associated with unfavorable clinical outcome. These findings further confirm the rationale for C5a antibody therapy.

Disclosure: Nothing to disclose

EPR2067

Early diagnosis of five cases of Gerstmann–Sträussler–Scheinker

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Background and aims: This article summarised 5 GSS cases in terms of clinical manifestation, electrophysiology, imaging and gene, providing the experience in the early diagnosis of GSS.

Methods: Retrospective analysis of 5 GSS cases that had been diagnosed by gene or clinically manifestation in the General Hospital of People's Liberation Army from 1 December 2015 to 31 December 2017.

Results: This article collected 5 GSS cases, 2 males (40%) and 3 females (60%). The average age was 47.40±8.59 years. All cases were chronic progressive aggravation, 1 died within 3 months due to complications, the others' course of disease averaged 30.00±10.55 months. All cases had cerebellar ataxia, cortical sensory disturbance and cognitive impairment as early core symptoms. 4 cases had insomnia, nystagmus or myoclonus in advanced stages. 1 case had a positive family history. The sensitivity of 14-3-3 protein was 40% and abnormal electroencephalogram appeared in 4 cases but only 1 had triphasic wave. Diffusion weighted imaging abnormally signals appeared in 5 cases but only 2 in cerebella. 4 cases who completed positron emission tomography-computed tomography were found having hypo-metabolism in cerebella. 4 cases were diagnosed by gene (3 cases were P102L mutation and 1 case was T188K mutation), and 1 case was clinically probable case. 4 cases were misdiagnosed of somatic disorder or spinocerebellar ataxia.

Low metabolism in cerebella of PET-CT.

PRNP; NM_000311; c.305C>T; reads(+)
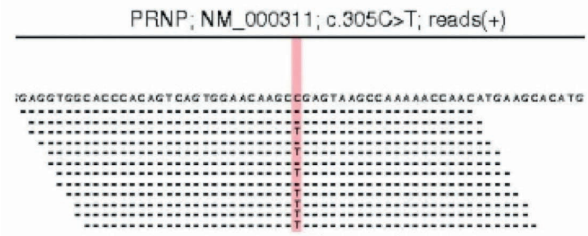
P102L gene mutution.

Conclusion: The GSS should be considered when cerebellar ataxia, cortical sensory disturbance and cognitive impairment are identified. The electroencephalogram and 14-3-3 protein have low sensitivity in GSS. PET-CT and gene examination play a critical role in this disease.

Disclosure: Nothing to disclose

Diffusion weighted imaging abnormally high signals in cerebella.

EPR2068

Histopathology of listeria meningitis

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Background and aims: Listeria monocytogenes meningitis is the third most common cause of bacterial meningitis in adult patients and has a high mortality and morbidity rate. In this study, we describe the clinical course and brain pathology results of 5 patients who died of listerial meningitis.

Methods: The cases were identified from two nation-wide prospective cohort studies and the neuropathology database in Amsterdam. Clinical course and results from diagnostic tests were derived from a chart review. Severity of vascular, parenchymal and ventricular damage and inflammation was scored according a pathology scale previously used in pneumococcal meningitis.

Results: All patients were immunocompromised and age ranged between 48-76 years. Three cases were cerebrospinal fluid culture confirmed, one brain culture confirmed and one diagnose was based on a positive blood culture and findings at neuropathological examination. Mild inflammation of meningeal arteries was found in 3 of 5 cases (60%), moderate to severe ventriculitis in 4 cases with available material (100%) and abscesses were found in 3 of 4 cases (75%). The inflammatory cells present in the meninges were a mix of monocytes/macrophages and neutrophils and frequent presence of efferocytosis. A moderate infarct was found in 1 of 4 cases (25%), mild to moderate hemorrhage in 2 of 4 cases (50%) and mild/moderate thrombosis of meningeal artery in 3 cases (60%).

Conclusion: Pathological examination of five listeria cases was characterised by presence of moderate to severe ventriculitis, abscesses and abundant efferocytosis which previously has been suggested to be exploited by L. monocytogenes for cell-to-cell spread.

Disclosure: Nothing to disclose

EPR2069

Complement factor H deficiency increases mortality in experimental pneumococcol meningitis through C3 depletion

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Background and aims: Complement factor H (CFH) inhibits alternative pathway activation and genetic variation influences susceptibility and outcome of bacterial meningitis. The aim of this study was to determine the role of CFH in pneumococcal meningitis.

Methods: CFH-deficient (n=28) and C57BL/6 wild-type (n=33) mice were inoculated intracisternally with 1µl of 10^7 CFU/ml Streptococcus pneumoniae. Animals were observed for 50 hours in a survival analysis and sacrificed after 5 and 20 hours in a time-point experiment. Bacterial outgrowth, complement component 3 (C3), interleukin-1beta (IL-1b) and macrophage inflammatory protein-2 (MIP-2) were determined. In a treatment model wild-type mice received adjuvant treatment with intraperitoneal human CFH (n=11) or PBS (n=12) at 16 hours after infection.

Results: CFH-deficient mice showed an increased mortality compared to wild-type mice, median survival 23 vs. 32 hours (Log-rank, p=0.0028). CFH deficiency was associated with decreased plasma C3 levels at both time points and increased bacterial outgrowth at 20 hours. CFH-deficient mice showed reduced brain levels of IL-1b (median 13 vs. 30 pg/ml, p=0.013) and MIP-2 (median 61 vs. 193pg/ml, p=0.009) at 5 hours and increased brain levels of IL-1b (median 754 vs. 532pg/ml, p>0.05) and MIP-2 (median 1556 vs. 748pg/ml, p=0.023) at 20 hours. The 72-hours mortality rates were similar between human CFH and PBS treated mice (45% and 50%, respectively).

Conclusion: CFH deficiency is associated with decreased bacterial clearance and increased mortality in experimental pneumococcal meningitis due to secondary C3 depletion. Treatment with human CFH did not influence outcome.

Disclosure: Funding: EU-FP7 EUCLIDS project

EPR2070

Performance of meningitis prediction rules in the at-risk population

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Background and aims: Community-acquired bacterial meningitis is a severe disease that needs immediate medical attention. Various prediction models have been developed to assess the likelihood of bacterial meningitis in suspected patients. Although they have been validated externally, it is necessary to look at the value of these models in a different, at-risk population.

Methods: We prospectively included patients who underwent a lumbar puncture for suspected meningitis or encephalitis. We performed a literature search for various prediction models for bacterial meningitis and applied them to this cohort. We calculated sensitivity and specificity for all models.

Results: From 2012 to 2015 we included 363 episodes of suspected meningitis or encephalitis. A total of 89 (24%) patients received a final diagnosis of an infection of the central nervous system, of whom 27 had bacterial meningitis. Ten prediction models for bacterial meningitis were identified. In seven of them all required parameters were available to use the model in our cohort. Sensitivity ranged from 12% to 96%, in which the highest sensitivity was reached with the model of Hoen et al. Specificity ranged from 32% to 99%, in which the highest specificity was reached with the model of Bonsu et al.

Conclusion: None of the models showed both high sensitivity and specificity. None of the existing scores performed well enough to recommend routine use in individual patient management.

Disclosure: Nothing to disclose

EPR2071

Community acquired Group B Streptococcal meningitis in adults

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Background and aims: Streptococcus agalactiae (GBS) is an uncommon cause of bacterial meninigitis in adults. We describe the clinical features, complications, treatment, and outcome of adults with GBS meningitis in a two nationwide surveillance study in the Netherlands.

Methods: In two prospective nationwide cohort studies performed between 1998-2002 and 2006-2017 we evaluated adults with community-acquired bacterial meningitis caused by GBS in the Netherlands.

Results: We assessed 33 patients with GBS meningitis with a median age 58 years of whom 22 were male (67%). The calculated annual incidence was 0.17 per 1.000.000 adults. Eleven patients (33%) had an immunocompromised status and in twelve patients (36%) an infectious focus outside the central nervous system was found, consisting of endocarditis in 4 patients (13%) and otitis/sinusitis in 4 patients (12%). The most common serotype was serotype III (n=12 [41%]). Patients with GBS meningitis more frequently had endocarditis (13% vs 1%, P=0.001) and alcoholism (18% vs 6%, P=0.01) while otitis or sinusitis occurred less frequently (12% vs 35%, P=0.008) compared to patients with meningitis due to other pathogens. Seven patients (21%) died and seven survivors an unfavorable outcomes such as blindness (n=2), cerebral infarction with neurological deficits (n=2). Nineteen patients (58%) made a full recovery. Serotype 5 was associated with death (mortality 3 of 4 [75%] serotype V vs 4 of 28 [14%] other serotypes P=0.025).

Conclusion: GBS is associated with concomitant endocarditis and alcoholism. Patients with GBS meningitis should receive cardiac ultrasound to rule out endocarditis. Mortality is associated with bacterial serotype.

Disclosure: Nothing to disclose

EPR2072

The contribution of variation in coagulation and fibrinolysis genes to cerebrovascular complications in community-acquired bacterial meningitis

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Background and aims: Bacterial meningitis is a severe infection of the brain often resulting in poor outcome due to cerebrovascular complications. Our aim was to determine whether genetic variation in coagulation and fibrinolysis genes contributes to cerebrovascular complications in bacterial meningitis.

Methods: We performed a nationwide prospective genetic association study in adult community-acquired bacterial meningitis patients. The exons and flanking regions of 16 candidate genes involved in coagulation and fibrinolysis pathways were sequenced. We analysed whether genetic variation in these genes resulted in a higher risk of cerebrovascular complications, unfavorable outcome and differences in thrombocyte count on admission. We used linear and logistic regression to compare genotype frequencies.

Results: From 2006 to 2011 a total of 1101 bacterial meningitis patients were included of which 752 (68%) supplied DNA for genotyping. After quality control, data of 622 patients of European ancestry could be used for further analyses. In 139 patients (22%) the episode of bacterial meningitis was complicated by cerebral infarction, and 188 (30%) had an unfavorable outcome. We identified the rs494860 variant in the protein Z (PROZ) gene as our strongest association with occurrence of cerebral infarction (odds ratio [OR] 0.49 [95% confidence interval 0.33-0.73]). The rs494860 variant is an expression quantitative trait locus contributing to variation in the PROZ protein mRNAs expression. No genetic variants were significantly associated with cerebral infarction, outcome or thrombocyte count after correction for multiple testing.

Conclusion: Our study does identify a genetic variation in the PROZ gene, effecting its transcription, as the strongest association with cerebral infarctions during bacterial meningitis.

Disclosure: Nothing to disclose

Movement disorders 4

EPR2073

A novel TMEM240 variant in SCA21 without cognitive impairment

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Background and aims: Variants in the transmembrane protein 240 (TMEM240) gene were described in French families with autosomal dominant, early-onset, slowly progressive ataxia, and cognitive impairment (SCA21). We characterised clinically and genetically a Portuguese family with SCA21.

Methods: Files review/patients observation through structured protocol.

Results: A1 is a 76y-old woman who developed dysarthria and gait ataxia, by age 15y. Diplopia and upper limbs incoordination were noticed in her 50s and dysphagia in her 70s. By age 66y, she needed a walking stick. On examination, she had dysarthria, fragmented pursuit, hypermetric saccades, upper/lower limbs dysmetria, brisk deep tendon reflexes, ataxic gait (SARA=18.5). Neuropsychological assessment (by age 76y) was normal. MRI disclosed marked cerebellar atrophy, more in the upper part, with anterior pons atrophy. Her youngest daughter (B1), 43y, developed gait ataxia by age 22y. In her 30s, handwriting deteriorated and speech became slurred. She has no cognitive deterioration. On examination, she has dysarthria, postural hand tremor, upper/lower limbs dysmetria, brisk deep tendon reflexes, ataxic gait (SARA=7). MRI showed mild upper cerebellar atrophy. Both bare a novel variant on TMEM240: c.486_487del (p.(Tyr163Profs*69)), resulting in a frameshift and extension of the reading frame. Another daughter of A1, 49y, is said to be affected. A daughter of B1, 22y, complains of disequilibrium and is under investigation. Neither is said to have cognitive impairment.

Conclusion: Both patients present a SCA phenotype, with minor pyramidal signs, but no cognitive deterioration. This is the first variant resulting in a larger protein. These cases contribute to enlarge the clinical spectrum of SCA21.

Disclosure: Nothing to disclose

EPR2074

Sex-specific pattern of sensori-motor network connectivity in de novo Parkinson's disease patients

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Background and aims: Clinical and epidemiological evidences support the presence of sex-specific expression of Parkinson's disease (PD), from the early to the late stages. In the present study, we aimed to investigate the potential sex-difference effect on the spontaneous neuronal activity within the sensori-motor network (SMN) in early untreated PD patients, using the amplitude of low-frequency fluctuation (ALFF) and its correlation with baseline and longitudinal clinical features.

Methods: 56 de novo PD patients and 23 matched healthy controls (HC) were enrolled in the study. Whole brain structural and functional imaging was performed on a 3T GE MR scanner. Functional data were analysed using BrainVoyager QX software. Linear logistic regression was used to investigate whether functional imaging data at baseline were predictors of motor impairment over a 2-year follow-up period.

Results: Compared with female PD patients and HC, male PD patients showed an increased ALFF connectivity within the SMN in the 5-slow band. No ALFF differences were detected between male and female HC and within female PD patients and HC. Male PD patients showed a higher risk to develop axial symptoms at 2-year follow-up. Functional abnormalities within the SMN at baseline showed to be an independent predictor of axial impairment overtime in the PD group.

Conclusion: Our findings revealed that the organization of the intrinsic functional connectivity within the SMN in PD differs between genders. We hypothesise that this specific pattern may be related to the presence of a gender-specific nigro-striatal dopaminergic pathway and might predict PD progression and development of motor complications over the disease course.

Disclosure: Nothing to disclose

EPR2075

Impaired motor planning in PD patients with fatigue: a seed-based RS-fMRI study

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Background and aims: Previous studies have consistently demonstrated that fatigue in Parkinson's Disease (PD) is associated with a dysfunction within brain areas involved in the motor planning, suggesting a pivotal role played by the supplementary motor area (SMA).
We aimed to investigate the functional connectivity of the SMA in de novo PD patients with and without fatigue, by using a seed-based resting-state functional MRI.
Methods: 20 PD patients with fatigue (f-PD), 20 PD patients without fatigue (nf-PD), and 20 age and sex-matched healthy controls (HCs) were enrolled. Presence and severity of fatigue was assessed with the Parkinson Fatigue Scale. Structural and functional imaging was performed on a 3T MR scanner. Statistical analysis was completed using BrainVoyager QX software. A seed-based approach was used to compare f-PD and nf-PD patients, selecting the SMA and the pre-SMA as regions of interest. Voxel-based morphometry (VBM) was used to exclude structural differences.
Results: Compared with nf-PD patients, f-PD patients showed a decreased connectivity within the left SMA and the left middle frontal gyrus as well as an increased connectivity within the left pre-SMA and the left post-central gyrus (p<0.05). VBM analysis showed no significant volume difference between all groups (P<0.05).
Conclusion: In the present study f-PD patients showed the presence of a disrupted connectivity between the SMA and several cortical areas involved in motor planning and executive attention. This aberrant functional connectivity may rely on an impairment during both programming and controlling the motor execution, likely leading to the difficulty in performing self-initiated movements which characterised f-PD patients.
Disclosure: Nothing to disclose

EPR2076

Spectrum of symptoms in prodromal synucleinopathy and their relation to the degeneration of nigrostriatal pathway

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Background and aims: Idiopathic REM sleep behavioral disorder (RBD) is a prodromal synucleinopathy. It is frequently associated with several motor and non-motor symptoms such as hyposmia, constipation, and orthostasis along with gradual loss of dopaminergic neurons in substantia nigra. Our aim was to compare prevalence and severity of degenerative symptoms in RBD and control group. Additionally, we investigated whether these symptoms are associated with the degree of nigrostriatal degeneration.
Methods: 75 RBD (5f, mean age(SD) 67.5(6.2)) and 41 control subjects (4f, mean age 65.3(8.4) were examined using Movement Disorders Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS-III), Montreal Cognitive Assessment (MoCA), University of Pennsylvania Smell Identification Test (UPSIT), Scales for Outcomes in PD-Autonomic (SCOPA-AUT), and orthostatic test. In 65 RBD patients, 123I-Ioflupane (DaTscan) SPECT was performed, putaminal indices were calculated using the BASGAN_V2 software and subsequently classified as normal, borderline, or abnormal.
Results: RBD patients had significantly more severe mean scores in MDS-UPDRS-III (p=0.01), MoCA (p=0.001), UPSIT (p=0.0001), and SCOPA-AUT (p=0001) compared to controls (Table1). Orthostatic test was positive in 33% RBD patients vs 0% controls (p=0.05). RBD patients with abnormal DaTscan had significantly higher MDS-UPDRS-III (p=0.01) and lower UPSIT (p=0.03) scores compared to patients with borderline/normal DaTscan result while no differences were found for age, symptom duration, MoCA, and SCOPA-AUT scores (Table2).

Comparison of RBD patients and control group

	RBD (total)	Controls	P value[r]
Number (females)	75 (6)	41 (4)	
Age in yrs*	67.5 ± 6.2	65.3 ± 8.4	0.12
MDS-UPDRS III	6.2 ± 5.6	3.5 ± 4.1	**0.008**
MoCA	23.7 ± 2.7	25.4 ± 2.0	**0.001**
UPSIT	22.6 ± 8.1	30.9 ± 4.6	**<0.0001**
SCOPA-AUT	11.8 ± 7.8	6.1 ± 4.2	**<0.0001**
Orthostatic test + (%)	33	0	**0.05**

*values reported as mean ± SD unless stated otherwise
[r] Student t-test

Table 1

Stratification of RBD cohort according to DaTscan results

	DaTscan normal	DaTscan borderline	DaTscan abnormal	P value[a]
Number (females)	25 (3)	27 (2)	13 (1)	
Age in yrs*	68.4 ± 6.7	67.2 ± 6.5	67.2 ± 6.1	0.76
Symptoms duration in yrs	6.8 ± 6.3	5.4 ± 4.3	7.2 ± 7.1	0.57
MDS-UPDRS III	5.4 ± 5.1	5.6 ± 4.1	10.8 ± 8.3	**0.01**
MoCA	23.6 ± 2.2	24.5 ± 3.1	22.8 ± 2.5	0.16
UPSIT	25.4 ± 8.2	22.5 ± 7.8	17.3 ± 4.6	**0.03**
SCOPA-AUT	10.8 ± 6.9	14.4 ± 8.1	11.2 ± 8.9	0.21

*values reported as mean ± SD
[a] ANOVA test

Table 2

Conclusion: RBD is associated with hyposmia, autonomic dysfunction, cognitive decline, and motor impairment indicating diffuse alpha-synuclein pathology. Subtle parkinsonian motor symptoms and hyposmia along with abnormal DaTscan are likely biomarkers of imminent conversion to manifest neurodegeneration.

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EPR2077

How to diagnose and manage progressive ataxia: guidelines for professionals

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Background and aims: The progressive ataxias are a group of rare, heterogeneous and complicated neurological disorders, knowledge of which is often poor among healthcare professionals. The patient support group Ataxia UK, recognising this lack of awareness, has developed guidelines for their diagnosis and management, focusing especially on hereditary ataxia (including Friedreich's ataxia and autosomal dominant spinocerebellar ataxia), cerebellar variant multiple system atrophy and "idiopathic" progressive ataxia.

Methods: 30 UK health professionals contributed to the production of the guidelines, their inputs reflecting diverse clinical experience in various aspects of ataxia diagnosis and management. After review of the published literature in their respective spheres, they provided summaries on "best" practice- including grading of evidence available for interventions, using the Guideline International Network (GIN) criteria. Where no specific published data existed, recommendations were based on data related to similar conditions and/or expert consensus.

Results: The guidelines comprise 128 recommendations, organised into four main sections (on diagnosis, medical interventions, allied health professional interventions and palliative care). By the GIN criteria, 6 recommendations are graded B, 7 graded C, 10 graded D and 105 graded GPP (Good Practice Points).

Conclusion: The guidelines aim to assist healthcare professionals when caring for patients with progressive ataxia, indicate evidence-based (where it exists) and best practice, and, overall, provide a useful resource for those managing ataxia patients. They also highlight the urgent need to develop effective disease-modifying therapies, and, given the large number of recommendations based on GPP, emphasise the need for further research to provide evidence for effective symptomatic interventions.

Disclosure: Nothing to disclose

EPR2079

Activities of daily living and quality of life in patients with advanced Parkinson's disease who are treated with or planning to use device-aided treatments

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Background and aims: To correlate activities of daily living (ADL) and quality of life (QoL) in advanced Parkinson's disease (APD) patients with ongoing or planned device-aided treatment (DAT) and to identify characteristics that may predict ADL and QoL response to DATs. ADL influences QoL in patients with APD. However, it is unknown how disease characteristics (eg, motor fluctuation/PD duration) affect ADL and patient QoL.

Methods: This was a post-hoc analysis of OBSERVE-PD, (a global, multicenter, cross-sectional, observational study). ADL was assessed using the Unified PD Rating Scale (UPDRS) Part II; QoL was assessed using PD 8-item questionnaire (PDQ 8). DATs included deep brain stimulation, levodopa-carbidopa intestinal gel infusion, and continuous apomorphine subcutaneous infusion. ADL and QoL correlation was assessed in APD patients eligible for DAT (planned and ongoing) using Pearson correlation coefficients.

Results: This analysis included 384 patients with ongoing DAT and 164 patients planning to initiate DAT. Despite greater disease duration and age [Table1], patients receiving DAT generally had better ADL/QoL scores than patients planning to initiate DAT [Table2]. Patients receiving DAT with >4 years motor fluctuation and >10 years since PD diagnosis also demonstrated slightly better ADL/QoL scores. ADL and PDQ-8 scores were strongly correlated for patients with ongoing DAT (r=0.54722;P<.0001) and planned DAT (r=0.55487;P<.0001).

Conclusion: Patients with planned DAT vs. ongoing DAT generally had worse ADL and QoL, suggesting DAT improves long-term patient-reported outcomes. ADL and QoL were strongly correlated in patients with ongoing and planned DAT. These data demonstrate the importance of assessing ADL/QoL in APD.

Disclosure: AbbVie Inc, participated in the study design, study research, collection, analysis, interpretation of data and writing, reviewing, and approving of this abstract for submission.

EPR2080

Abnormal α-synuclein deposits in skin nerves: inter and intra-laboratory reproducibility

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Background and aims: Phosphorylated α-synuclein at serine 129 (p-syn) in skin nerves is a promising test for the in vivo diagnosis of synucleinopathies. Here we aimed to establish the intra and inter-laboratory reproducibility of intraneural p-syn positivity in two laboratories (Würzburg, Germany and Bologna, Italy) with a major expertise in this analysis.

Methods: We enrolled 42 patients (26 from Würzburg and 16 from Bologna) affected by Parkinson's disease (PD: 21 patients), REM sleep behavior disorder (RBD: 11), Multiple System Atrophy (MSA: 4) and small fiber neuropathy (SFN: 6). Skin biopsy was performed in C7 paravertebral spine region and distal leg. The analysis was standardised in both laboratories and made blinded on a single skin slide double stained with p-syn and PGP 9.5 (pan-neuronal marker). 50 skin slides were analysed. Slides differently classified were re-evaluated to understand the reasons of the discrepancy.

Results: The intra-laboratory analysis showed an excellent reproducibility both in Würzburg (concordance of classification 100% of slides; K=1; p<0.001) and Bologna (96% of slides; K=0.92; p<0.001). Inter-laboratory analysis showed a reproducibility in 45 slides (90%; K=0.8; p<0.001) and a different classification in 5 slides which was mainly due to fragmented skin samples or weak PGP 9.5 signal.

Conclusion: 1) p-syn analysis showed an excellent inter and intra-laboratory reproducibility supporting the reliability of this technique as in vivo biomarker for synucleinopathies; 2) the few ascertained discordances were important to further improve the standardisation of this technique.

Disclosure: Nothing to disclose

Movement disorders 5

EPR2081

Quantitative gait analysis in idiopathic normal pressure hydrocephalus using instrumental timed up and go test

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Background and aims: Gait disturbance is the most frequent symptom in idiopathic normal pressure hydrocephalus (iNPH), and it is characterised by a short-stepped, magnet-like and broad-based gait. The timed up and go test (TUG) is widely used to assess gait and balance. In this study, quantitative measurements were performed twice, using iPhone speed sensors and free "SENIOR QUALITY " software. Herein, we report the characteristics of gait in iNPH compared with those in controls.

Methods: 33 patients with suspected iNPH and 86 control subjects were recruited. Data were automatically collected during TUG and 6 components of gait (Standing, Go, Turn, Back, Backturn and Sitting) were automatically computed. Statistical comparisons were performed to compare those with iNPH and controls.

Results: Correlations of total time between first and second TUGs were high (>0.9) in both the iNPH and control groups. In comparing first and second TUGs, statistically significant shortening of time was noted in Go, Backturn and Sitting in the controls. In those with iNPH. mean values were decreased in the second TUG in all components except for Turn, but these results were not statistically significant. Comparison between the iNPH with control groups revealed that all components of iNPH were slower in the first TUG, while only the Go, Back and Backturn components were slower in the second TUG.

Conclusion: The instrumental TUG enables quantitative measurements of six components of TUG. This provides further insight into the pathophysiology of gait disturbances in various disorders.

Disclosure: The first author, MI, received honoraria from Johnson & Johnson, Japan and Medtronic Japan.

EPR2082

Impact of infusion-based therapies initiation on levodopa equivalent daily dose in advanced Parkinson's disease patients: a 2-year retrospective study in a french expert center

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Background and aims: In Parkinson's disease (PD), cumulative levodopa equivalent daily dose (LEDD) is associated with the onset of motor complications. Subthalamic deep brain stimulation (STN-DBS), subcutaneous apomorphine infusion (Apo) and intrajejunal levodopa-carbidopa infusion (IJLI) are the treatment options for patients with refractory motor complications. While cumulative LEDD is dramatically reduced after STN-DBS, its evolution after infusion-based therapies initiation is unclear. Thus, the aim of our study was to assess the evolution of cumulative LEDD after initiation of Apo or IJLI in PD patients.

Methods: We conducted a retrospective study in a movement disorders unit, between January 2015 and July 2017. LEDD was calculated before initiation and after the titration period necessary to reach the optimal clinical state, and included the LEDD of the injected drug.

Results: 68 patients were included: 21 received IJLI and 46 received Apo. Cumulative LEDD significantly increased after IJLI initiation (1483±788mg/d vs 1224±582mg/d before; p<0.01) and after Apo initiation (1571±579mg/d vs 1203±444mg/d before; p<0.001). The L-dopa daily dose did not significantly decreased after Apo initiation (865±513mg/d vs 984±425mg/d before; p=0.23). The increase in LEDD after Apo initiation is comparable to IJLI (+33.5±42.3% vs +32.6±76.1%; NS).

Conclusion: IJLI and Apo induced an increase in LEDD when the dosage of the injected drug was included in the evaluation, what was not done in most of previous studies. These results suggest that infusion-based therapies allow to reach higher LEDD than pulsatile oral conventional treatment, and that STN-DBS is the only option to decrease LEDD.

Disclosure: Nothing to disclose

EPR2083

Foot clearance pattern: a distinctive gait variable in vascular Parkinson's disease

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Background and aims: Foot clearance (height's foot above ground during swing phase and foot angles before and after swing phase, Figure 1) has been related to the risk of falling in people with Parkinson's disease PD). The literature on foot clearance is scarce, especially in Vascular PPD (VPD).
Objective: To investigate foot the clearance pattern of patients with VPD and IPD patients, and levodopa response.
Methods: Physilog sensors (GaitUp®) were used to measure the clearance variables of each stride during 60-meter continuous course in a self-selected pace in 15 healthy subjects, 15 IPD patients and VPD patients in (Off phase) and 1 h after (On phase) the acute administration of suprathreshold morning levodopa dose. Two features (mean and coefficient of variation) of each time series were statistically compared using Mann-Whitney test (comparison between groups) and using Wilcoxon signed ranks test (intragroup) (significant P-values <0.05).
Results: VPD patients presented lower lift-off angle, strike angle, maximum heel and toe height, all of these refractive to levodopa. Patients with IPD and VPD, particularly VPD, presented higher variability at the beginning (lift-off angle, maximum heel) and the end (maximum toe 2, strike angle) of swing phase.
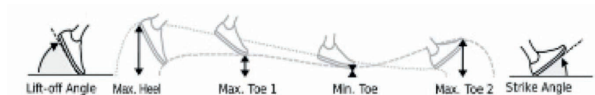
Figure 1: Illustration of clearance variables. (Adapted from Gait Up®)
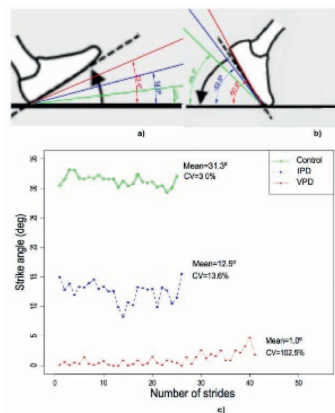
Figure 2: Strike angle (panel a)) and lift-off (panel b)) of foot clearance in VPD (green line), compared to a healthy subject (red line) and an IPD patient (blue line). Panel; c) Representative times series of strike angle over a continuous course of 30 meters, showing higher variability over the mean (CV=102.5%) in VPD.

Conclusion: Foot clearance analysis allowed to identify unique foot and heel patterns, potentially less amenable to be identified on clinical examination, with VPD patients displaying difficulty lifting the foots from the ground.
Disclosure: Nothing to disclose

EPR2084

The prevalence of dystonic tremor and tremor associated with dystonia in patients with cervical dystonia

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Background and aims: Link between dystonia and tremor has been known for decades, but at present question arises whether they are two separate illnesses or just different manifestations of one disease. We distinguish two types of tremor in dystonia: dystonic tremor, which appears on body part affected by dystonia, and tremor associated with dystonia (TAWD) in locations where dystonia does not occur. Dystonia has always been considered a basal ganglia disease. However, theory of neuronal network dysfunction, involving many areas of brain, currently prevails. Role of cerebellum seems especially important, which promotes theory, that TAWD might not be just a coincidence of essential tremor and cervical dystonia, but one of symptoms of cerebellar dysfunction in dystonia.

Methods: Prevalence of different forms of tremor was determined in a group of patients with cervical dystonia, treated with regular local injections of BoNT-A.

Results: In total, 123 patients with CD were included in the pilot study, 28 men (22.76%) and 95 women (77.24%). Mean age of patients was 59.8 years. Dystonic tremor of the head was present in 70 patients (56.91%). TAWD was in all 14 cases (11.38%) observed on upper limbs as static or intentional tremor.

Conclusion: In this pilot study, we point out the presence of TAWD as one of the clinical signs of cervical dystonia, occurring in 11.38% of patients in the studied group. Dystonic tremor occurred in more than half of the patients and appears to be a relatively common part of clinical picture in patients with cervical dystonia.

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EPR2085

Accelerometric evaluation of motor performance in PD patients before and after STN-DBS treatment

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Background and aims: Conventional assessment of motor fluctuations and dyskinesia in Parkinson's disease (PD) patients relies on subjective self-reporting and patient diaries. We have used wrist-worn accelerometers to objectively monitor motor symptoms in PD patients before and after STN-DBS.

Methods: We studied 13 advanced PD patients (6 women, mean age 61 ± 10.5) in the period 1 year before and again 4-12 months after bilateral STN-DBS, when the patients were considered stabilised on DBS. Patients were wearing a wrist-worn accelerometric device (Parkinson's Kinetigraph-PKG) over a period of 6 consecutive days. The percentage of daily time spent in moderate to severe dyskinesia and in bradykinetic state were recorded, and the fluctuation and dyskinesia score (FDS) was calculated as a measure of fluctuation, derived from variations of dyskinesia and bradykinesia scores produced by the PKG. These were compared before and after STN-DBS surgery using Wilcoxon Signed-ranks Test.

Results: The pre-DBS rank was significantly higher than the post-DBS one for the time spent with dyskinesia (Mdn=0.41 vs. Mdn=0.1, Z=2.97, p<0.01). However, there was no significant difference in bradykinesia (Mdn=0.35 vs. Mdn=0.49, Z=0.85, p=0.064). The FDS was significantly lower after STN-DBS (Mdn=17.5 vs. Mdn=9.2, Z=2.97, p<0.01).

Conclusion: Our study shows an objective statistically reliable reduction of dyskinesia. No change in bradykinesia was probably due to l-dopa overdose before the operation to avoid "off" periods at the cost of dyskinesia. The improvement of FDS score after operation suggests more stable daily motor performance. PKG offers a reliable and objective measure of patient's motor condition.

Disclosure: Nothing to disclose

EPR2086

Probable novel presenilin 1 mutation (p. Arg41Ser) as cause of early-onset Parkinsonism

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Background and aims: Although Alzheimer's disease (AD) and Parkinson's disease (PD) are multifactorial neurodegenerative disorders having distinct genetic risk factors, studies have revealed a possible genetic links between them. Mutations in presenilin-1(PSEN1) accounts for the majority of cases of early-onset autosomal dominant AD as well as sporadic forms. Atypical presentations have been reported including extrapyramidal signs (parkinsonism, myoclonus, dystonia). In the last years, mutations involving the PSEN1 and PD genes such as PARK2, PINK1 and LRRK2 have been demonstrated.
Objective: Report a case of PSEN1 mutation presenting with early-onset Parkinsonism (EOPD) phenotype.
Methods: A 46-year–old Argentinian woman with a remarkable medical history of chronic iron deficiency anemia,and a positive family history of psychiatric disorders started at age 35 with progressive asymmetric left resting tremor, bradykinesia and rigidity. Wilson's and Niemann-Pick type C disease resulted negative. EOPD was diagnosed. L-dopa/carbidopa (LD/C) and rotigotine were slowly titrated, with clinical improvement. Two years later, she reported mild difficulties with memory and attention during the last two years.
Results: Neuropsychological examination showed a predominant frontal subcortical cognitive decline. Brain MRI showed moderate signs frontal atrophy and 18FDG-PET reduced metabolism in frontal cortex. PiB-PET (Pittsburgh compound) image was amyloid negative. Because of EOPD and family history a Next Generation Sequencing-NGS was performed on DNA extracted from whole blood. NGS analysis revealed a novel missense PSEN1 mutation position 14:73637540, A>T, p.Arg41Ser. Parental DNA analysis could not be examined.
Conclusion: This missense PSEN1 was considered a potential causative mutation, given the phenotype and the occurrence of the mutation in a very conservative region
Disclosure: Nothing to disclose

EPR2087

(Dys)prosody in Parkinson's disease: effects of medication and disease duration on different prosodic functions

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Background and aims: Sentence modality and speech chunking are two prosodic functions crucial to communication. It is currently unknown whether/how the expression of these linguistic functions is impaired in Parkinson's disease (PD), and how disease duration and medication affect prosodic functions in PD.
Methods: 20 PD patients were compared to 20 controls during the production of sentences eliciting various prosodic patterns (Table1). Patients fell in two groups according to disease duration (G1: 1-5 years; G2: ≥10 years), and medication (OFF: no medication; ON: one hour after a dopaminomimetic drug intake). Prosodic analysis was done with PRAAT, using the P-ToBI system to annotate nuclear contour types and phrasing breaks. A deviance scale from '1' to '-1' was computed by subject, with the language target prosody as '1' and the most deviant prosody in the data as '-1'. Group performance was examined by a One-Way ANOVA. A mixed ANOVA assessed the effects of disease duration and medication.

Table 1. Participants' mean age, age range and gender, by group.

Participants	Mean age	Age range	Females
Controls (n=20)	60	43 - 74	10
PD – G1 (n=10)	66	40 - 82	6
PD – G2 (n=10)	64	41 - 79	6

Table 1. Participants' mean age, age range and gender, by group.

Results: Both the expression of sentence modality and speech chunking were disturbed in PD, as patients overall performed significantly worse than controls (Fig.1). However, medication improved the expression of modality, while no effects of disease duration were found (Fig.2, left). Differently, for speech chunking there was no main effect of medication, or of disease duration, but a significant interaction between medication and disease duration: G1 chunking improved in ON, unlike G2 chunking (Fig.2, right).
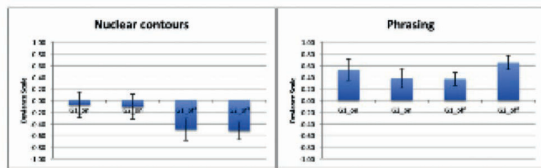
Figure 2. PD: medication and disease duration. Left panel: Nuclear contours (data for all sentence types); Right panel: Phrasing (expected speech chunking).
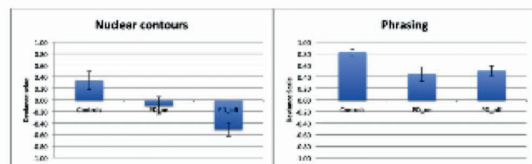
Figure 1. Controls and PD. Left panel: Nuclear contours (data for all sentence types); Right panel: Phrasing (expected speech chunking).

Conclusion: These findings are the first to demonstrate that different prosodic functions are affected differently in PD, with implications for PD neurophysiology and therapy.

Disclosure: Research developed within the project Dysarthria in Parkinson's disease: Lusophony vs. Francophony comparison (FCT-ANR/NEU-SCC/0005/2013), funded by FCT-ANR, within the Program Blanc Accords Bilatéraux France/Portugal. Additional support was provided by CLUL (Grant UID/LIN/00214/2013).

EPR2088

The diagnostic accuracy of the hummingbird and morning glory sign in patients with neurodegenerative parkinsonism

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Background and aims: The hummingbird (HB) and morning glory flower signs (MGF) reflect midbrain pathology on MRI. Therefore, we aimed to determine diagnostic accuracy and reproducibility of midbrain atrophy patterns in a large cohort of patients with neurodegenerative parkinsonism and healthy controls (HC).

Methods: Retrospective analysis of midbrain atrophy patterns on T1-weighted MRI by at least two independent experienced and two junior raters.

Results: 95 patients with progressive supranuclear palsy (PSP), 289 with Parkinson's disease (PD), 97 with multiple system atrophy (MSA) and 79 HC were included. Presence of the HB sign had a specificity of 99.5% and a PPV of 96.1% for a diagnosis of PSP, while sensitivity was suboptimal (51.6%). Presence of the MGF sign yielded a specificity of 97.7% for a diagnosis of PSP, but sensitivity was only 36.8%. Cohen's kappa revealed almost perfect agreement between both experienced rater (HB: k 0.945; MGF: k 0.918;p<0.001), strong agreement in the assessment of the HB sign (k 0.871;p<0.001) and moderate agreement in the assessment of the MGF sign (k 0.651;p<0.001) between the two junior raters. There was also an almost perfect agreement for the comparison of consensus rating of the HB sign between the junior and the experienced raters (k 0.901;p<0.001), for the MGF sign only a strong agreement could be achieved (k 0.719;p<0.001).

Conclusion: Midbrain atrophy patterns are useful in the differential diagnosis of neurodegenerative parkinsonism but both the HB and MGF sign suffer from low sensitivity.

Disclosure: Nothing to disclose

Movement disorders 6

EPR2089

Variability of presynaptic nigrostriatal dopaminergic function and clinical heterogeneity in a Dopa-responsive dystonia family with GCH-1 gene mutation

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Background and aims: Mutation of guanosine triphosphate cyclohydrolase 1 (GCH-1) is the most common and best characterized condition that manifests as Dopa-responsive dystonia (DRD). Since the gene product is related to tyrosine hydroxylation, impairment of dopamine production in the nigral cell seems to be responsible for DRD. However, results of the functional imagings were still controversial. The aim of this study was to evaluate presynaptic nigrostriatal dopaminergic function by brain TRODAT SPECT imaging in a Taiwanese DRD family.

Methods: Three of five members of the DRD family were found to have a heterozygous T241C mutation in exon 1 of GCH-1. We studied TRODAT SPECT imaging in those three members. We further analyse the correlation between the phenotypic presentation of DRD and the nigrostriatal dopaminergic function

Results: There was presentation of intrafamilial variability in the DRD family; one was a classic DRD (proband), one presented with parkinsonism which was distinguishable from typical PD, and the other one was an asymptomatic gene carrier. The proband was a 10-year-old girl with classic DRD and normal presynaptic nigrostriatal dopaminergic function. Her grandmother, a 79-year-old woman, presented with slowly progressive PD and excellent response to dopaminergic therapy for 21 years. Her brain TRODAT imaging revealed a markedly and asymmetrically reduced uptake of dopamine transporter at the bilateral striatum. Her father, a 54-year-old man, was an asymptomatic gene carrier and his brain imaging revealed asymmetrically reduced nigrostriatal dopaminergic transmission in the bilateral striatum.

Conclusion: We conclude variability of presynaptic nigrostriatal dopaminergic function in patients with DRD is related to their clinical heterogeneity.

Disclosure: Nothing to disclose

EPR2090

Quantitative assessment of postural instability by measuring minimal weight load for stepping reaction in pull test

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Background and aims: We developed an apparatus for quantitative assessment of pull test in Parkinson's disease (PD). Before applying this apparatus to PD patients, we investigated whether several physical parameters in healthy subjects might affect the amount of minimal weight load for inducing backward stepping in pull test.

Methods: 26 adult healthy subjects (23 ± 3.7 y.o., male : female=10 : 12) participated in the experiment. The subject wore a vest, in which a lope was connected at the back. A basket was attached at the other end of the lope. By putting a heavy bob into the basket, the subject at standing position was pulled backwards unexpectedly (Fig. 1). A minimal weight for inducing stepping reaction (MWS) was measured. During the experiment, EMGs of both tibialis anterior muscle (TA) and soleus muscle (SOL) were recorded. All the experiment process was recorded with a video camera.
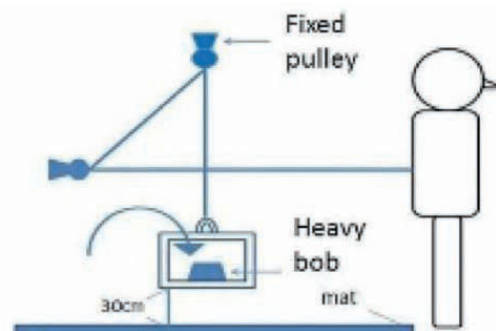
Fig 1: Apparatus Mimicking Pull Test

Fig. 1

Results: Mean MWS was 1.73 ± 0.73 kg. Among several physical parameters investigated, grasp power had a significant correlation with the MWS ($r=0.408$, $p<0.05$) (Fig. 2). Other physical parameters including height, weight, foot size etc. had no statistical correlation with the MWS. The large variations among each subject were observed in the latency of TA EMG activity after weight load.

Fig 2: Correlation between minimal weight for stepping and grasp power (r =0.408, p<0.05)
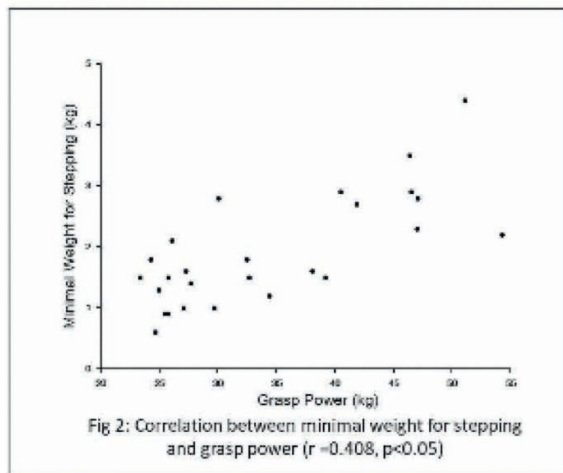
Fig. 2

Conclusion: Considering that mean grasp power represents whole body muscle strength, whole body muscle strength may affect the result of pull test.

Disclosure: JSPS KAKENHI Grant Grant-in-Aid for Scientific Research C Number JP16K01510.

EPR2091

Genotype-phenotype correlation in ADCY5-related movement disorders

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Background and aims: Mutations in ADCY5 gene might derive in different phenotypes: benign hereditary chorea (BHC), facial dyskinesia and paroxysmal dyskinesia with hypotonia. Our aim is to describe the variability in clinical manifestation among patients with different mutations in ADCY5.

Methods: We report a family clinically affected with BHC and a sporadic case with paroxysmal dyskinesia and hypotonia. Our family index case is a 34-year-old woman with a childhood onset chorea and facial dyskinesia with mild dystonia and myoclonus. Some of her relatives had been studied in our Movement Disorders Unit for BHC, suggesting an autosomal dominant pattern of inheritance. The sporadic case was an eighteen-year-old male without delivery problems. He developed hypotonia with six months and nocturnal paroxysmal dyskinesia during the first two years of life, increasing frequency of these events among childhood.

Results: Cerebral MRI were normal in all patients. Neurophysiological studies showed myoclonus in both, family index and sporadic cases. Genetic tests for the most common causes of dystonia, paroxysmal dyskinesia and myoclonus were performed with negative results. In the familiar index case a pathogenic mutation c.2176G>A (p.Ala726Thr) in gene ADCY5 was found. In the sporadic case a de novo mutation c.1252C>T (p.Arg418Trp) in ADCY5 was demonstrated.

Conclusion: We described two mutations in gene ADCY5 causing different phenotypes: BHC and paroxysmal dyskinesia with hypotonia and myoclonus. Facial dyskinesia or nocturnal exacerbations of dyskinesia are clinical features that help through the diagnosis. De novo mutations in ADCY5 can be present, this etiology should be considered even without positive family history.

Disclosure: Nothing to disclose

EPR2092

The overlap syndrome of three neurodegenerative diseases – a case report

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Background and aims: Progressive supranuclear palsy (PSP), frontotemporal dementia (FTD) and corticobasal syndrome (CBS) are neurodegenerative diseases classified as tauopathies. Clinical and/or histopathological features of these diseases may coexist in one patient within an overlap syndrome. In such cases, mutations or polymorphism of genes attributed to different neurodegenerative diseases are often found. The concomitance of features of PSP, FTD and CBS is observed in 10-30% of overlap syndromes.

Methods: A 51-year-old man had four years history of progressive psychomotor slowness, reduction of spontaneous activity, deficits in memory and attention, behavioural disorders (hygiene neglect, binge eating), dysarthria, excessive salivation, frequent falls and uncontrolled laughter. The symptoms have become a burden for the patient at home and in the workplace. Neurological examination revealed psychomotor slowness, difficulties in performing complex tasks, pseudobulbar features, oculomotor abnormalities (bradykinesia, limited vertical movements), oromandibular and truncal dyskinesias, extrapyramidal symptoms (hypomimia, postural reflexes disturbance, rigidity of right limbs with foot dystonia and "alien" lower limb phenomenon), right-sided pyramidal symptoms and cerebellar features.

Results: Brain magnetic resonance imaging displayed moderate frontal, temporal and mesencepahlic atrophy with signs of neuronal necrosis. Neuropsychological testing confirmed disturbances in cognition, visuospatial organization, executive functions, impaired impulse control and stiffness of emotional reactions. The patient was diagnosed with an overlap syndrome comprising progressive supranuclear palsy, frontotemporal dementia and corticobasal syndrome.

Conclusion: We presented a rare case of an overlap of three tauopathies. The concomitance of clinical features typical for different neurodegenerative diseases may generate diagnostic difficulties and is usually associated with a poor prognosis.

Disclosure: Nothing to disclose

EPR2093

The effect of bilateral subthalamic stimulation on postural sway and its correlation with disease-related factors in Parkinson's disease

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Background and aims: The effect of bilateral subthalamic stimulation (STN-DBS) on the postural instability in Parkinson's disease (PD) is not unequivocal in different studies. We aimed to analyse it and explore its influencing factors.

Methods: 24 PD patients treated with STN-DBS and 18 age-matched healthy subjects performed Instrumented Clinical Test of Sensory Organisation and Balance test while wearing an Opal motion sensor on the lumbar region. Sway area (m2s4) of the trunk (Table1) was calculated with Mobility Lab software (APDM Inc.) during stimulation-off state (NON) and with optimal bilateral stimulation (BON) after 12 hours medication withdrawal. Pre- and postoperative clinical data were collected and compared.

Results: The age of the patient group was 65(10) years [median (interquartile range)], the elapsed time since operation: 19(27) months. The preoperative UPDRS III. scores in MED-OFF state were 30(29) points; its postoperative improvement was 81(51)%. Sway values in PD, in NON state were higher than that of controls (Table1). PD group was divided into Group1 (sway decreased with neurostimulation) and Group2 (sway increased in BON state). Sway values in these groups were not different in NON state, but Group2 had higher values in BON state (Table2). Age and the elapsed time since the operation were not different in the two PD groups. However, Group2 had higher preoperative UPDRS III. scores (24(13.5) and 48(33); p=0.004).

Table1. Sway values of the PD group in NON state compared to control values

	Sway (m²s⁴) [median (IQR)]				
	Eyes opened Ground	Eyes closed Ground	Eyes opened Foam	Eyes closed Foam	Combined Sway
Patient group	0.036 (0.04)	0.048 (0.04)	0.089 (0.091)	0.249 (0.19)	0.116 (0.07)
Control group	0.015 (0.01)	0.024 (0.02)	0.045 (0.04)	0.167 (0.17)	0.068 (0.07)
p	0.006	0.029	0.006	0.127	0.036

Table 1.

Table2. Sway values of the NON and BON state in the two patient groups

	Sway values (m²s⁴) [median (IQR)]									
	Eyes opened Ground		Eyes closed Ground		Eyes opened Foam		Eyes closed Foam		Combined sway	
	NON	BON	NON	BON	NON	BON	NON	BON	NON	BON
Group 1.	0.027 (0.04)	0.014 (0.01)	0.033 (0.05)	0.027 (0.02)	0.075 (0.11)	0.046 (0.03)	0.181 (0.16)	0.13 (0.12)	0.09 (0.04)	0.06 (0.04)
Group 2.	0.045 (0.04)	0.061 (0.06)	0.056 (0.04)	0.08 (0.13)	0.093 (0.08)	0.13 (0.15)	0.301 (0.15)	0.33 (0.25)	0.13 (0.07)	0.17 (0.11)
p	0.44	0.001	0.06	0.01	0.32	< 0.001	0.1	< 0.001	0.13	< 0.001

Table 2.

Conclusion: Our data suggest that worse preoperative motor performance is a risk factor for stimulation-induced postural instability after STN-DBS in PD. Further predictive factors should be explored.

Disclosure: Nothing to disclose

EPR2094

Eyes that are both quick and slow: three patients with PSP syndrome and gaze evoked nystagmus – new observation.

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Background and aims: Nystagmus is an atypical finding in progressive supranuclear palsy (PSP). In fact, presence of nystagmus in patient with parkinsonism points toward multiple systemic atrophy. Since the diagnosis of different parkinsonian conditions is primarily clinical, it is important to determine phenotypic spectrum of the disease. We present three patients with PSP syndrome and horizontal, gaze-evoked nystagmus (GEN).

Methods: Patients were clinically examined, video recorded and followed-up up to 5 years. Extensive diagnostic work up, including brain MRI and FDG PET, spinal tap and genetic testing was performed. Pub Med was searched for articles describing GEN in PSP patients.

PATIENT SEX AND AGE	MAIN CLINICAL FEATURES	TYPE OF NYSTAGMUS	BRAIN MRI	BRAIN FDG - PET CT
Male. 66	-Early falls -Parkinsonism, unresponsive to levodopa - Axial rigidity -Postural instability -Eyelid apraxia – Vertical gaze palsy -Slowing of saccades in all directions	Gaze evoked, horizontal nystagmus in both directions	Mesencephalic and frontal lobe atrophy	Decreased activity in basal ganglia and frontal lobes. Normal activity in cerebellum.
Male, 68	-Postural instability -Symmetrical parkinsonism, unresponsive to levodopa – Vertical gaze palsy - Slowing of saccades in all directions	Initially vertical, gazed evoked nystagmus on looking up and gazed evoked horizontal nystagmus in extreme positions. At last follow up, gaze evoked horizontal nystagmus, more prominent on looking to left.	Mesencephalic atrophy	Slightly increased activity in basal ganglia. Normal activity in cerebral cortex and cerebellum.
Male, 61	-Postural instability with early falls -Dysarthria -Parkinsonism unresponsive to levodopa –Axial rigidity -Vertical gaze palsy - Slowing of saccades in all directions	Gaze evoked horizontal nystagmus in both direction, present only in some head positions (and no vertigo)	Mesencephalic atrophy	Decreased activity in the pons and both frontal lobes. Normal activity in cerebellum.

Table 1: Patient information regarding sex, age, PSP symptoms, head MR and PET CT.

Results: All three patients (Table) had parkinsonism poorly responsive to levodopa and vertical gaze paresis with slowing of vertical and horizontal saccades, indicating PSP syndrome. The atypical finding was horizontal GEN, with no other cerebellar signs. Imaging results were characteristic for PSP and alternative diagnosis were excluded. We found only two cases of nystagmus in PSP in the literature.
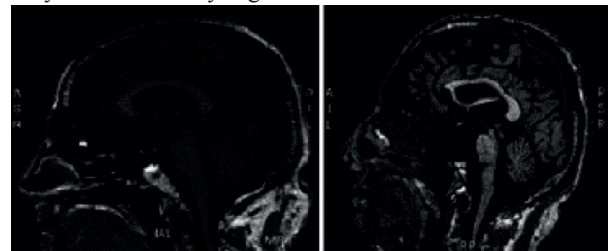
Picture 1: Head MR of the second patient (on the left) and of the third patient (on the right).

Conclusion: The same pontine structures are responsible for voluntary saccades and the fast phase of nystagmus, thus the co-occurence of nystagmus and gaze paresis might be contraintuitive. However, in our PSP patients, it might be explained by gradual neurodegenerative process, which first affects voluntary saccades causing saccadic slowing as an early manifestation of gaze paresis. At the sime time, reflex saccades responsible for the fast component of nystagmus, are relatively unaffected. With disease progression, reflex saccades become impaired and the nystagmus fades away. GEN may frequently be overlooked in PSP, as it appears only temporarily.

Disclosure: Nothing to disclose

EPR1078

Dopaminergic adverse-events in patients that switched from entacapone to opicapone: the BIPARK-I open-label experience

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Background and aims: Assess the occurence of dopaminergic adverse-events (AEs) in levodopa-treated Parkinson's Disease (PD) patients that switched from entacapone (ENT) to opicapone in the BIPARK-I open-label part.

Methods: After completing the BIPARK-I double-blind part, ENT-patients switched to a 1-year open-label extension, in which all subjects received OPC. This post-hoc analysis investigated the occurence of dopaminergic AEs, namely, dyskinesia, nausea, vomiting, hallucinations (including delusion, illusion and disturbance in attention), and orthostatic hypotension on those entacapone 'switchers'. Dopaminergic AEs were defined as new or worsening post-treatment from baseline or double-blind.

Results: 100 patients switched from ENT to 1-year OPC open-label extension. By the end of double-blind, 4% of ENT-patients reported at least 1 dopaminergic AE. After switching to OPC, cumulatively, 22% of ENT switched-patients reported at least 1 dopaminergic AE. Most common AE was dyskinesia (20% cases) that presented an earlier onset. About 45% of ENT switched-subjects with dopaminergic AEs had a levodopa daily-dose reduction of ~25%. By the end of the 1-year OPC open-label extension, actual (by-day) frequency reported was 4% and 1%, respectively for dyskinesia and nausea. One case each of dyskinesia and orthostatic hypotension led to patient withdrawal.

Conclusion: After switching to OPC, we observed an increase in the rate of dopaminergic AEs by ENT switched-patients. This was largely due to worsening or new emergence of dyskinesia, which appeared to be controlled by levodopa reductions. These observations support an enhanced dopaminergic efficacy of OPC and an early follow-up may be warranted to perform any required levodopa adjustments in a timely manner.

Disclosure: Nothing to disclose

EPR2096

Effects of probiotic bacterial strains on peripheral inflammation in Parkinson's disease

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Background and aims: Parkinson's disease (PD) is characterised by loss of dopaminergic neurons and intraneuronal accumulation of alpha-synuclein, both in the basal ganglia and in peripheral sites, such as the gut. Recent findings demonstrate that PD patients display a pro-inflammatory phenotype. In this context, the present in vitro study was focused on the direct effects of probiotic bacterial strains on inflammatory pathways in PD patients

Methods: We enrolled 40 PD patients and 40 matched controls. Peripheral Blood Mononuclear Cells (PBMCs) were isolated and cultured with the following bacterial strains: Lactobacilli (salivarius, plantarum, acidophilus, rhamnosus) and Bifidobacteria (breve and lactis). The modulation of the in vitro release of the major pro- (Tumor Necrosis Factor-alpha and Interleukin-17A) and anti-inflammatory (Interleukin-10) cytokines by PBMCs was investigated, as well as the production of free oxygen radicals (ROS). To provide a surrogate marker of inflammatory profile, we expressed cytokine data as Th1/Th2 ratio.

Results: All strains were able to inhibit inflammatory cytokines and ROS production in both patients and controls. The most striking results in patients were obtained with L. salivarius: 55 and 94% reduction of Th1/Th2 ratio and ROS compared to baseline. A relevant decrease of Th1/Th2 ratio was provided by L. plantarum and B. breve (39 and 38%), whereas ROS production was reduced of 85 and 77% by L. plantarum and L. acidophilus.

Conclusion: Probiotics exert promising results in modulating the release of cytokines towards an anti-inflammatory profile and in counteracting oxidative stress. Further data are mandatory to confirm the role of bacteriotherapy in PD

Disclosure: Nothing to disclose

MS and related disorders 4

EPR2097

Clinical predictors of long-term outcome in multiple sclerosis patients: a prospective cohort study

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Background and aims: Randomised clinical trials have shown that interferon (IFN)-beta reduced relapse frequency and relapse-related accumulation of disability in multiple sclerosis (MS). The aim of this study is to describe the accumulation of long-term disability in a cohort of IFN-beta treated MS patients and to assess whether clinical data have long-term prognostic value.
Methods: This is a prospective study of 419 (236 IFN-beta-treated, 183 untreated) relapsing-remitting (RR) MS patients recruited consecutively, at the Clinic of Neurology, Belgrade. Out of this original cohort, 10-year follow-up data were available on 364 (233 IFN-beta-treated, 131 untreated) subjects. The median time since recruitment was 9.7 years and 19.1 years since MS onset.
Results: The composite predictor, no evidence of clinical disease activity (NEDA-2), from baseline through second year of the study was detected in 60.9% IFN-beta-treated and 7.6% untreated patients (p<0.001). The baseline Expanded Disability Status Scale (EDSS) score (p<0.001), baseline to year 2 increase in EDSS (p<0.001), annualized relapse rate from baseline to year 2 (p<0.001), and NEDA-2 (p=0.002) were significant predictors for secondary progressive MS conversion, and likelihood of confirmed EDSS worsening up to scores ≥4 and ≥6 in IFN-beta-treated group. In untreated group, all those variables were significant predictors for all three end points, except annualized relapse rate from baseline to year 2.
Conclusion: Our observational study showed the necessity of IFN-beta treatment in patients with RRMS, in order to prevent disease progression and permanent disability, and additionally that NEDA-2 was significant predictor for long-term worsening disability.
Disclosure: Nothing to disclose

EPR2098

Dynamic functional network connectivity in CIS patients: a longitudinal study

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Background and aims: Time-varying properties of resting-state (RS) functional network connectivity (FNC) at earliest stages of multiple sclerosis (MS) have never been studied. We investigated the trajectory of longitudinal dynamic FNC (dFNC) changes in patients with clinically isolated syndrome (CIS) suggestive of MS.
Methods: RS fMRI data were acquired from 50 CIS patients and 13 healthy controls (HC) at baseline (within 3 months from first attack), year 1 and year 2. Independent component analysis identified 41 relevant networks, which were subsequently classified according with their functional system. Between-group differences of dFNC strength and dynamism measures were analysed.
Results: 47 (94%) patients developed MS at year 2. HC and CIS patients presented 2 dFNC states: State1 (frequency=69%), characterised by low FNC, and State2 (frequency=31%) characterised by high FNC. At baseline, compared to HC, CIS patients showed increased dFNC mainly for sensorimotor and default-mode networks in State 2, which was maintained at follow-up. Reduced dFNC for executive and visual networks that decreased over time, mainly in State 1, was also observed. FNC dynamism tended to increase over time in CIS patients vs HC, with: a) an increasingly higher distance travelled through meta-states at year 1 and year 2, and b) higher number of meta-states and more frequent switches between meta-states at year 2.
Conclusion: The analysis of time-varying RS FNC patterns in CIS patients highlights the relevant role that sensorimotor, default-mode, executive, and visual networks play at the first stages of MS, while helping to establish a potential target for MS early diagnosis.
Disclosure: Partially supported by a grant from the Ministry of Science, Republic of Serbia (# 175031).

EPR2099

Long-term fingolimod treatment in patients with RRMS: MRI outcomes from the LONGTERMS study

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Background and aims: Assessment of long-term efficacy of disease-modifying therapies for multiple sclerosis (MS) is an important aspect of MS disease management in routine clinical practice. We assessed the radiological stability in patients with relapsing-remitting MS treated with fingolimod for up to 120 months.

Methods: LONGTERMS is an open-label, single-arm, extension study evaluating the long-term safety, tolerability and efficacy of fingolimod in patients who previously participated in phase 2/3/3b studies. The full analysis set included all patients randomised to fingolimod 0.5 mg. The selected MRI endpoints were annualised rate of new or newly enlarging T2 lesions (ARneT2), the proportion of patients free from gadolinium-enhancing (Gd+) T1 lesions, percent brain volume change (PBVC) from the first dose of fingolimod by visit, and the annualised rate of brain atrophy (ARBA; an average annual percentage change in brain volume).

Results: At baseline, 3168 patients (women, 71.2%; age [mean± standard deviation (SD)], 38.0±9.1 years; median exposure to fingolimod, 528.5 days [range, 75–3805]; Expanded Disability Status Scale [mean±SD], 2.4±1.5) were included. ARneT2 gradually decreased from 1.362 at Month (M) 0–12 to 0.922 at M0–60 to 0.71 at M0–120. Of the 924 evaluable patients, 48.3% remained free from Gd+ T1 lesions up to M60. PBVC remained low from the first dose of fingolimod (least squares mean: M12, -0.38; M60, -1.57; M120, -3.28). Change in brain volume, as assessed by ARBA, was stable throughout the study (mean: M12, -0.37; M60, -0.33; M120, -0.32).

Conclusion: These results support the long term efficacy of fingolimod in maintaining low disease activity.

Disclosure: This study was funded by Novartis Pharma AG, Basel, Switzerland. Detailed disclosures of each author will be included in the poster.

EPR2100

International consensus on quality standards for multiple sclerosis care: results from a modified Delphi process

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Background and aims: The importance of prompt intervention in multiple sclerosis (MS) was described in the widely endorsed report, Brain health: time matters in multiple sclerosis.1 The present study aimed to define standards for the timing of key steps in the care pathway.

Methods: An international group of 29 MS neurologists was recruited to participate in a Delphi process. Across five rounds, they defined 'core', 'achievable' and 'aspirational' standards (to reflect a minimum, good and high standard of MS care, respectively). A Reviewing Group of 31 MS nurses, experts with MS and allied healthcare professionals reviewed the results and provided feedback.

Results: Consensus was reached (≥75% agreement; n=21) on core, achievable and aspirational standards for 21 steps in the MS care pathway, covering symptom onset, referral, diagnosis, treatment decisions, lifestyle, monitoring, and managing new symptoms. For example, the panel agreed that MS teams should complete a diagnostic workup for MS within 2 months of referral to a neurologist as a core standard, and that completion within 4 weeks of referral should be achievable for most MS teams, with completion within 7 days as an aspirational standard. Here, we will present core, achievable and aspirational standards for key steps in the MS care pathway.

Conclusion: These standards will inform tools for clinics and people with MS and act as a future benchmark for established and developing MS clinics across the globe aiming to deliver the highest quality care.

Reference

1. Giovannoni G et al. Mult Scler Relat Disord 2016;9 Suppl 1:S5–S48.

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EPR2101

Prespecified subgroup analyses of ocrelizumab efficacy in patients with primary progressive Multiple Sclerosis from the Phase III ORATORIO Study

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Background and aims: The Phase III ORATORIO study (NCT01194570) demonstrated the efficacy of ocrelizumab versus placebo on a broad range of clinical and imaging outcomes in patients with primary progressive multiple sclerosis.

Methods: The effect of ocrelizumab (600mg) versus placebo on 12-week CDP was analysed in prespecified subgroups (age, sex, region, BMI, body weight, EDSS score, T1 gadolinium-enhancing lesions, prior MS disease-modifying treatment, duration of MS since symptom onset) by Cox proportional hazard models including treatment-subgroup interaction effects. Additional analyses of outcomes were performed for subgroup comparisons that showed a trend for differences in treatment effect (nominal interaction $p < 0.3$ on 12-week CDP). The study was not powered to demonstrate efficacy within, or differences between, subgroups.

Results: No differences in the magnitude of ocrelizumab treatment effect on 12-week CDP between all prespecified subgroups were statistically significant (all interactions $p > 0.05$; ocrelizumab n=487; placebo n=244). Numerical differences in treatment effect were observed within subgroups based on sex, baseline T1 gadolinium-enhancing lesions and age (interaction $p < 0.3$). On 12-week CDP, males seemed to derive more benefit; however, male and female patients benefited from ocrelizumab on key clinical and imaging secondary and exploratory endpoints. Although the effect of ocrelizumab was generally larger in patients with baseline T1 gadolinium-enhancing lesions and/or at a younger age, older patients and those with no baseline T1 gadolinium-enhancing lesions also derived benefit across key endpoints.

Conclusion: Directionally consistent point estimates favouring ocrelizumab versus placebo were seen across all clinical and MRI endpoints in prespecified subgroups of the ORATORIO study.

Disclosure: Sponsored by F. Hoffmann-La Roche Ltd.

EPR2102

Case report of a fingolimod treated patient with possible progressive multifocal leucoencephalopathy, without prior immunosuppression

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Background and aims: Progressive multifocal leukoencephalopathy (PML) is rarely encountered in MS patients as a potential side effect of treatment with some disease modifying drugs, notably natalizumab and more recently fingolimod and dimethyl fumarate, usually in immunocompromised or priorly immunosuppressed patients.

Methods: Herein, we report a case of a fingolimod-treated multiple sclerosis (MS) patient with no lymphocytopenia and no prior exposure to immunosuppressants, who developed possible PML.

Results: A 36-year-old woman, with relapsing-remitting MS previously treated with interferon b-1β, was switched to fingolimod due to breakthrough disease activity. After three years she presented with right pyramidal weakness, right inferior quadrantanopia, progressive cognitive dysfunction, apathy and mixed aphasia. Absolute white blood cell count was 10,51K/μl and absolute lymphocyte count was 1,93 K/μl (>30% from baseline). Fingolimod was discontinued and methylprednisolone was initiated. Brain MRI revealed a left frontal and temporal lobe lesion with no contrast enhancement. She tested negative for HIV and DNA PCR for JC virus was repeatedly negative. Proton magnetic resonance spectroscopic imaging revealed evidence of PML. A course of plasmapheresis followed and mirtazapine was also administered. Repeated brain MRIs showed improvement along with clinical improvement.

Conclusion: Even patients without previous immunosuppressive therapy or low lymphocyte count, may be at risk for developing PML. In fingolimod treated patients no guidelines exist for PML surveillance and the clinical course of PML in naïve-immunosuppressed patients, may be different compared to patients receiving natalizumab. Vigilant clinical and radiologic monitoring is needed in order to timely diagnose this possibly critical side effect.

Disclosure: Nothing to disclose

EPR2103

Siponimod improves cognitive processing speed in patients with SPMS: Results from Phase 3 EXPAND Study

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Background and aims: Symbol Digit Modalities Test (SDMT) and Paced Auditory Serial Addition Test (PASAT) are commonly used in clinical trials to assess cognitive processing speed (CPS). The SDMT is more reliable and sensitive than the PASAT. A 4-point change in the SDMT is proposed to define a clinically meaningful change. The Brief Visuospatial Memory Test-Revised (BVMTR) evaluates visual/spatial memory and is valid in MS patients. We report the effect of siponimod on CPS and visual/spatial memory in secondary progressive multiple sclerosis (SPMS) patients.

Methods: Patients from the EXPAND study (siponimod, 1099; placebo, 546) underwent SDMT, PASAT and BVMT-R at 6-month intervals with flexible follow-up per patient. Between-group comparisons for change from baseline were performed using a repeated measures model, adjusted for treatment and baseline scores. Subgroup analyses were performed for patients with/without relapses (rSPMS/nrSPMS) in 2 years before baseline. Cox models assessed the time to 6-month sustained 3 and 4 points change on SDMT.

Results: Siponimod reduced the risk of 3- and 4-point-confirmed worsening on SDMT versus placebo by 28.6%(p=0.0002) and 21.3%(p=0.0157) respectively (Figure 1).Month 24-SDMT scores improved (3points/4points) in 44.8%/40.8% of patients receiving siponimod versus 38.8%/30.2% receiving placebo (Figure 2A&B). Difference in mean change from baseline (2.48) favoured siponimod (p=0.0004). Between-group scores for PASAT/BVMTR were similar. Compared with baseline, SDMT scores improved with siponimod in both rSPMS and nrSPMS patients; for PASAT a difference was only seen in
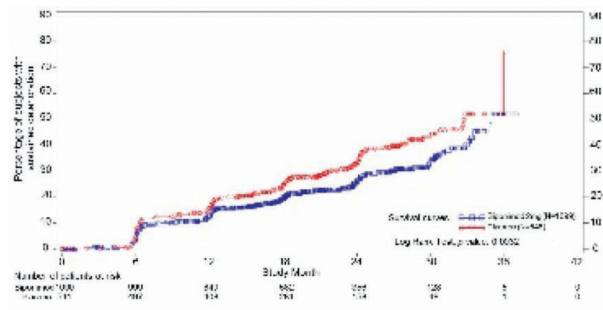
CI, confidence interval; SDMT, Symbol Digit Modalities Test

Figure 1. Percentage of patients with sustained deterioration based on SDMT score (cut-off 4 points)

PASAT, Paced Auditory Serial Addition Test; SDMT, Symbol Digit Modalities Test; SE, standard error; SPMS, secondary progressive multiple sclerosis

Table 1. Change from baseline in the SDMT and PASAT scores by visit in patients a) with superimposed relapses (rSPMS) and b) without superimposed relapses (nrSPMS) in the 2 years before the study start
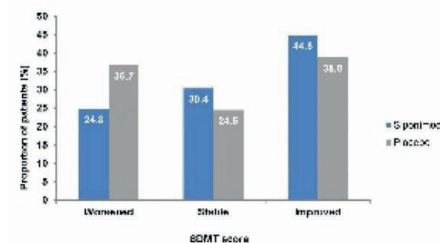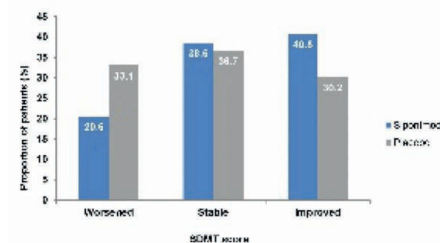
Figure 2. Proportion of patients with deteriorated, improved and stable SDMT scores with cut-off 3 points (A) and 4 points (B) at Month 24

Conclusion: Siponimod demonstrated a significant and clinically meaningful positive effect on CPS as measured by SDMT in SPMS patients with/without relapses.

Disclosure: This study was funded by Novartis Pharma AG, Basel, Switzerland. Detailed disclosures of each author will be included in the poster.

EPR2104

Effect of Teriflunomide on substantial disability worsening in patients with relapsing forms of MS in a Pooled Analysis of the phase-3 TEMSO and TOWER studies

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Background and aims: In 2 phase-3 studies (TEMSO, NCT00134563; TOWER, NCT00751881), teriflunomide 14mg significantly reduced the risk of 12-week confirmed disability worsening (12wCDW) vs placebo in patients with relapsing forms of MS. In a post-hoc analysis of the pooled TEMSO/TOWER dataset, the effect of teriflunomide 14 mg on more substantial disability worsening using 3 exploratory definitions of 12wCDW was assessed.

Methods: In TEMSO and TOWER, 12wCDW, defined as a ≥ 1.0-point increase in Expanded Disease Severity Status Scale (EDSS) score from baseline (≥ 0.5 point when baseline was >5.5), was a key secondary endpoint. We assessed 12wCDW using both the original definition (OD) and the following exploratory definitions: D1: ≥ 1.5 points (baseline ≤ 5.5) or ≥ 0.5 point (baseline >5.5); D2: ≥ 2.0 points (baseline ≤ 5.5) or ≥ 0.5 point (baseline >5.5); D3: ≥ 2.0 points (baseline ≤ 5.5) or ≥ 1.0 point (baseline >5.5). Risk of 12wCDW was assessed using a Cox proportional hazards model.

Results: For the pooled TEMSO/TOWER dataset, risk of 12wCDW by OD was reduced for teriflunomide 14 mg (n=728) vs placebo (n=751): hazard ratio (HR) (95% confidence interval [CI]), 0.695 (0.542, 0.892), P=0.0037. The effect of teriflunomide was maintained using higher thresholds of EDSS increase (D1: HR 0.600 [95% CI 0.415, 0.868], P=0.0055; D2 and D3: HR 0.613 [95% CI 0.380, 0.988], P=0.0436).

Conclusion: Teriflunomide significantly reduced the risk of 12wCDW when more-stringent exploratory definitions were used. These observations are consistent with primary analyses in both studies and provide further insight into the positive impact of teriflunomide on disability worsening in patients with relapsing MS.

Disclosure: Study supported by Sanofi.

MS and related disorders 5

EPR2105

Decreased cerebrospinal fluid antioxidative capacity is associated with disease severity and progression in early Multiple Sclerosis (MS)

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Background and aims: Oxidative stress (OS) is a major feature of multiple sclerosis (MS) and promotes cell damage and neuronal death. The antioxidative capacity (AOC) acts as an important defence mechanism and may limit OS-induced toxic effects. An imbalance of OS and AOC may facilitate tissue damage in MS. Various OS species have been investigated so far; however, the role of AOC in MS remains inconclusive. We therefore aimed to compare AOC in serum and cerebrospinal fluid (CSF) between MS patients and controls, and assess its relation with clinical measures.

Methods: We included serum and CSF of 69 patients (clinically isolated syndrome (CIS)/MS) and 67 controls (other non-inflammatory neurological diseases) (Table 1). AOC was determined as the sample's ability to inhibit 2,2'-azobis(2-amidinopropane) dihydrochloride-induced oxidation of dihydrorhodamine. Clinical follow-up was available in all patients.

Table 1. Demographic and clinical data & AOC results

	CIS/MS n=56/13	Controls n=67	p-value
n Female	47 (68.1)	45 (67.2)	n.s.[a]
Age (years)	32.2 (26.6-39.8)	32.7 (25.2-44.9)	n.s.[b]
Disease duration (months)	0.5 (0.3-4.9)	N/A	
n CSF OCB positive	66 (95.7)	N/A	
EDSS	1.5 (0.0-3.0)	N/A	
n DMT	1 (1.4)	N/A	
Time FU (years)	4.3 (1.8-7.0)	N/A	
EDSS last FU (remission)	0.0 (0.0-1.5)	N/A	
n DMT last FU	34 (53.6)	N/A	
Serum AOC (%)	46.4 (41.3-49.9)	47.0 (43.0-50.0)	n.s.[b]
CSF AOC (%)	29.0 (19.6-40.8)	32.8 (23.0-41.4)	n.s.[b]

AOC=antioxidative capacity; *CSF*=cerebrospinal fluid; *CIS*=clinically isolated syndrome; *DMT*=disease modifying treatment; *EDSS*=Expanded Disability Status Scale; *FU*=follow-up; *MS*=multiple sclerosis; *n*=number of subjects; *N/A*=not applicable; **n.s.** = not significant; *OCB*=oligoclonal bands.
Unless otherwise indicated, data are given for time at sampling. Values are given as number (%) or as median (interquartile range). Significance (p<0.05) was assessed by chi-square test[a] or Mann-Whitney *U* test[b].

Table 1. Demographic and clinical data & AOC results

Results: AOC did not differ between CIS/MS patients and controls in serum and CSF, respectively. CSF AOC was lower in patients with active disease (clinical relapse ≤14 days before sampling, n=37) vs. non-active disease or controls (Figure 1), and correlated with Expanded Disability Status Scale at sampling (Figure 2). CIS patients who later converted to clinically definite MS (n=21) had lower CSF AOC compared to non-converters (p=0.01).

Figure 1. Lower CSF antioxidative capacity in clinical active MS
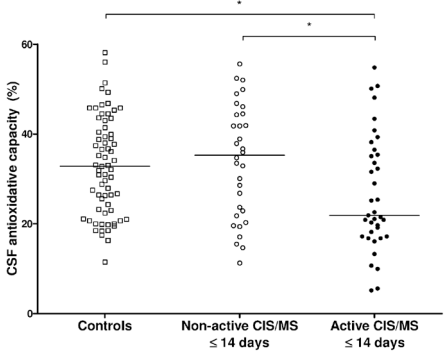
Cerebrospinal fluid (CSF) antioxidative capacity was significantly decreased in CIS/MS patients who were in an active state of disease (clinical relapse within 14 days prior to sampling) compared to non-active CIS/MS and controls. Significance was assessed by Kruskal-Wallis test and post-hoc Dunn's multiple comparison test. Horizontal bars indicate median values. * p<0.05.

Figure 1. Lower CSF antioxidative capacity in clinical active CIS/MS

Figure 2. Lower CSF antioxidative capacity correlated with EDSS
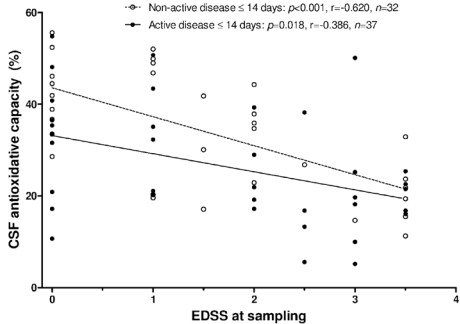
Cerebrospinal fluid (CSF) antioxidative capacity significantly correlated with patient's Expanded Disability Status Scale (EDSS) score at sampling (p<0.001, r=-0.492, n=69), also for patients with active disease (clinical relapse ≤ 14 days prior to sampling) and non-active patients separately. Significance was assessed by Spearman's Rank-Order Correlation. Linear regression lines are drawn for both subgroups.

Figure 2. Lower CSF antioxidative capacity correlated with EDSS

Conclusion: Decreased CSF AOC is associated with disease activity and progression in MS patients, and seems to be either a critical factor to counteract MS pathology, or reduced as a consequence of active or progressing disease. Further research is warranted towards the potential of AOC as a treatment target in MS.

EPR2106

Disability improvements in each functional system of the EDSS in active RRMS patients following treatment with alemtuzumab: results from CARE-MS I extension

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Background and aims: In treatment-naïve RRMS patients from CARE-MS I (NCT00530348), alemtuzumab (12mg/day, baseline: 5 days; 12 months later: 3 days) significantly improved clinical/MRI outcomes versus SC IFNB-1a over 2 years (y). Durable efficacy was demonstrated in a 4-years extension (NCT00930553). Alemtuzumab efficacy on disability improvement at the level of functional systems (FS) of the EDSS was assessed over 6 years.

Methods: Assessments: percentage achieving stable/improved EDSS scores ($\leq$0.5-point change/$\geq$1.0-point decrease from baseline [mean$\pm$SD, 2.0$\pm$0.8]), FS scores (0-point change/$\geq$1.0-point decrease from baseline FS score), and 6-month confirmed disability improvement (CDI; $\geq$1.0-point EDSS decrease confirmed over 6 months). Assessments in patients with 6-month CDI over 6 years (n=214): percentage with EDSS score (<4; $\geq$4); number of improved FS/patient; percentage with stable/improved FS scores.

Results: 349 patients enrolled in the extension; 321 (92%) completed Y6. At Y6, 81% showed stable/improved EDSS scores versus baseline, and 77%–88% showed stability/improvement across all FS. Through Y6, 34% achieved 6-month CDI; 100% of these patients had an EDSS score <4; 75% improved in >1 FS. Improvements occurred in each FS; most frequently in the sensory (45%), pyramidal (42%), and cerebellar (38%) FS.

Conclusion: At Y6, the majority (77%–88%) of alemtuzumab-treated patients showed stability/improvement across all FS. The robustness of these results is underscored by the high retention rate (92%) in the extension. Improvements were seen for each of the FS in patients with 6-month CDI, with 75% showing improvements in >1 FS, indicating a broad treatment effect with alemtuzumab in improving multiple aspects of disability.

EPR2107

Comparison of biodistribution following subcutaneous and intravenous administration of a novel Zirconium-89 labelled anti-CD20 antibody using imaging

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Background and aims: Anti-CD20 therapies have shown clinical efficacy in multiple sclerosis by acting on lymph node resident B-cells that facilitate autoimmune activation. We aim to investigate subcutaneous administration of a novel Zirconium-89 (89Zr) labelled anti-CD20 antibody, and to compare imaging and biodistribution data with that of intravenous administration in control mice.

Methods: Biodistribution of 89Zr-labelled anti-CD20 antibody was examined in healthy mice, following either an intravenous tail vein injection or a subcutaneous right lower flank injection. Biodistribution was assessed using positron emission tomography/computed tomography (PET-CT) and gamma counting of excised organs at early (4–24 hours) and later (72 hours to 7–10 days) time points.

Results: PET-CT data demonstrated that the proportion of 89Zr-anti-CD20 antibody remaining in the whole body at 7 days following intravenous injection (63±5%) is comparable to the proportion remaining following subcutaneous injection (55±4%). In gamma counting experiments at early time points following intravenous injection, the highest levels of 89Zr-anti-CD20 antibody were found in the circulation and in highly perfused organs, while following subcutaneous injection, the highest levels were found in inguinal lymph nodes and circulating blood (Table).

Organ	Mode of administration	Time-points		
		24 h	72 h	7 days
Blood	i.v.	17.0 ± 0.7	11.8 ± 0.7	6.3 ± 1.0
	s.c.	26.5 ± 3.6	24.7 ± 2.8	13.4 ± 0.8
Spleen	i.v.	24.8 ± 9.3	11.4 ± 1.3	28.8 ± 5.5
	s.c.	11.1 ± 1.6	21.4 ± 3.3	21.3 ± 1.2
Lymph nodes	i.v.	7.5 ± 0.5	11.6 ± 3.4	8.3 ± 2.0
	s.c.	25.4 ± 9.0	47.9 ± 0.5	26.8 ± 16.0

ID/g, injected dose per gram; i.v., intravenous; s.c., subcutaneous; SD, standard deviation

Comparison of intravenous and subcutaneous injections of the Zirconium-89 labelled anti-CD20 antibody biodistribution data (% ID/g [mean±SD]) from blood, spleen, and lymph nodes of healthy mice (n=3) using gamma counting

Conclusion: The route of administration affects the distribution of the 89Zr-anti-CD20 antibody. Subcutaneous administration results in effective absorption from the injection site and subsequent distribution preferentially to lymph nodes and to a lesser extent to the spleen as compared to the distribution following intravenous injection.

EPR2108

Estimated prevalence of secondary progressive Multiple Sclerosis in the USA and Europe: results from a systematic literature search

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Background and aims: The prevalence of secondary progressive multiple sclerosis (SPMS) has not been widely reported in the literature. We aimed to estimate its prevalence in the USA and EU-5 countries.

Methods: A systematic literature search was conducted using MEDLINE, Embase and the Cochrane Database of Systematic Reviews via the OVID platform to identify publications providing epidemiological data on SPMS. Studies published in English up to September 2017 that reported on the prevalence of multiple sclerosis (MS) or SPMS, or the proportion of patients with SPMS, were included. Articles duplicating data in later publications or from the same patient cohort were excluded. Prevalence per 100,000 people was estimated based on data within included publications and expressed as an unweighted average (range); when MS prevalence was not reported, other sources were used.

Results: In total, 96 of 3487 identified studies were included in the review. Of these, 22 (published 1997–2016) contained information to estimate the prevalence of SPMS in the USA (four studies) or EU-5 countries (18 studies across the UK, Germany, Italy, France, and Spain). The highest estimated prevalence was in the UK, then the USA, Germany, Italy, France, and Spain (Table). Moreover, two of these studies also reported proportion of patients with relapsing SPMS (Germany, 52.7%; France, 39.5%).

Country (Number of studies*)	Prevalence per 100,000 people, unweighted average (range)
UK (2)	57.8 (40.9–74.6)
USA (4)	37.1 (27.0–45.0)
Germany (3)	33.3 (13.1–60.8)
Italy (5)	26.2 (19.4–33.0)
France (1)	25.5 (NA)
Spain (7)	10.9 (2.8–16.7)

*Number of published studies containing information to estimate the prevalence of SPMS (by country)

NA, not applicable; S'MS, secondary progressive multiple sclerosis

Estimated prevalence of SPMS (in decreasing order) in the USA and EU-5 countries

Conclusion: There was wide variation in the estimated prevalence of SPMS within and across countries, and in the proportion of patients with relapsing SPMS. This may be because of differences in SPMS definition, study design or study duration, which should be explored in future studies.

Disclosure: This study was funded by Novartis Pharma AG, Basel, Switzerland. Vivek Khurana and Harsh Sharma are employees of Novartis Healthcare Pvt. Ltd., Hyderabad, India. Jennie Medin was an employee of Novartis Pharma AG, Basel, Switzerland during the conduct of the analysis.

EPR2109

The diagnosis of multiple sclerosis with markers of "better explanation": accuracy of the "central vein sign" in uncovering pathogenic mechansms different from inflammatory demyelination

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Background and aims: In systemic autoimmune diseases with neurological involvement, brain lesions are mainly and periarteriolar and micro-ischemic. In these diseases central vein sign (CVS) frequency in the white matter is lower than 50% (Maggi et al, in press).

In this study differences in the CVS frequency are analyzed in MS and in MS patients with clinical, laboratory or MRi markers of "better explanation" of the diagnosis (MS-plus) not fulfilling the criteria of another diagnosis.

Methods: Relapsing remitting MS (RRMS) patients or MS-plus were included and CVS frequency was evaluated by brain MRI with a T2* sequence. For identifying patients with MS, a treshold frequency below 50% of lesions with the CVS (the 50% rule) was selected for excluding MS, as previously described (Maggi et al, in press).

Results: Patients recruited: 30 definite MS; 34 MS-plus. The CVS frequency was higher in MS than in the MS-plus: 91% vs 17.5% (p< 0.0001). A CVS frequency not fulfilling the 50% rule, was observed in 100% the MS and in 40% of the MS-plus patients (p< 0.0001). In most of the MS-plus patients above the 50% rule, the CVS frequency was 70-83%, within the range of the definite MS. The most frequent red flags observed in the MS-plus fulfilling the 50% rule, were normal CSF exam and presence of serum autoantibodies.

Conclusion: The low frequency of the CVS observed in most of the MS-plus suggests a non inflammatory-demyelinating underlying pathology. CVS seems a useful marker for increasing the accuracy of the MS diagnostic criteria.

Disclosure: Nothing to disclose

EPR2110

Patient-centred approach in monitoring Dimethyl-Fumarate: data from a real-life experience

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Background and aims: The most frequent side effects (SEs) of Dimethyl-Fumarate (DMF) include flushing and gastrointestinal events (GI). We investigated about the safety issues in a cohort of 120 Relapsing Multiple Sclerosis (RMS) patients treated with DMF 120 mg BID for 7 days (standard titration) or for 2-4 weeks (slower titration), and then increased to 240 mg BID.

Methods: At the time of DMF first prescription, anthropometric measures were assessed. Any SEs were reported immediately upon the occurrence or during the scheduled follow-up.

Results: The observation period was 10.3±5 months. The mean Body Mass Index (BMI) was 23.6±4.38. In our cohort 45% of patients experienced GI and 66.1% flushing. We found a direct correlation between female sex and SEs (r=0.17; p =0.029): GI (r=0.22, p =0.004), nausea/ vomiting (r =0.18, p =0.024), and flushing (r= 0.2; p= 0.011). Multivariate analysis confirmed that male sex was a protective factor against GI (p=0.035; OR=0.287; 95% CI=0.9-0.941) and flushing (p= 0.004; OR= 0.42; 95% CI =0.05-0.365). Stratifying patients according to their "weight category", we found that normal-weight patients (18.5 <BMI <24.99) had higher incidence of AEs (p=0.044), especially GI (p=0.023). A slower titration did not influenced SEs, but among patients with standard titration, a higher BMI was a protective factor for GI (p= 0.003).

Conclusion: Clinicians should evaluate demographic and anthropometric characteristics of MS patients in order to optimize tolerability during MS therapies.

Disclosure: Dr. Paolicelli received honoraria for consultancy and/or speaking from Biogen Idec, Merck-Serono, Almirall, Sanofi-Aventis, TEVA, Novartis and Genzyme. Dr. Manni, Dr. Iaffaldano A, Dr.D'Onghia, Dr. Zoccolella and Dr. Felica have declared that no competing interests exist. Dr. Iaffaldano P. has served on scientific advisory boards for Biogen Idec and Bayer, and has received funding for travel and/or speaker honoraria from Genzyme, Sanofi-Aventis, Biogen Idec, Teva and Novartis. Dr. Trojano received honoraria for consultancy or speaking from Biogen, SanofiAventis, Merck Serono, Novartis, Genzyme, TEVA, and Bayer-Schering and research grants from Merck Serono, Biogen, and Novartis.

EPR2111

A post-marketing observational monocentric study of efficacy and tolerability of Dimethyl fumarate

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Background and aims: Dimethyl fumarate-DMF is a novel oral therapy for multiple sclerosis. Pivotal studies demonstrated a promising clinical and neuroradiological efficacy of DMF but there are still few reports in real life setting.

Methods: Analysis of intention-to-treat was conducted on 298 patients with a follow-up (FU) of at least 24 months; their basal characteristics are shown in Table1. 18% were naïve, 70% switch from 1°line therapy for inefficacy or intolerance, 12% switch from 2°line therapy. All patients had a brain MRI at DMF initiation and once a year and a neurological examination every 3 months. 76 (25.5%) patients discontinued DMF: 10.1% for disease activity, 10.8% for adverse events (shown in Table2) 3.4% for pregnancy, 1.3% for patient's decision.

Table 1. Basal characteristics of 298 pts	
Sex	68,8%F F:M=3:1
Mean age at DMF start	37,41 (18,15 - 64,39)
Disease duration at DMF start	10,3 (0,04 − 42,18)
Mean n° of tretaments	1,63 (0 − 6)
IS	16,1% yes
Mean of relapses in the last year	0,5 (0 − 3)
Median EDSS	1,5 (0 − 7,5)
Mean of new T2 lesions in the last year	0,9 (0 − 18)
Mean of Gd+ lesions at basal RM	0,3 (0 − 7)

Table 2. Discontinuation for adverse events	
Flushing	N=2 (0,7%)
GI effects	N=11 (3,7%)
Lymphopenia	N=15 (5%)
Liver enzyme elevation	N=3 (1%)
Allergic reaction	N=1 (0,34%)

Results: After 2 years of FU 61% had NEDA-3. Mean ARR was 0.09 (Wilcoxon; p<0.001) and mean of new T2 lesions was 0.404 (Wilcoxon; p<0.001). ARR and MRI activity were also significantly reduced in subgroups. The analysis of ARR and MRI activity in naïve patients could be biased by higher ARR and MRI activity before DMF. Mild gastrointestinal and flushing symptoms were reported within 12 months in the 9.1% and 32.2% of patients respectively while at 24 months frequency was reduced to 6.04% and 23.5%. Since January 2016 we adopted a slower DMF titration schedule and we noticed a lower rate of drug

discontinuation. Lymphopenia of different grades occurred in 17.4% of patients at 12 months and 6.4% at 24 months of FU.

Conclusion: Our data confirm the efficacy of DMF as 1°line treatment and its good tolerability

Disclosure: I received honoraria for speaking and consultancy activity from: Biogen-Idec Merck-Serono Sanofi-Genzyme Novartis TEVA

EPR2112

Prognostic value of serum neurofilaments in patients with clinically isolated syndromes

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Background and aims: MS is a leading cause of youth disability and axonal damage occurs since the early phases of disease. The aim of this study was to evaluate serum neurofilament light chains (Nfls) in patients with Clinically Isolated Syndromes (CIS) and their prognostic value for the development of Clinically Defined Multiple Sclerosis (CDMS) and McDonald 2017 MS (2017MS).

Methods: We evaluated baseline serum Nfls as well as clinical, MRI, and CSF data on 222 CIS patients (mean follow-up 100.6 months) hospitalised from 2000 to 2015 at San Raffaele Hospital, Italy.

Results: At 2 years 45 patients (20%) developed CDMS and 141 patients (63.5%) developed 2017MS. Serum Nfls (median 22.0, IQR 11.6-40.4 pg/ml) and CSF Nfls (median 839, IQR, 387–1647 pg/ml) were highly correlated (r=0.58, p<0.001). Nfls were significantly higher in patients with a recent relapse, high T2 lesion load and Gd enhancing lesion at baseline MRI. Serum Nfls were prognostic both for CDMS and 2017MS, with a 3-fold and a 2-fold decrease of CDMS and 2017MS risk respectively in patients with very low and low Nfl levels. The results were unaltered following adjustment for known MS prognostic factors. Nfls were associated with baseline disability by the EDSS but not with disability worsening in the follow-up.

Conclusion: Serum Nfl levels have prognostic value for conversion to MS in CIS patients. Nfls may have a dual role as biomarkers in MS, with measured peak levels being a quantitative marker of acute inflammatory activity, while steady state levels reflecting chronic inflammatory and neurodegenerative processes

Disclosure: Nothing to disclose

MS and related disorders 6

EPR2113

Efficacy of cladribine tablets 3.5mg/kg added to interferon-beta in patients with SPMS or relapsing-RRMS: a post-hoc analysis from ONWARD

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Background and aims: In the CLARITY study, treatment with cladribine tablets 3.5mg/kg (CT3.5) significantly improved clinical outcomes vs. placebo in patients with RRMS. The ONWARD study showed similar benefits for CT3.5 administered as add-on therapy to interferon-beta (IFN-beta) in patients with SPMS or RRMS.

Methods: ONWARD was a 2-year, randomised, double-blind study in patients aged 18–65 years, with EDSS scores 1.0–5.5, who experienced ≥1 relapse during the 48 weeks prior to the study while receiving IFN-beta therapy. At baseline, there were 26 patients with SPMS (placebo+IFN-beta, N=9; CT3.5+IFN-beta, N=17) and 171 with RRMS. The effect of treatment with CT3.5 on key outcomes during ONWARD was examined in the SPMS and RRMS subgroups in this post hoc analysis.

Results: At baseline, there were no clinical differences in relapses in the prior year between the subgroups. Mean EDSS was higher in the SPMS vs. the RRMS subgroup. CT3.5 demonstrated a significant reduction in ARR vs. placebo in both subgroups: 89% and 50% for SPMS and RRMS respectively (Figures 1 and 2). Time to 3- and 6-month confirmed EDSS progression was not significantly different in either subgroup. Treatment with CT3.5 was associated with reductions in mean numbers of T1 Gd+ and T2 lesions vs. placebo in both RRMS and SPMS subgroups.
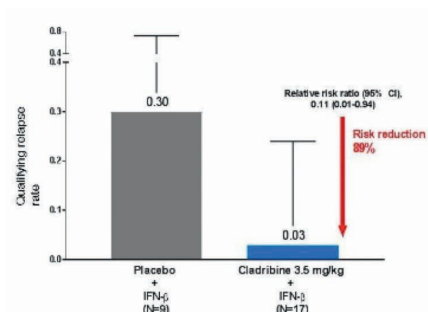
Figure 1: Qualifying relapse rate (annualised, adjusted) in patients with SPMS treated with cladribine tablets 3.5 mg/kg + IFN-beta or placebo + IFN-beta in ONWARD
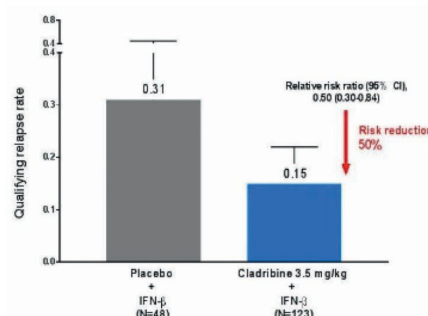
Figure 2: Qualifying relapse rate (annualised, adjusted) in patients with RRMS treated with cladribine tablets 3.5 mg/kg + IFN-beta or placebo + IFN-beta in ONWARD

Conclusion: Despite limitations due to the very low number of SPMS patients, the available data indicate that CT3.5 mg/kg administered with IFN-beta showed evidence of increased efficacy in patients with SPMS and RRMS in the ONWARD study compared to placebo+IFN-beta.

Disclosure: This study was sponsored by EMD Serono Inc, a business of Merck KGaA, Darmstadt, Germany (in the USA), and Merck Serono SA, Geneva, an affiliate of Merck KGaA Darmstadt, Germany (ROW).

EPR2114

Screening for transcription factor binding inside the 200 non-MHC MS susceptibility regions

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Background and aims: In the last decade, genome wide association studies (GWAS) have broadened our understanding of multiple sclerosis (MS) genetic background. The recent MS genomic map has expanded the number of known susceptibility variants outside the major histocompatibility complex (MHC) to about 200. Given the more detailed knowledge of MS genetic architecture, we aimed at defining common upstream regulators by screening for transcription factor (TF) binding inside disease susceptibility regions.

Methods: Non-MHC variants were obtained from the latest MS genomic map. MS regions were defined as the genomic intervals of +/-50 kb around each variant. Experimental data of TF binding (ChIP-seq tracks) in GM12878 cell line were extracted from ENCODE. We analyzed ChIP-seq data against MS regions using Genomic HyperBrowser (http://hyperbrowser.uio.no/hb/). Significant TF were those with a similarity score between TF binding track and MS track>5 as measured by the Forbes coefficient:ratio of observed versus expected overlap, and p-value<0.05.

Pathway analysis on significant TFs was performed using Panther.

Results: NFkB emerged as the main TF binding to MS regions, thus potentially regulating multiple disease susceptibility loci. Other factors include P300, STAT3, STAT5A, NFATC1. The complete list of TFs with Forbes coefficient>5 is presented in Figure1. Panther analysis showed that significant TFs were preferentially involved in immune processes, WNT and JAK-STAT signaling and gonadotropin releasing hormone receptor pathways (Figure2).

Rank	TF	Similarity to MS track	P-value	Overlap between MS and TF binding track (bps)	Genome coverage of TF binding track (bps)
1	NFKB	7.1	0.0196	244676	5581526
2	p300	6.32	0.0196	54038	1384960
3	IKZF1	6.24	0.0196	187456	4861605
4	CEBPB	6.05	0.0196	105571	2826832
5	CHD1	5.51	0.0196	95183	2794092
6	STAT3	5.45	0.0196	88321	2620701
7	WHIP	5.44	0.0196	186585	5546448
8	TBLR1	5.44	0.0196	185993	5538829
9	POL2	5.39	0.0196	379845	11407040
10	MAX	5.35	0.0196	9567	289491
11	BCL11A	5.23	0.0196	146060	4518044
12	STAT5A	5.23	0.0196	125087	3872056
13	MTA3	5.15	0.0196	202361	6360004
14	BHLHE40	5.15	0.0196	141896	4459874
15	YY1	5.1	0.0196	26240	833452
16	CDP	5.09	0.0196	414850	13197610
17	FOXM1	5.02	0.0196	314243	10133142
18	BCL3	5.01	0.0196	153385	4954966
19	NFATC1	5	0.0196	168288	5446547

Significant TF binding tracks overlapping with MS regions (Forbes coefficient>5, p-value<0.05)

Conclusion: MS susceptibility regions are targeted by NFkB and other TFs involved in immune-related pathways. The precise identification of upstream regulators could help better define how MS loci are functionally interconnected in disease-specific networks.

Disclosure: Nothing to disclose

EPR2115

Cesarean delivery and artificial lactation are associated with an earlier age of disease onset in Multiple Sclerosis

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Background and aims: Age at onset (AAO) in multiple sclerosis (MS) is an important marker of disease severity and may have prognostic significance. Understanding what factors can influence AAO may shed light on the etiology of this complex disease, and have applications in the diagnostic process.
Methods: The study cohort consists of 2055 eligible patients followed-up prospectively at San Raffaele Hospital. AAO was defined as the year of the first symptom suggestive of inflammatory central nervous system demyelination. Predictors of AAO were evaluated by linear regression.
Results: In our cohort of patients, the mean age at onset of MS was 28.4 years (SD 8.4 years), and the female:male ratio was 2.2:1. A significant percentage of patients (225 patients, 10.9%) were born from a cesarean delivery, and most of them (1230 patients, 59.9%) received maternal breastfeeding, while the remaining received artificial lactation. Compared with those born from a natural delivery, onset of symptoms was 5.2 years earlier for those with cesarean delivery (p<0.001). Also, artificial lactation was associated with an earlier diagnosis (-2.2 years earlier) compared to patients who had been breastfed, in which the duration of the breastfeeding period was directly associated with the age of onset of MS.
Conclusion: An earlier AAO in MS patients born from a cesarean delivery and receiving artificial lactation was observed, and the results suggest that environmental factors which act at the population level may significantly influence disease severity characteristics in genetically susceptible populations.
Disclosure: Marzia Romeo – Received honoraria from Genzyme Gloria Dalla Costa – Reports no disclosures Francesca Sangalli – Reports no disclosures Bruno Colombo – Received honoraria from Biogen Idec, Genzyme e Merck Serono Lucia Moiola – Received honoraria from Sanofi-Genzyme, Biogen Idec, TEVA, Merck Serono and Novartis Marta Radaelli – Received honoraria from TEVA and Genzyme Federica Esposito – Received honoraria from TEVA, Almirall e Genzyme Giancarlo Comi – Received honoraria from Novartis, Teva, Sanofi-Genzyme, Merck Serono, Biogen Idec, Excemed, Roche, Almirall, Chugai, Receptos, Forward Pharma Vittorio Martinelli – received honoraria from Genzyme, Biogen Idec, TEVA, Bayer, Merck Serono and Novartis

EPR2116

No evidence of disease activity achievement over 4 years of peginterferon beta-1a treatment in newly diagnosed patients with relapsing Multiple Sclerosis: subgroup analyses of ADVANCE/ATTAIN

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Background and aims: In the phase-3 ADVANCE study year (Y) 1, relapsing MS (RMS) patients were randomized 1:1:1 to placebo or peginterferon beta-1a every 2 weeks or every 4 weeks; for Y2, placebo patients were re-randomised to peginterferon beta-1a every 2 or 4 weeks. ADVANCE completers entering the ATTAIN extension study (Y3-4) maintained their ADVANCE Y2 dosing regimen. This analysis evaluated attainment of no evidence of disease activity (NEDA) over 4 years in Newly Diagnosed (ND) patients from ADVANCE who continued into ATTAIN.
Methods: The proportion of patients treated with peginterferon beta-1a every 2 weeks in the ATTAIN intent-to-treat population who achieved overall NEDA (no relapses, 24-week confirmed disability worsening, gadolinium-enhancing lesions, or new/newly enlarging T2 lesions) was evaluated over 4 years in ND (diagnosed ≤1 year prior to enrolment and disease-modifying therapy naïve, n=343) and Non–Newly Diagnosed (NND, n=379) subgroups. Annualised relapse rate (ARR) during ATTAIN was analysed based on ADVANCE 2-year NEDA status.
Results: In ADVANCE Y1, both ND and NND patients treated with peginterferon beta-1a every 2 weeks were significantly more likely to achieve NEDA compared to placebo (Table). In Y2–4, yearly NEDA remained consistent for both subgroups. Patients who achieved NEDA in ADVANCE had lower ARR during ATTAIN than non-NEDA patients (ND: 0.057 vs 0.211, P=0.0003; NND: 0.073 vs 0.237, P=0.0001).

Table. Proportion of patients achieving NEDA in the overall population and ND and NND subgroups

% of patients with overall NEDA [total N]	ND		NND		Overall	
	Placebo	Peginterferon beta-1a every 2 weeks	Placebo	Peginterferon beta-1a every 2 weeks	Placebo	Peginterferon beta-1a every 2 weeks
Year 1	13 (53)	24 (116)	14 (76)	46 (124)	14 (264)	34 (743)
		P=0.0010		P=0.003		P=0.003
Year 2	–	55.0 (120)	–	54.5 (94)	–	54.7 (219)
Year 3	–	56.0 (116)	–	57.1 (79)	–	56.5 (179)
Year 4	–	55.0 (132)	–	54.4 (94)	–	55.7 (281)

Conclusion: Both ND and NND patients treated with continuous peginterferon beta-1a every 2 weeks exhibited sustained yearly NEDA rates over 4 years. NEDA achievement in the first 2 years predicted positive long-term clinical outcomes.
Disclosure: This study was supported by Biogen. DLA: equity interest in NeuroRx during the conduct of the study; personal fees from Acorda, Biogen, EMD Serono, Genentech, Genzyme, Hoffman-La Roche, Innate Immunotherapy, MedImmhune, Mitsubishi, Novartis, Receptos, Sanofi, and Teva outside the submitted work; grants from Biogen and Novartis. MLN, JY: employees of and may hold stock and/or stock options in Biogen.

EPR2117

Modulation of cortico-subcortical functional connectivity occurs after symptomatic treatment of fatigue in patients with Multiple Sclerosis

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Background and aims: To investigate longitudinal changes of brain resting state (RS) functional connectivity (FC) in multiple sclerosis (MS) patients with fatigue undergoing different symptomatic treatments for this symptom.

Methods: 45 fatigued MS patients were randomly, blindly assigned to treatment with fampridine (n=15), amantadine (n=15) or placebo (n=15) and underwent clinical, neuropsychological and RS fMRI at baseline (T0) and after four weeks (W4) of treatment. 15 matched healthy controls were acquired twice. RS FC analysis of the main brain functional networks was performed using independent component analysis and SPM12.

Results: At T0, compared with controls, MS patients showed increased intra-thalamic RS FC and abnormal fronto-parietal RS FC of several cortical networks. At W4, decreased global, physical and cognitive (p=0.001/0.003/0.01) modified fatigue impact scale (MFIS) scores were found in fampridine patients and, to a lesser extent, in amantadine patients (p=0.04). Placebo patients also showed improved global, physical and psychosocial MFIS (p=0.02/0.01/0.02). At W4, fampridine patients showed increased RS FC of the bilateral precuneus in the default mode and executive control networks, and increased RS FC of the right inferior frontal gyrus in the salience and frontoparietal attention networks. At W4, increased RS FC in frontal regions and decreased RS FC in temporoparietal regions were detected in placebo and amantadine patients. A significant decrease over time of intrathalamic RS FC was found in fampridine and amantadine patients.

Conclusion: Treatment with fampridine (and, to a lesser extent, with amantadine) ameliorates fatigue in MS. Concomitant modifications of RS FC suggest an improved regulation of cortico-subcortical circuits.

EPR2118

Patterns of regional gray matter and white matter atrophy in patients starting fingolimod or natalizumab: a 2-year tensor-based morphometry study

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Background and aims: To compare the effects of fingolimod (FTY) and natalizumab (NAT) on preventing regional gray matter (GM) and white matter (WM) atrophy in relapsing-remitting multiple sclerosis (RRMS) after two years of treatment.

Methods: 55 RRMS patients starting FTY (n=25) or NAT (n=30) underwent 3T brain scans at baseline (T0), month-6 (M6), year-1 (Y1) and year-2 (Y2). The longitudinal patterns of regional GM/WM volume changes were assessed using tensor-based morphometry (SPM12, p<0.05, FWE-corrected).

Results: At T0, no between-group volumetric difference was found. At M6 vs T0, FTY-patients experienced GM atrophy of bilateral cerebellar cortex and hippocampi, right thalamus and cingulate cortex. At Y1 vs M6 and Y2 vs Y1, a further atrophy of bilateral cerebellar cortex, left thalamus, several fronto-temporo-occipito-parietal regions, and cingulate cortex occurred in FTY-patients. NAT-patients showed a significant atrophy of left cingulate cortex and thalamus and bilateral fronto-temporo-parietal regions only at Y2 vs Y1. At M6 vs T0, both groups showed a significant atrophy in supratentorial WM clusters, while cerebellar WM volume loss occurred in FTY-patients only. At Y1 vs M6 and Y2 vs Y1, supratentorial WM atrophy progressed in both groups, while cerebellar WM atrophy occurred in FTY-patients. Compared to NAT-patients, FTY-patients showed only a significant cerebellar cortical and WM atrophy at M6 vs T0.

Conclusion: The anti-inflammatory effects of NAT and the pleiotropic effects of FTY on the immune system and in the central nervous system differently modified GM/WM atrophy progression in RRMS patients, with NAT having a more significant effect on preventing regional atrophy.

Disclosure: Nothing to disclose

EPR2119

Is it possible to continue a really effective therapy in a patient with a severe hypersensitivity drug reaction?

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Background and aims: Alemtuzumab (ALEM) is a highly effective monoclonal anti-CD52 antibody approved for patients with active multiple sclerosis (MS). The most common ALEM's adverse events (AE) are infusion reactions (IRs). Three out of 100 IRs are severe and contraindicate treatment prosecution with the traditional schedule.

Methods: A case report

Results: A 45-year-old female, diagnosed with MS in 1998, was treated with several therapies, but only had a complete response to natalizumab. However, natalizumab had been discontinued for a high progressive multifocal leucoencephalopathy risk. After last treatment failure with fingolimod, she was started on ALEM without any AE and with an optimal clinical and neuroradiological response. However, one year later, while she was receiving her second infusion, she suddenly developed severe hypotension, cough, dysphagia and diffuse urticaria/angioedema. She was then treated with intravenous corticosteroids, antihistamines and fluids. Four months later, 1:1000 intradermal tests with ALEM were strongly positive at 20' reading. A diagnosis of IgE-mediated anaphylaxis to ALEM was then confirmed. Since no other effective alternatives were available to treat her MS, ALEM was infused following Castells' desensitization protocol. No mild or severe AE were observed. The treatment was effective with regard to disease activity and quality of life improvement.

Conclusion: This is the first case of ALEM-desensitisation in a MS patient. This procedure allowed a safe administration of the only effective treatment for this highly active patient, despite her previous severe IR to the drug. Desensitisation is a crucial procedure to induce temporary drug tolerance, when no effective alternatives are available.

Neurogenetics 2

EPR2121

European expert consensus recommendations for neurological therapeutic goals for patients with Fabry disease

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Background and aims: In Fabry disease, a hereditary lysosomal storage disease, alpha-galactosidase A deficiency causes globotriaosylceramide accumulation in various organs, significantly reducing life expectancy. Enzyme replacement therapy (ERT) ameliorates symptoms of Fabry disease and slows or reduces organ damage. Cerebrovascular complications (ischaemic stroke, chronic white matter hyperintensities [CWMH]), peripheral neuropathy (predominantly due to small-fibre involvement), and neuropathic pain are the major neurological symptoms. Achieving evidence-based therapeutic goals, individualised to patient characteristics and disease status, can facilitate effective patient management. We formulated consensus recommendations based on expected and achievable responses to ERT and adjunctive therapies administered for neurological disease complications.

Methods: An international multidisciplinary team of 26 experts developed neurological therapeutic goals for Fabry disease based on consensus opinion and evidence obtained from a PRISMA-compliant systematic analysis of literature on ERT published through January 2017.

Results: ERT can be effective in slowing the progression of CWMH and managing neuropathic pain. Amelioration of neuropathy and pain using ERT has been demonstrated in studies utilizing the Total Symptom Score, the Mainz Severity Scale Index, or the Brief Pain Inventory scale. There is also evidence that a higher dose of ERT leads to more substantial pain improvement. We recommend initiating ERT upon pain onset to alleviate pain and to slow CWMH progression. Secondary stroke prevention might reduce the risk of stroke recurrence.

Conclusion: Timely initiation and appropriate dosage of ERT and adjunctive therapies, i.e. personalised and outcome-oriented medicine for patients with Fabry disease, facilitates the achievement of therapeutic neurological goals (Table).

Patient subgroup	Treatment goals
Neuropathic pain due to small-fibre involvement	
Early-stage disease	• Reduce intensity of pain and frequency of pain crises • Slow or stop progression of polyneuropathy
Late-stage disease	• Reduce pain to manageable levels • Slow or stop progression of polyneuropathy
Paediatric patients	• Reduce intensity of pain and frequency of pain crises
Pain due to entrapment neuropathy (large-fibre involvement)	
All patients	• Reduce intensity of pain and manage pain due to nerve compression/entrapment (e.g. carpal tunnel syndrome)
Transient ischaemic attack (TIA)/stroke	
All patients	• Prevent occurrence/recurrence of TIA/stroke and delay age at onset of first TIA/stroke event
CWMH	
Early-stage disease	• Attempt to avoid development of CWMH
Late-stage disease	• Delay progression of number and volume of CWMH

Therapeutic neurological goals in patients with Fabry disease.

EPR2122

The neuropsychological phenotype of CACNA1A disorders: a retrospective cohort analysis

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Background and aims: The CACNA1A gene encodes the α1-subunit of the neuronal calcium channel P/Q. Autosomal dominant CACNA1A mutations underlie three allelic disorders: familial hemiplegic migraine type 1 (FHM1), episodic ataxia type 2 (EA2) and spinocerebellar ataxia type 6 (SCA6). The main clinical features are migraine with hemiplegic aura in FHM1, paroxysmal attacks of ataxia in EA2 and progressive cerebellar ataxia in SCA6. Several case reports suggest that also cognitive and behavioral features belong to the phenotype of CACNA1A disorders, but studies on large case series are lacking.

Methods: Genetically confirmed CACNA1A cases were identified from the database of our Ataxia Unit. Findings from neuropsychological examination, history of psychiatric comorbidities, developmental delay and poor school performance were retrieved through retrospective chart review.

Results: 44 CACNA1A cases were identified. Neuropsychological testing was available in 25 of them (11 FHM1, 10 EA2, 4 SCA6). Diffuse cognitive deficits were documented in 23 cases (92%). Impairments were more evident in figural memory (82,6%, 19/25), visuo-constructive abilities (75%, 16/24), executive functions (100%, 17/17) and attention (68,4% 13/19). Two SCA6 patients had normal neuropsychological tests. Delayed psychomotor milestones were recalled in 8 patients (5 FHM1, 3 EA2). Poor school performance was reported in 8 cases (3 FHM1 and 5 EA2). Psychiatric comorbidities were diagnosed in 8 patients (2 FHM1, 6 EA2).

Conclusion: Diffuse cognitive deficits were documented in our CACNA1A cohort, as well as a high prevalence of developmental delay and psychiatric symptoms. FHM1 and EA2 cases exhibited a neuropsychiatric phenotype while SCA6 patients did not have this comorbidity.

Disclosure: Nothing to disclose

EPR2123

Is it muscle or nerve? - Novel heterozygous variant c.3542G>A; p. Ser1181Asn in POLG explaining a mixed neuro-myopathic phenotype

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Background and aims: Pathogenic variants in POLG can cause a broad variety of central and peripheral nerve symptoms. In one family, we report the novel variant c.3542G>A; p.Ser1181Asn putatively causing a mixed neuro-myopathic phenotype.

Methods: The patients were followed-up at the neuromuscular outpatient clinic of the RWTH Aachen University. An NGS-based diagnostic multigene panel provided by the CeGaT GmbH was analysed in the index patient, a further co-segregation was performed in one unaffected and two affected sisters as well as in the affected father.

Results: With an adolescent onset, the index patient (55) presented with an advanced distal tetraparesis, corresponding atrophies and sensory loss, afferent ataxia, double vision, and a slight bilateral ptosis. One sister (57) showed a Charcot-Marie-Tooth resembling phenotype with calf atrophies and pedes cavi, likewise. A second sister (51) as well as the father (80) predominantly reported exercise-induced muscle pain and proximal weakness. Muscle biopsies obtained from the father and the first mentioned sister showed ragged-red fibers indicating mitochondrial damage. All affected family members were heterozygous for the yet undescribed variant c.3542G>A; p.Ser1181Asn in POLG, whereas an unaffected sister had two wild-type alleles. The mutation spectrum of POLG contains several known pathogenic variants in the vicinity of c.3542G>A; p.Ser1181Asn. The amino acid position is highly conserved lying within the palm-domain. In-silico predictions were indicative for pathogenicity. The allele frequency of 0.02% is compatible with an autosomal dominant inheritance.

Fig 1: Genotype and phenotype in one family with the heterozygous variant c.3542G>A; p.Ser1181Asn in POLG
A: Pedigree. All affected family members are denoted in black; the index patient is indicated by an arrow. B: A mixed neuropathy and myopathy phenotype; the lines affected ankles (ego orders, oldest sister on the left, youngest sister on the right of the bench).
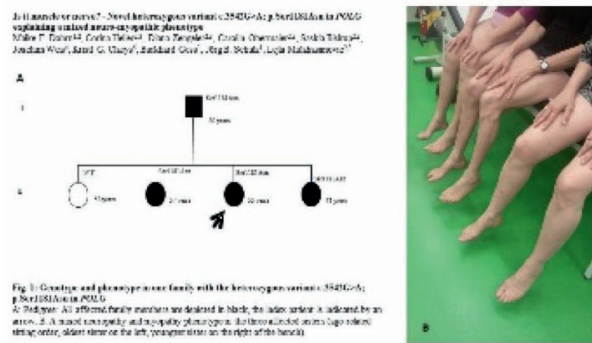
Figure 1: Genotype and phenotype in one family with the heterozygous variant c.3542G>A; p.Ser1181Asn in POLG

Conclusion: The novel heterozygous variant c.3542G>A; p.Ser1181Asn in POLG is likely pathogenic explaining a neuro-myopathic phenotype.
Disclosure: Nothing to disclose

EPR2124

Neurological variants of ataxia telangiectasia - clinical and genetic features

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Background and aims: Variant Ataxia-Telangiectasia is a rare autosomal recessive disorder with a milder phenotype compared to the classic form. Here, we describe the clinical features of the largest cohort of individuals with variant Ataxia-Telangiectasia to date and explore genotype-phenotype correlations.
Methods: Cross-sectional clinical data were retrospectively collected for individuals who have attended the National UK and Dutch Ataxia-Telangiectasia clinics. Patients were classified as variant Ataxia-Telangiectasia based on mutarions with retained ATM kinase activity, or mutations in the initiator methionine codon.
Results: The study includes 57 individuals from 50 families. Mean age at assessment was 37.5 years. Most individuals had their first symptoms by age ten (81%).

There was a diagnostic delay of more than 10 years in 68% and more than 20 years in a third of probands.
Three neurological phenotypes were observed, where only a third of included individuals had predominant ataxia and ten probands (18%) a pure extrapyramidal presentation. Individuals with extrapyramidal presentations had milder neurological disease severity. There were no significant respiratory or immunological complications, but fourteen individuals had a history of malignancy.
The presence of missense mutations was associated with milder neurological disease severity and a higher risk of malignancy.
Conclusion: Individuals with variant ataxia atelangiectasia require malignancy surveillance and tailored management. However, our data suggest that the condition is often mis or underdiagnosed. This is likely due to atypical clinical features (including mild severity, exclusive extrapyramidal symptoms, normal eye movements, absent ocular telangiectasia and normal AFP levels) in some individuals, which clinicians may not be aware of.
Disclosure: Nothing to disclose

EPR2125

A study on combined brain positron Emission Tomography (PET) – Magnetic Resonance Imaging (MRI) using Fluorodeoxyglucose (18FDG) (FDG-PET/MRI) in premanifest Huntington's disease gene-expansion carriers

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Background and aims: Huntington's disease (HD) is an autosomal dominantly inherited neurodegenerative disorder, caused by an expansion of a trinucleotide (CAG) repeat in the huntingtin gene. There is no cure and only sparse symptomatic treatment. Structural brain imaging is the most applied and well documented technique to demonstrate longitudinal structural changes in premanifest and manifest HD gene-expansion carriers. Changes in the striatum are registered as far as 15 years before symptom onset with MRI. PET studies have found hypometabolism in the Caudate nucleus, Putamen and the temporal and frontal cortex years before clinical diagnosis along with hypermetabolism in Thalamus prior to symptom onset. By a combined brain PET–MRI using FDG, we wished to simultaneously characterise the structural and metabolic brain changes in premanifest HD gene-expansion carriers.

Methods: We recruited 22 premanifest HD gene-expansion carriers and 17 controls from the Neurogenetics Clinic, Danish Dementia Research Centre, Rigshospitalet, Copenhagen, Denmark. We included individuals with a CAG repeat ≥39 and a Unified Huntingtin's Disease Rating scale-99 total motor score ≤5.

Results: We found significantly reduced volumes of the Putamen bilaterally and the Globus Pallidus in the right hemisphere. Further we found significantly reduced metabolism in the Putamen bilaterally with a significant correlation between CAG age product and the FDG activity which, however, disappeared when correcting for the reduced volume of Putamen.

Conclusion: Our results indicate that the hypometabolism and atrophy of Putamen are evolving simultaneously.

A follow-up study on the cohort will shed more light on the sequential evolution and correlation of structural and metabolic changes.

Disclosure: Nothing to disclose

EPR2126

Cerebral creatine deficiency syndromes: a single-centre experience from diagnosis to treatment

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Background and aims: Cerebral creatine deficiency syndromes (CCDS) are a group of inborn errors of metabolism caused by deficiencies of the creatine transporter SLC6A8 or the enzymes L-arginine:glycine amidinotransferase and guanidinoacetate methyltransferase (GAMT). Typical clinical findings comprise intellectual disability, seizures and movement disorders. Diagnostic workup includes brain MR spectroscopy (MRS) and urinary measurements of guanidinoacetate (GAA), creatine and creatinine. Early creatine supplementation can stabilize symptoms and improve outcome. The aim of this study was to characterize a group of patients with GAMT deficiency regarding clinical, MRS and biochemical findings, as well as treatment response.

Methods: Retrospective review of the medical records of patients with GAMT deficiency followed in our Metabolic Disorders consultation.

Results: We present 7 patients with a mean age of 25 years (9-34) and mean age at onset of 22 months (6-36), with an adult age diagnosis in 2 patients. All patients presented with developmental delay, usually moderate and involving language. Epilepsy was present in 6 patients. Three patients developed behavioural disorders later during childhood. All patients presented low creatine peak in brain MRS and elevated GAA (30-75 times higher than reference values) with low creatine values and normal creatine/creatinine ratio in urine. Creatine supplementation was started in every patient, with clinical stabilisation and normalisation of creatine peak in MRS.

Conclusion: Our patients demonstrate the typical clinical presentation of CCDS. Despite pediatric onset, CCDS sometimes remain undiagnosed until adult age. Since supplementation usually presents good results, neurologists must recognise CCDS and perform an early diagnostic workup with brain MRS and urinary biochemical studies.

Disclosure: Nothing to disclose

EPR2127

L-2-hydroxyglutaric aciduria in a young Greek female with mild mental retardness, pyramidal semiology and ataxia

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Background and aims: L-2-hydroxyglutaric aciduria (L-2-HGA) is a rare neurometabolic disorder with autosomal receive inheritance. Biochemically, is characterised by elevated concentration of L-2-hydroxyglutaric acid (L-2-HG) in plasma, urine and cerebrospinal fluid. This is caused by dysfunction of L-2-hydroxyglutarete dehydrogenase (L2HGDH), an enzyme catalysing the oxidation of L-2-hydroxyglutaric to 2-ketoglutaric, due to mutations of LHGDH gene.

Methods: We evaluated an adolescent female referred to our clinic for mental retardness, gait disorders and dysgraphia. We performed a thorough clinical investigation, complete laboratory work-up and targeted genetic analysis. Patient also had a baseline and a follow-up brain MRI after a 4-year interval.

Results: We present the case of a 24-year-old female with L-2-HGA. Patient reached with delay major neurodevelopmental milestones and presented learning difficulties at school. Mild mental retardness was confirmed after proper paidopsychiatric evaluation. Patient presented with pyramidal semiology, gait disorders, dysmetria, dysarthria and dysgraphia. Brain MRI revealed mild cerebellar atrophy and hyperintense signal in T2-W and FLAIR sequences at subcortical white mater and basal ganglia with sparing of deep white matter and corpus callosum. Strongly elevated exertion of L-2-HG was detected in urine sample. DNA sequencing of L2HGDH gene identified two heterozygous mutations and confirmed the diagnosis.

Conclusion: L-2-HGA is a rare neurometabolic disorder with characteristic clinical, laboratory and neuroimaging presentation. When clinical suspicion is high proper genetic analysis of L2HGDH gene will confirm the diagnosis. Since first described in 1980 by Duran et al approximately 90 patients with L-2HGA have been described worldwide. To our knowledge this is the first report of L-2-HGA in Greece.

Disclosure: Nothing to disclose

Neurogenetics 3

EPR2128

Late-onset leukoencephalopathy with brainstem and spinal cord involvement and lactate elevation (LBSL): Russian experience

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Background and aims: Leukoencephalopathy with brainstem and spinal cord involvement and lactate elevation (LBSL) is a recently described rare autosomal recessive hereditary disease of the nervous system, associated with DARS2 gene mutations. Clinically it is characterised by progressive pyramidal, cerebellar, and dorsal column dysfunction. MRI is highly specific. Neuroimaging findings are heterogeneous cerebral white matter abnormalities accompanied by a selective involvement of the brainstem and spinal cord tracts and MR spectroscopy shows high lactate level. Usually LBSL manifests in an early childhood, adult-onset forms are extremely rare. We hereby present 9 cases of the disease manifested in the adulthood.

Methods: Nine patients (4 female, 5 male; 29±7.8 years) with the previously made diagnoses of spinocerebellar ataxia, hereditary spastic paraplegia, multiple sclerosis. All the patients received a complete neurologic examination, neuropsychological testing, brain MRI and MR-spectroscopy, DARS2 gene sequencing.

Results: All patients showed different combination of pyramidal, cerebellar and dorsal column symptoms. In six patients different polyneuropathy symptoms were found and in eight patients psychoneurological symptoms were found. MRI and MRS revealed findings typical for LBSL (fig.1, 2). DARS2 gene sequencing revealed a high spectrum of different pathogenic mutations. The frameshift mutation in intron 2 of the DARS2 gene was revealed in all cases (fig.3). The second mutation differed among the patients.
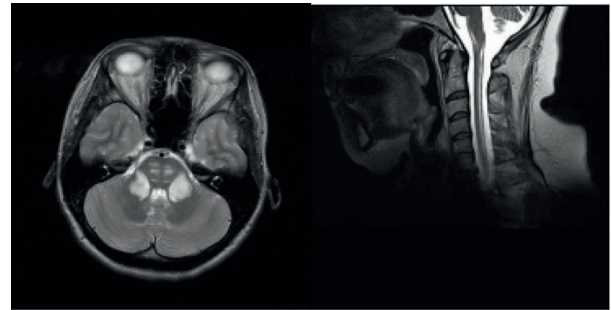
Fig.1. T2 WI showing hyperintense signal from pons, middle cerebellar peducles, spinal cord.
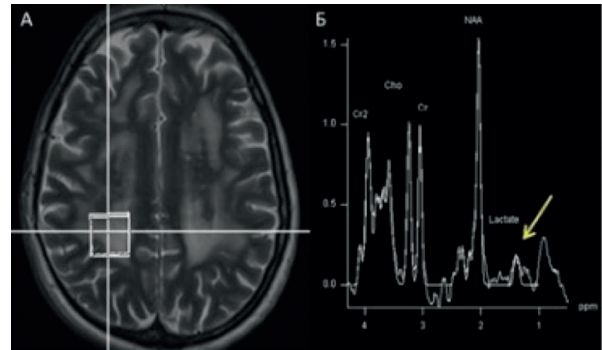
Fig.2. Single voxel MR spectroscopy of the affected white matter showing high lactate level
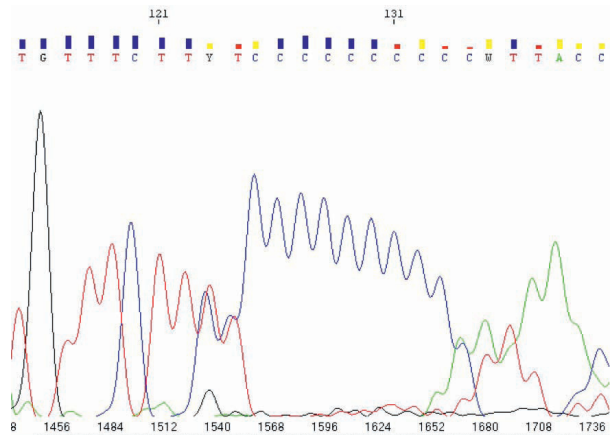
Fig.3. Frameshift mutation c.228-21_20delTTinsCC (rs367543010) in intron 2 of the DARS2 gene

Conclusion: It is deemed to conclude that late onset LBSL is not as rare as it was supposed to be. We reckon LBSL shall be considered to be a possible diagnosis in adult patients with ataxia, pyramidal dysfunction and leukoencephalopathy signs on MRI.

Disclosure: Nothing to disclose

EPR2129

Linguistic characteristics of genetic primary progressive aphasias: a retrospective study of 27 cases carrying GRN and c9orf72 mutations

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Background and aims: Primary progressive aphasia (PPA) is a neurodegenerative disorder characterized by an early and progressive impairment of language. The current classification recognizes three variants: non-fluent/agrammatic (nfaPPA), semantic (svPPA) and logopenic (lvPPA). Genetically determined PPA cases are mainly due to mutations in frontotemporal lobar degeneration (FTLD)-related genes. We aimed at defining the clinical, neurolinguistic and neuroimaging features of a cohort of French PPA patients with a mutation in GRN or c9orf72 genes.

Methods: From 600 patients with genetically determined FTLD included in a French clinical and genetic research network on FTLD, we selected 27 PPA cases who underwent neuropsychological and linguistic evaluation (with Boston Diagnostic Aphasia Evaluation and/or Montreal-Toulouse batteries), CSF biomarkers dosage, structural and functional neuroimaging. Twenty-four PPA patients had a GRN mutation and three a c9orf72 expansion. We described and compared their performances in main language domains at a relatively initial stage (2,2 years from onset) and subsequent disease evolution across PPA subtypes and genotypes.

Results: Among GRN patients, nfvPPA and lvPPA were equally represented (8 cases each), whereas svPPA and mixed phenotypes (5 and 3 cases respectively) displayed the greatest global impairment. In the c9orf72 cohort the age of onset was the earliest (mean 48,3 years) and the progression the slowest. Seven GRN patients later manifested parkinsonism, two of which with CBS phenotype. GRN mutations determined the greatest impairment and the most severe evolution.

Conclusion: This is the largest cohort of PPA cases carrying FTLD mutations described so far. This study allows to define linguistic characteristics of PPA according to their genotype.

Disclosure: Nothing to disclose

EPR2130

Hereditary spastic paraplegia (HSP) type 15 in five Portuguese patients

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Background and aims: Autosomal-recessive hereditary spastic paraplegias (HSP) are typically associated with a complex phenotype. HSP15 is caused by mutations in the ZFYVE26 gene, encoding spastizin. We aim to describe a cohort of five Portuguese HSP15 patients from four different families, further contributing to its genetic and phenotypical characterization.

Methods: Descriptive analysis of the patients' clinical, genetic, imaging and electrophysiological data.

Results: Onset of spastic gait ranged 8-16y. All patients had cognitive dysfunction: three had a delay in cognitive acquisitions; one had cognitive regression by age 6y; the other presented learning difficulties at elementary school and cognitive deterioration by late adolescence. Three were wheelchair bound after a mean disease duration of 14 years. Other non-pyramidal features included neuronopathy/peripheral neuropathy (in 5), levodopa-responsive juvenile-onset Parkinsonism (1), cerebellar syndrome (1). Two patients were born from consanguineous and one from non-consanguineous parents. Parents of the other two patients were from the same small village, though denied consanguinity. All performed brain MRI (4 to 15y after onset), showing a thin corpus callosum (in 4), white-matter abnormalities (4) and cortical atrophy (2). Sequencing revealed four novel and two previously known variants in ZFYVE26; two patients were homozygous and three compound heterozygotes.

Conclusion: We describe five molecularly confirmed cases of HSP15, including four novel genetic variants. Cognitive dysfunction and neuronopathy/peripheral neuropathy were present in all five patients, though the last is a frequent but not universal sign. Levodopa-responsive juvenile-onset Parkinsonism has been described so far in only two HSP15 patients (one of Portuguese ancestry).

Disclosure: Nothing to disclose

EPR2131

Mutations in endocytic recycling protein Rab11FIP3 are associated with ataxia and intellectual disability

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Background and aims: The aim of this work is to identify the genetic cause of disease in two siblings affected with infantile-onset ataxia and intellectual disability.
Methods: Family members were genotyped with Infinium OmniExpressExome-8 v1.4 BeadChip. Two affected brothers and one healthy brother underwent whole-exome sequencing. Linkage analysis was performed with Allegro software. Exomic variants were filtered with Enlis Genome software. A skin biopsy was performed on one affected sibling, from which a fibroblasts culture was derived, in order to study the effect of mutations on patient's cells. Plasmids harboring the two mutations were transfected in HeLa cells.
Results: Using a combined approach of genome-wide linkage analysis and whole-exome sequencing, we found RAB11FIP3 compound heterozygous mutations in two siblings showing infantile-onset ataxia and intellectual disability. Patient's fibroblasts displayed a significant delocalization of Rab11FIP3 protein and morphological anomalies consistent with Rab11FIP3 function. Overexpressed mutated protein showed immunoblot abnormalities in comparison to overexpressed wild-type protein.
Conclusion: In conclusion, the identified RAB11FIP3 mutations are associated with a novel autosomal recessive ataxic syndrome with intellectual disability.
Disclosure: Nothing to disclose

EPR2132

Promoter methylation of full and intermediate C9orf72 expansion in Russian population

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Background and aims: C9orf72 repeat expansion is the most frequent cause of familial frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS). It was also identified in some cases of Parkinson's disease (PD). DNA methylation of C9orf72 gene plays a role in the pathogenesis of FTD and ALS, but it is not studied enough.
Methods: We investigated the promotor methylation of full C9orf72 expansions in FTD/ALS patients (n=12), intermediate expansions in PD patients (n=8) and non-expanded alleles in healthy controls (n=8) from a Russian population. The expansion lenght was evaluated by repeat-primed PCR. The full expansion comprised >40 repeats; the intermediate expansion 13-20 repeats. CpG islands of C9orf72 gene were defined using MethPrimer program and the methylation status was determined via sequencing of amplified fragments of bisulfite-converted DNA.
Results: We identified 2 cases with the hypermethylation of C9orf72 promoter in the full expansion group. These patients were sublings from one family. We had detailed information only about a brother (a sister did not visit the clinic due to a disease severity). This patient had an atypical ALS presentation: an onset with parkinsonism, a long duration of ALS symptoms, cognitive impairments with a temporal lobes atrophy and a positive family history. There were no cases of the promoter hypermethylation in the intermediate and control groups.
Conclusion: This is the first data on the C9orf72 promoter methylation in Russian population. The frequency of the promoter methylation among full expansion carriers was 9,1% (1/11) that consistent with previous studies in other populations. The study was supported by RSF 17-75-20211.
Disclosure: RSF 17-75-20211

EPR2133

Mitochondrial ATP6 mutation m.9176T>C leading to mild late-onset manifestation of a neurologic multisystem disorder

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Background and aims: Pathogenic mutations in the ATP6 gene of the mitochondrial DNA (mtDNA) which encodes for a subunit of the mitochondrial ATP synthase (respiratory chain complex V) typically lead to severe early-onset multisystemic diseases such as Leigh syndrome (LS) or to the syndrome of neuropathy, ataxia and pigmentary retinopathy (NARP). In addition, there is increasing evidence for ATP6 mutations causing milder phenotypes with variable age of onset, including adult-onset spinocerebellar ataxia (SCA) or axonal distal hereditary motor neuropathy. More recently, an association between the homoplasmic ATP6 mutation m.9176T>C and acetazolamide-responsive episodic weakness mimicking periodic paralysis as well as hereditary spastic paraplegia-like disorders has been reported.

Methods: Case report including brain pathology, exome sequencing and muscle biochemistry.

Results: This 67-year-old male reported gait disturbance and weakness since age 45 years. Clinical examination revealed cerebellar ataxia, peripheral neuropathy, and mild parkinsonism. Dopamine transporter scan confirmed a presynaptic dopaminergic deficit. Pedigree analysis revealed ten affected maternal relatives. The patient's sister who was symptomatic from age 8 years died at age 66 years. Brain pathology showed age-related findings (Braak I, Thal 3, CERAD 0) and mild gliosis. Exome sequencing identified the known pathogenic ATP6 mutation m.9176T>C in the mtDNA. Respiratory chain analysis in muscle revealed an isolated deficiency of Complex V.

Conclusion: Distinct homoplasmic mutations in the ATP6 gene (m.9176T>C) should be considered as a cause for mild adult-onset multisystemic neurological disorders with spinocerebellar ataxia, neuropathy and parkinsonism.

Disclosure: Nothing to disclose

Neuroimaging 2

EPR2134

The association between patterns of grey matter atrophy and white matter disruption in relapsing-remitting Multiple Sclerosis

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Background and aims: Few recent MRI studies have used source-based morphometry (SBM) to show non-random patterns of either grey matter (GM) atrophy or white matter (WM) disruption in patients with longstanding multiple sclerosis (MS). We used here SBM to assess patterns of both GM atrophy and WM disruption in relapsing-remitting (RR) MS patients with relatively mild disability and explore their relation and relevance to patients' disability.

Methods: We assessed RRMS patients (n=41) with mild disability (median EDSS=1.5). Symbol digit modalities test (SDMT) was abnormal on 8 patients. A 3T MRI was acquired. WM lesion volume was 6.7±11.5 cm3. Patterns of brain changes were assessed on maps of GM volume, fractional anisotropy (FA) and mode of anisotropy (MO) with SBM. Patient data were compared with those of demographically matched normal controls (NC, n=28).

Results: MS patients had GM atrophy in 3/6 patterns (p≤0.01) and WM disruption (altered FA and/or MO) in 3/4 patterns (p<0.05). The three GM patterns in deep GM (DGM), sensorimotor cortex/parancigulate/superior frontal gyrus and temporo-occipital cortex correlated with the WM pattern in the posterior corona radiata (PCR) (r=0.62 to 0.67, p<0.001). DGM component also correlated with the two WM components in PCR and callosal splenium (r=0.61 to 0.7, p<0.001). Correlations were found between temporo-occipital atrophy and SDMT (r=0.52, p<0.001) and between splenium disruption and EDSS (r=-0.55, p<0.001).

Conclusion: In RRMS with mild disability, GM atrophy and WM disruption occur in distinct anatomical patterns, which are inter-related and have great relevance for both physical and cognitive disability.

Disclosure: Nothing to disclose

EPR2135

Peak width of skeletonised mean diffusivity (PSMD), a promising imaging marker for white matter diseases: preliminary results in Multiple Sclerosis and CADASIL

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Background and aims: Peak width of skeletonised mean diffusivity (PSMD) is a new, fully automated, MRI-based biomarker, that has shown clinical relevance in cerebral small vessel diseases. We aimed here to explore its relevance in other white matter (WM) disorders such as multiple sclerosis (MS) and cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL).

Methods: In this ongoing study, we studied thus far 22 MS (age: 43.9±9.3 years, expanded disability status scale: 2 [1-5.5], symbol digit modalities test: 41±11), 13 CADASIL (age: 44.1±8.3 years, mild disability), and 27 normal controls (NC, age: 44.2±11.24 years). MRI data were acquired on a 1.5 T scanner. PSMD was computed from diffusion tensor imaging data through "skeletonisation" of WM tracts and histogram analysis.

Results: No age and sex heterogeneity was found among the three groups. Patients with MS and CADASIL had similar WM lesion volume (LV, 12.4±2.2 cm^3 vs 14.6±10.7cm^3, p=0.54). Both patient groups showed higher PSMD than NC (2.8±0.3 10^-4 mm2/s, p≤0.001) but in MS PSMD was higher than in CADASIL (4.6±0.6 vs. 3.8±0.9 10^-4 mm^2/s, p=0.008). In both patient groups PSMD correlated with LV (r=0.6, p=0.004 in MS; r=0.7, p=0.007 in CADASIL) whereas no correlations with clinical variables were found.

Conclusion: Our preliminary results showed that, in presence of a similar LV, diffuse microstructural brain damage as detected by PSMD is more pronounced in MS than in CADASIL. PSMD can thus represent a useful marker for a robust quantification of microscopic brain damage in WM disorders.

Disclosure: Nothing to disclose

EPR2136

Automated pipeline to assess clinically relevant white matter lesions (WMLs)

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Background and aims: WMLs reflects vascular damage in Alzheimer's disease, and are often quantified through visual assessment (i.e. Age-Related White Matter Changes Scale-ARWMC, Wahlund et al, 2001). Visual scales require an expert rater clinician, are time-consuming, and showing high intra-rater and inter-rater variability. Therefore, several automated methods have been developed for WMLs quantification, but their clinical relevance has been poorly investigated. The aim of this study is to provide an automated pipeline able to assess clinically relevant WMLs in mild cognitive impairment (MCI) patients.

Methods: We included 134 MCI patients consecutively enrolled in the PharmaCog study (Galluzzi et al., 2016). WMLs visual assessment was performed using ARWMC, automated assessment using in-house pipeline: i) lesion prediction algorithm execution for WMLs segmentation (raw masks), ii) focal and periventricular lesions removal (final masks), iii) WMLs regionalisation as in ARWMC (frontal/parieto-occipital/temporal/infratentorial/basal ganglia). The concordance of ARWMC and WML volumes from raw or final masks was performed using Kendall's rank correlation tau.

Results: At global level, ARWMC showed a moderate concordance with volumes of final masks (tau=0.46-p<.001), higher than that with raw masks (tau=0.35-p<.001). At regional level, the concordance with final masks was higher in frontal (tau=0.51-p<.001) and parieto-occipital regions (tau=0.39- p<.001).

Conclusion: Our pipeline improved the concordance between the widely-used ARWMC scale and raw automated methods, may be useful in research and clinical settings to evaluate vascular damage. These analyses will be replicate on healthy subjects' cohort to provide normative data. PharmaCog is funded by the EU-FP7 for the Innovative Medicine Initiative (grant n°115009).

Disclosure: Nothing to disclose

EPR2137

Detecting whole-brain and gray matter atrophy in Multiple Sclerosis: assessment by MRI

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Background and aims: In this study, the comparison between different available methods for whole-brain and gray matter (GM) atrophy estimation using MRI (ANTs v1.9, CIVET v2.1, FSL-SIENA(X) v5.0.1, Icometrix-MSmetrix v1.7, SPM v12) in multiple sclerosis (MS) was performed, for their potential clinical application.
Methods: The dataset consisted of (1) 8 simulated MR images and longitudinal data (two weeks) from 10 healthy controls to assess cross-sectional and longitudinal accuracy of atrophy measures; (2) test-retest MR images of 29 MS patients acquired within the same day at different scanner field strengths/manufacturers to evaluate precision; (3) longitudinal data (one year) from 24 MS patients to assess the agreement between methods. Tissue segmentation, image registration and white matter (WM) lesion filling were also evaluated.
Results: High values of accuracy (0.87-0.97) for whole-brain and GM volumes were found, with the lowest values for MSmetrix. ANTs showed the lowest mean error (0.02%) for whole-brain atrophy in healthy controls with a coefficient of variation (CoV) of 0.5%. SPM showed the smallest mean error (0.07%) and CoV (0.08%) for GM atrophy. On average, good repeatability (p>0.05), but poor reproducibility (p<0.05), were found for all methods. The WM lesion filling technique mainly affected ANTs, MSmetrix and SPM results (p<0.05).
Conclusion: From this comparison, it would be possible to select software for atrophy measurement, depending on the requirements of the application (research center, clinical trial) and its goal (high accuracy and repeatability or high reproducibility). For clinical application, an improved reproducibility is required for all methods.
Disclosure: Nothing to disclose

EPR2138

Dynamic inter-regional coordination patterns as specific predictors of consciousness

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Background and aims: To date, specific signatures of conscious states in humans remain elusive. Contemporary theories concur that such markers can be traced to temporally evolving brain processes instead of static descriptions of brain activity.
Methods: Dynamic fMRI connectivity patterns (states) by means of clustering of phase-based coherence was estimated on 47 healthy and 112 patients diagnosed in vegetative state/unresponsive wakefulness syndrome (VS/UWS) or in a minimally conscious state (MCS). To validate whether the patterns captured properties of awareness, out-of-sample generalization was performed on patients with cognitive-motor dissociation (i.e. lacking overt conscious behaviour yet evidenced using functional neuroimaging), and on anesthetised patients, under the premise that complex signatures would disappear uniformly across all subjects.
Results: A pattern of long-range positive/negative coherence had a higher probability of occurring in healthy and MCS patients. A pattern of low inter-areal coordination, mostly similar to anatomy, was more likely to occur in VS/UWS. Inter-state transitioning was flexible for healthy and MCS and more rigid for VS/UWS patients. Unconscious patients were more likely to avoid the exploration of the complex connectivity state. The generalisation to cognitive-motor dissociation predicted the occurrence of the complex-connectivity state. The generalisation to propofol anaesthesia showed an equalization of occurrence probabilities of all patterns regardless of clinical diagnosis.
Conclusion: The dynamics of inter-areal coordination contain information specific to conscious awareness. The rigid and less metastable dynamics in VS/UWS could account for the limited mental capacities in these patients. The minute identification of these patterns and their external manipulation could account for non-invasive restoration of consciousness.
Disclosure: Nothing to disclose

EPR2139

Location of T2-W lesions discriminate between radiologically isolated syndrome and preclinical CADASIL

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Background and aims: The radiologically isolated syndrome (RIS) refers to asymptomatic subjects who show brain abnormalities on magnetic resonance imaging (MRI) suggestive of multiple sclerosis (MS). Asymptomatic subjects with genetically proven cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) can show brain MRI abnormalties before symptom occurrence, with a pattern similar to that of MS and RIS.

To use lesion mapping to investigate spatial differences in white matter (WM) lesion distribution and frequency between the two groups of asymptomatic subjects with CADASIL and RIS.

Methods: Using T2-W lesions masks a lesion probability map was created and a voxel-wise analysis of lesion distribution and frequency of lesion occurrence was performed in 23 RIS (17F/6M) and 18 asymptomatic CADASIL (8F/10M).

Results: Age- and T2-W lesion load were not different in the two groups (p>0.1). Asymptomatic subjects with CADASIL showed significantly higher frequency of lesions in the right external capsule and superior longitudinal fasciculus. The percentage of voxels occupied by lesions in these regions was significantly higher in CADASIL than in RIS (CADASIL: 10.4%±4.2%; RIS: 0.97%±1.37%; p<0.001), with a value of 4% that was able to best discriminate between the 2 groups.
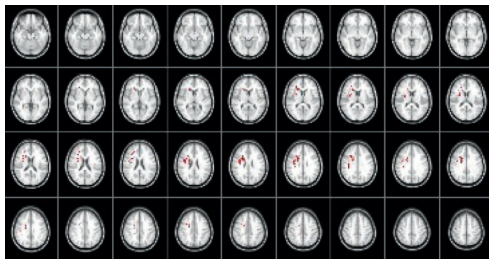
Lesion Probability Map

Conclusion: Present results suggest differences in lesion location between asymptomatic subjects with CADASIL and RIS could be of crucial relevance in the differential diagnosis of these conditions.

Disclosure: Nothing to disclose

EPR2140

Cerebellar atrophy patterns in Paraneoplastic Cerebellar Degeneration (PCD) and Spinocerebellar Ataxia type-1 (SCA1)

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Background and aims: Brain and more specifically cerebellar atrophy is a major radiological finding in both Paraneoplastic Cerebellar Degeneration (PCD) with anti-Yo antibodies and Spinocerebellar Ataxia type-1 (SCA1). We sought to analyse the different brain volumetric patterns of cerebellar atrophy in these diseases.

Methods: Patients were recruited in Paris, Lyon and Barcelona reference centres with either anti-Yo PCD (n=16) or SCA1 (n=17). T1 weighted MRI were used. We used 30 MRI from OASIS and IXI databases as controls paired by age. We have applied VolBrain and CEREbellum Segmentation (CERES) algorithms to obtain cerebellar volumetric data. We performed multivariate analysis to compare cerebellar atrophy patterns in the different diseases using R package SCCAN. We also performed whole brain analysis using a Voxel Based Morphometry (VBM) method. All p-values were corrected for multiple testing.

Results: In univariate analysis, most of the atrophic regions (p<0.05) were common between PCD and SCA1 patients compared to controls. Lobule IV, and V were atrophic only in PCD patients (p=0.003 and p=0.04 respectively), whereas atrophy of lobule IX was only found in SCA1 patients (p=0.009). Cerebellum cortical thickness was significantly lower in PCD versus controls (p<0.001), and versus SCA1 (p<0.001). Multivariate analysis using SCCAN and VBM confirmed these results (p<0.05) (Figure 1) Interestingly, we identified two complementary patterns of cerebellar atrophy in PCD (Figure 2).
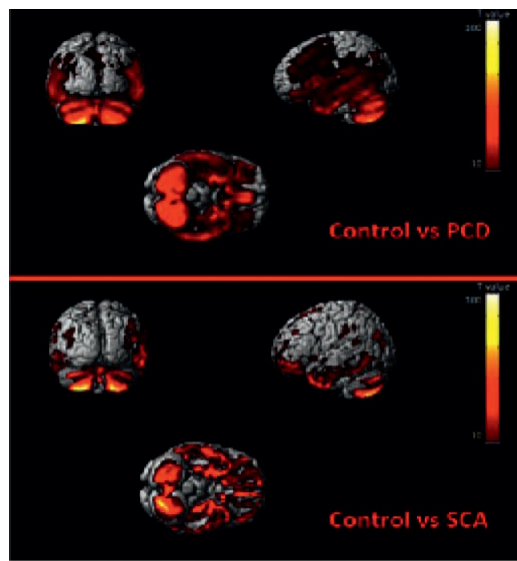
Figure 1: Visualisation of statistically different voxels, using Voxel Based Morphometry (VBM) method through Statistical Parametric Mapping (SPM), between control and both PCD subjects (upper figure) and SCA1 subjects (lower figure). Normalization was made with age and intra-cranial volumes. Family Wise Error Rate correction for multiple testing, p-value set to 0.05 and voxel cluster size set to 10.

Figure 1: Visualisation of statistically different voxels, using Voxel Based Morphometry (VBM) method through Statistical Parametric Mapping (SPM), between control and both PCD subjects (upper figure) and SCA1 subjects (lower figure). Normalisation was made with age and intra-cranial volumes. Family Wise Error Rate correction for multiple testing
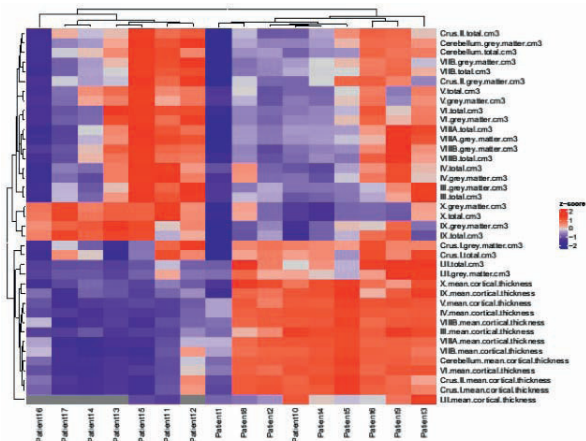
Figure 2. Heatmap representation of PCD cerebellar volumetric features showed two clusters of patients. The volumetric features were transformed using a z-score

Figure 2. Heatmap representation of PCD cerebellar volumetric features showed two clusters of patients. The volumetric features were transformed using a z-score.

Conclusion: The cerebellar atrophy related with PCD is more diffuse and is associated with a broader reduction of cerebellar cortical thickness than in SCA1. These differences can be explained by a differential pathophysiology.
Disclosure: Nothing to disclose

Neurological manifestations of systemic diseases; Neuro-oncology

EPR2141

Impact of Patisiran on Norfolk Quality of Life Questionnaire Diabetic Neuropathy (QOL-DN) in patients with Hereditary transthyretin-mediated Amyloidosis: results from the Phase-3 APOLLO study

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Background and aims: Hereditary transthyretin-mediated (hATTR) amyloidosis is a multi-system, rapidly progressive, life-threatening disease. Clinical manifestations can include polyneuropathy, cardiomyopathy and gastrointestinal symptoms impacting patients' quality of life (QOL). In the Phase-3 APOLLO study, patisiran, an investigational RNAi therapeutic, resulted in a statistically significant improvement in neuropathy (mNIS+7) and quality of life (Norfolk QOL-DN) at 18-months compared to placebo and was generally well tolerated. Here we describe the impact of patisiran on individual domain scores of the Norfolk QOL-DN.

Methods: APOLLO was a multi-centre, international, randomized (2:1), double-blind, study of patisiran 0.3mg/kg or placebo IV q3W in hATTR amyloidosis patients with polyneuropathy (NCT01960348). Norfolk QOL-DN assessed 5 domains: small fibre, large fibre, and autonomic nerve function, symptoms (including walking, arising from a seated position, sensation in extremities and gut motility), and activities of daily living (ADL). Scores range from -4 to 136; lower scores indicate QOL improvement.

Results: APOLLO enrolled 225 patients: mean age 60.5 years (24-83); 74% males; 43% V30M. Patisiran treatment led to significant improvement relative to placebo in the Norfolk QOL-DN overall score LS mean difference (SEM) [95%CI] (p-value) -21.1 (3.1) [-27.2, -15] (p=1.1×10^{-10})

and improvement within each domain at 18-months (Table 1). Patients on placebo had worsening QOL over time while the patisiran group improved relative to baseline (Table1).

		Placebo n=77	Patisiran n=148
Norfolk QOL-DN Overall (LS Mean Change from Baseline (SE))	-	14.4 (2.73)	-6.7 (1.77)
Individual Domains (Mean Change from Baseline)	Physical Functioning/Large Fibre	9	-1.9
	ADL	5.3	0.5
	Symptoms	2.3	-1.2
	Small Fibre	2.8	0.3
	Autonomic	0.8	-0.3
	Total Score	20.2	-2.6

Table 1. Norfolk QoL-DN Overall and Domain Scores from Baseline after 18-months of Treatment

Conclusion: Patisiran treated patients reported improvement or preservation in quality of life over 18-months related to strength, digestive health, ability to perform everyday activities, and steadiness on their feet. Those who did not receive patisiran reported a decline.

EPR2142

Patisiran-LNP Pharmacokinetics (PK), Pharmacodynamics (PD), and Exposure-Response (E-R) relationship in patients with hereditary Transthyretin-Mediated (hATTR) amyloidosis with polyneuropathy

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Background and aims: APOLLO is a global phase-3 study evaluating clinical efficacy, safety, PK, and PD of patisiran-LNP, a first-in-class investigational RNAi therapeutic that inhibits the hepatic synthesis of wild-type and mutant transthyretin (TTR) protein in adult patients with hATTR amyloidosis with polyneuropathy. Here we report PK, PD, anti-drug antibody (ADA), and E-R relationships for TTR reduction, efficacy and safety.

Methods: A total of 148 adult patients received patisiran-LNP 0.3mg/kg intravenously q3W over 18 months (NCT01960348). Sparse PK samples were collected for the determination of plasma concentrations of ALN-18328 (siRNA) and 2 novel lipid excipients (DLin-MC3-DMA and PEG2000-C-DMG). Serum samples were collected for determination of serum TTR concentrations and ADA. Steady-state PK exposures were divided by 4 quartiles and TTR and efficacy (mNIS+7 change from baseline) were summarized by each PK exposure quartile. Similarly, incidence of adverse events (AEs) were analysed by 4 PK exposure quartiles.

Results: Patisiran-LNP exhibited linear and time-independent PK with chronic dosing of 0.3mg q3w over 18 months. There were no differences in PK, TTR reduction or efficacy in any subgroup [age, sex, ADA status, hepatic impairment (mild) and renal impairment (mild to moderate)]. Incidence of ADA was low (3.4%), with no impact on PK, PD, efficacy or safety. Also, TTR reduction, efficacy and incidence of AEs were similar across 4 PK exposure quartiles.

Conclusion: Steady-state PK was similar across subgroups. Intra-subject variability in PK did not affect TTR reduction and clinical efficacy. Incidence of AEs were not associated with patisiran-LNP concentrations.

Disclosure: This research was supported by Alnylam Pharmaceuticals.

EPR2144

Cognitive functioning and health-related quality of life in patients with newly diagnosed primary central nervous system lymphoma: a systematic literature review

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Background and aims: Background: Incidence of primary central nervous system lymphoma (PCNSL) is increasing and prognosis improving due to improved treatment, however, declined cognitive functioning remains a major challenge in the treatment of PCNSL. This cognitive decline, in conjunction with other symptoms caused by the disease and/or its treatment, may compromise health-related quality of life (HRQoL).

Objectives: To give a comprehensive overview of current knowledge on cognitive functioning and HRQoL in PCNSL, including an evaluation of patient- and treatment related factors which can influence cognitive functioning and HRQoL.

Methods: We reviewed literature on cognitive functioning and HRQoL in newly diagnosed adult patients with PCNSL in several electronic resources, including Pubmed and Embase, up to January 4, 2018. Articles were selected using predetermined in- and exclusion criteria.

Results: 42 original articles were included. The tumor itself has a large impact on cognitive functioning and HRQoL. On the short-term, induction chemotherapy resulted in improvement of cognition and HRQoL in most patients. On the long-term only additional Whole Brain Radiotherapy (WBRT) has a negative impact on cognitive functioning, but the magnitude of this impact is not always clinically relevant. HRQoL scores were worse compared to controls. Moreover, scores were worse after chemoradiation when compared to chemotherapy only, particularly on the long-term.

Conclusion: Only chemoradiation seems to have a negative effect on HRQoL and cognition in PCNSL patients. Although prolonged progression-free survival is achieved with combined therapy, information on the impact of treatment on cognition and HRQoL should also be included in clinical decision-making, regarding starting or withdrawing treatment modalities.

Disclosure: Nothing to disclose

EPR2145

Rapidly progressive dementia in an anti-Yo positive patient

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Background and aims: Paraneoplastic cerebellar degeneration (PCD) related to the anti-Yo antibody typically manifests as a subacute pancerebellar dysfunction. Although psychiatric comorbidity is commonly apparent, severe cognitive impairment is rare.

Methods: Case report

Results: A 59-year-old healthy woman, developed a subacute history of apathy and loss of initiative, followed by a progressive gait unsteadiness, with inability to walk within four months. She presented a severe dysexecutive syndrome, characterised by apathy, psychomotor slowing, attention and working memory deficit, ideomotor, oculomotor and constructional apraxia, decreased verbal fluency, speech perseveration, palilalia and agraphia without alexia; primitive signs were present; and a pancerebellar dysfunction with downbeat nystagmus and speech, limb and gait ataxia. The brain MRI revealed small nonspecific hyperintensities in supratentorial white matter. The CSF analysis was normal and bacterial cultures, neurotropic virus PCR and 14-3-3 protein were negative. Screening of prion protein mutations was negative. Body CT scan, upper and lower digestive endoscopy and pelvic, breast and thyroid echographic exams were unremarkable. Whole-body PET-FDG identified two small abdominal hypermetabolic foci, which were biopsied suggesting metastasis of unknown primary tumour, and a right cerebellar hot-spot. Antineuronal antibody anti-Yo was positive. A tractography MRI revealed disruption of the fronto-ponto-cerebellar tract, between the left frontal cortex and the right cerebellar peduncles.
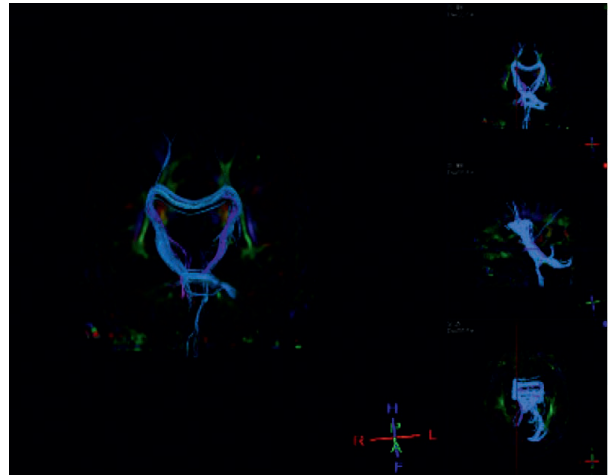
Conclusion: Metabolic changes in PET-FDG along with dysfunction of the ipsilateral cortico-ponto-cerebellar tract suggests a possible mechanism for the cognitive impairment in this patient. A cognitive-affective syndrome has been described in the context of cerebellar lesions. This case supports the development of a Schmahmann syndrome in the setting of PCD.

Disclosure: Nothing to disclose

EPR2146

Primary diffuse large B-cell lymphoma of the dura – a case report

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Background and aims: Primary dural lymphoma (PDL) is
a rare subtype of primary central nervous system lymphoma
(PCNSL) arising primarily from the meninges without brain
or systemic involvement. The most frequent
histopathological diagnosis is marginal zone B-cell
lymphoma (MZL) and presentation as diffuse large B-cell
lymphoma (DLBCL) is extremely rare.
Methods: We report a case of a PDL with skull and
epicranial involvement in an immunocompetent patient.
Results: A 43-year-old woman with no previous medical or
surgical history, presented to our outpatient clinic with
progressive frontal headaches over the last year and two
enlarging frontal scalp masses in the past four months.
Neurological examination was unremarkable. MRI revealed
diffuse pachymeningeal thickening with contrast
enhancement, predominantly on the frontoparietal region,
with diffuse bone infiltration and soft tissue thickening
along the scalp. Partial excision of the epicranial lesions
revealed a DLBCL. CSF analysis was negative for
malignant cells and bone marrow biopsy was normal. 18F-
FDG PET/CT imaging showed avid FDG uptake by the
epicranial lesions, but no evidence of systemic involvement.
The patient was transferred to a tertiary referral hospital and
completed 6 cycles of high dose systemic chemotherapy
regimen – R-HCVAD. MRI after four cycles of
chemotherapy demonstrated a significative reduction of the
pachymeningeal thickening.
Conclusion: Despite being uncommon, PDL should be
considered in the differential diagnosis of scalp masses and
distinguished from meningiomas. Whether this DLBCL
arised de novo or as a transformation/progression from
MZL is unknown. Given the scarcity of cases, there is no
standard treatment established for PDL.
Disclosure: Nothing to disclose

Neurorehabilitation 2

EPR2147

Effects of gait training using the Hybrid Assistive Limb (HAL®) in patients with spinocerebellar degeneration

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Background and aims: Patients with spinocerebellar degeneration (SCD) are severely disturbed in gait and routine daily activity. The effect of neuro-rehabilitation is usually not enough in SCD. The hybrid assistive limb (HAL®) (the wearable robot suit) assist kinesis during voluntary control of hip and knee joint motion. The aim of this study is to investigate the effect of HAL® on gait disturbance in SCD.

Methods: 15 patients with SCD took part in the experiments (mean age: 59.1 ± 17.4 years old; mean disease duration: 13.7 ± 9.5 years). Eight patients with SCA6, one SCA1, two SCA8, one SCA31 were diagnosed. The remaining one patient was cortical cerebellar form. The walking speed and the number of steps were counted to calculate step length. During the 2-minute walk test, the total distance walked was recorded. Evaluation were conducted before treatment (baseline), after training and 2 weeks later. The patients received HAL® treatment for fifteen sessions during three weeks in hospital. Each treatment session lasted 60 minutes per day for three weeks. One therapist operated the walking device and the other operated the computer.

Results: The walking speed was significantly faster from baseline to after training (0.74m/sec vs 0.98m/sec). The total walking distance in the 2-minute walk test were significantly longer observed (71.2m vs 94.8m).

Conclusion: Significant improvements in gait speed, step length, and cadence for the 10-m walk test.

Conclusion: The study showed that gait training using the HAL® in SCD patients can improve gait disturbance and ADL.

Disclosure: Nothing to disclose

EPR2148

Diagnosis and treatment of post-stroke depression in China: a cross-sectional survey of 350 senior clinicians in neurology, geriatrics and rehabilitation department

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Background and aims: Integration incidence rate of post-stroke depression (PSD) in China was very serious. This study aimed to investigate the PSD diagnosis and treatment given by physicians in China.

Methods: A total of 361 physicians working in neurology, geriatrics and rehabilitation medicine departments (8:1:1) at 145 hospitals in 16 cities were selected to answer a PSD questionnaire designed with 41 entries and pre-tested in 29 physicians. The descriptive statistics were used to analyse the 350 feedback PSD questionnaires.

Results: (1) The questionnaire had high reliability (Cronbach's alpha of 0.769) and good structural validity. (2) Physicians (13%) lacked the knowledge of the available screening methods, particularly those who working in geriatrics and rehabilitation departments, would missed diagnosis of PSD. Physicians (87%) would diagnosis less than 30% of their stroke patients with PSD, and another 13% physicians reported it less than 10%. (3) More than half (57%) of physicians agreed that prophylaxis for PSD should be given to patients with stroke, but most (>70%) physicians in these considered non-drug therapy as the first option. 25% of physicians would initiate pharmacology therapy for mild PSD. 79% of physicians would initiate pharmacology therapy (24%) or pharmacologic and non-pharmacologic combination treatment (55%) for moderate-to-severe PSD. (4) The reexamination rate of PSD was not high due to the patients neglect.

Conclusion: This study provides novel insights into the diagnosis and treatment protocol of PSD in China. A general awareness about PSD from neurologists, geriatrics, rehabilitations and also the patients really should be raised.

Disclosure: Nothing to disclose

EPR2149

Rehabilitation after stroke with brain-computer-interface-exoskeleton technology and multimodal cognitive stimulation

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Background and aims: Cognitive dysfunction occurs in more than half of poststroke patients. It reduces the rehabilitation potential and process of adaptation in society. Therefore, comprehensive rehabilitation aimed at restoring motor and cognitive deficits, appears to be most correct you to restore your lost due to stroke functions. The aim of the study: to assess the effect of additional multi-modal stimulation on the recovery of cognitive functions in poststroke patients wich were treated with the brain-computer-interface-exoskeleton technology (BCI-exoskeleton).

Methods: 20 patients treated with BCI-exoskeleton. 10 patients underwent further multimodal stimulation using stabilometric platform using biofeedback and cognitive training (main group). 10 patients of the control group were treated with the BCI-exoskeleton. All patients underwent testing before and after a course of neurorehabilitation using the Frontal Assessment Battery (FAB), memorizing 10 words by AR Luria, Kohs Block Design Test, the Schulte Table, Montreal Cognitive Assessment (MoCA), the Stroop test, The hospital Anxiety and Depression Scale (HADS), The Motivation to Success by T. Ehlers, State-Trait Anxiety Inventory.

Results: After the course of neurorehabilitation in conjunction with multimodal stimulation in main group there was revealed the significantly greater improvement than in the control group of the recovery of impaired cognitive functions on the majority tests (p<0,05). There was achieved the trend to improvement of the emotional-volitional sphere in patients of the main group - the reduction of anxiety and depression, and increase of motivation to success.

Conclusion: Additional multi-modal stimulation in neurorehabilitation with using of BCI-exoskeleton improves cognitive functions and emotional-volitional sphere of poststroke patients.

Disclosure: Nothing to disclose

EPR2150

Effect of body-oriented therapy on executive abilities in children with ADD

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Background and aims: It is known that children with ADHD (Attention Deficit Hyperactivity Disorder) and ADD (Attention Deficit Disorder) have deficit in executive abilities. The gaol of this study was to reveal the effect of body-oriented therapy on executive abilities in preschool children with ADD. We compared the efficacy of two methods of treatment (body-oriented therapy for children vs. conventional motor exercises) in a randomised controlled pilot study.

Methods: 15 children with ADD between 5 to 7 years of age were included and randomly assigned to treatment conditions according to a 2×2 cross-over design. The body-oriented therapy included yogas' exercises and breathing techniques. To assess the executive functions and attention in children we used 4 subtests from NEPSY (Tower, Auditory Attention and Response Set, Visual Attention, Statue). Effects of treatment were analyzed by means of an ANOVA for repeated measurements.

Results: The ANOVA has revealed (p<.05) that for all 4 subtests on executive functions and attention the body-oriented therapy was superior to the conventional motor training, with effect sizes in the medium-to-high range (0.58-0.89).

Conclusion: The findings from this pilot study suggest that body-oriented therapy can effectively influence the executive abilities in preschool children with ADD. However, it is necessary to further research the impact of body-oriented therapies on the prevention and treatment of ADD in children.

Disclosure: The research was supported by Act 211 Government of the Russian Federation, agreement no. 02.A03.21.0006.

EPR2151

Impact of visuospatial training on preschool children with SLI

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Background and aims: It was shown that children with specific language impairments (SLI) have deficits not only in producing and understanding language but also in visuospatial abilities (Kiselev et al., 2016). We assume that training programmes that are aimed to develop the visuospatial abilities can help children with SLI. The goal of this study was to assess the impact of visuospatial training on the language abilities in children with SLI.

Methods: The participants were 21 children aged 5–6 years (mean age=5.7) with SLI. Children were randomly assigned to the intervention and comparison group. Children from intervention group participated in 36 weeks of visuospatial training. This programme trains the child to do different visuospatial exercises both on motor and cognitive level. This programme is built on the conceptual framework derived from the work of Luria's theory of restoration of neurocognitive functions (Luria, 1963, 1974).

We used the subtests from Luria's child neuropsychological assessment battery to assess language abilities in children before and after the intervention period.

Results: Analysis of covariance tested the effect of visuospatial training programme on five language subtest from Luria's child neuropsychological assessment battery. Group differences ($p<0.05$) were found for subtest that assess understanding prepositions that describe the spatial relations between objects. Posttest mean for the intervention group were significantly ($p<0.05$) greater than the control group.

Conclusion: Visuospatial training in preschool children with SLI benefits specific language abilities for understanding sentences with spatial prepositions.

Disclosure: The research was supported by Act 211 Government of the Russian Federation, agreement no. 02.A03.21.0006.

EPR2152

Efficacy of home-based training in virtual environment in patients with stroke

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Background and aims: The growing level of VR technology allows using portable devices such as Kinect systems for in-home rehabilitation, providing continuous therapy. Studies of Hondori et al. and Capecci et.al showed that Kinect has motion capture accuracy required for clinical appliance and rehabilitation. The aim of our research was to study the efficacy of home-based VR training in patients with stroke.

Methods: 14 post-stroke patients were included in this study (mean age 52 [27; 68], months after stroke 9,5 [2; 23]). Main group (6 patients) received in-home training course on the Rehabunculus system without daily participation of medical personnel. The control group (8 patients) was trained at home without virtual biofeedback. Evaluation methods: Fugl-Meyer Assessment scale (FM), Action Research Arm Test (ARAT), motion capture system. To evaluate dynamics in VR exercise performance in the main group were used Rehabunculus motion analysis statistics of movement trajectories.

Results: FM upper limb scores showed significant increasing of upper limb range of motion, gross upper limb function and tendency to hand movements increasing. Also, patients received in-home Rehabunculus treatment significantly improved gait skills, resulted in increasing of performed steps per minute during "Step forward" exercise, step length with simultaneous decreasing of step height. Control group showed an insufficient tendency to FM increasing of passive range of motion and balance.

Conclusion: Rehabunculus system is the unique tool for in-home rehabilitation which allows providing continuous, self-guided and effective motor rehabilitation for neurological patients.

Disclosure: Nothing to disclose

EPR2153

Non-invasive neuromodulation of neural networks in Alzheimer's disease: cognitive and clinical effects

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Background and aims: There is increasing evidence that human brain is organised into large-scale networks. Among these, the Default Mode Network (DMN) and the Salience Network (SN) show abnormal connectivity patterns in Alzheimer's disease (AD), i.e. reduced connectivity in the DMN and increased connectivity in the SN. In this study, we tested the cognitive/clinical effect of neuromodulation of the above networks in AD through transcranial direct current stimulation (tDCS).

Methods: 20 AD patients participated in the study. Each patient underwent a clinical (neuropsychiatric inventory and geriatric depression scale) and cognitive assessment (memory, language and visuo-spatial functions), before and after ten daily 25-minutes tDCS sessions. Patients were randomized into two groups: anodal DMN stimulation (right parietal cortex), cathodal SN stimulation (right frontal cortex). Clinical and cognitive outcomes were compared by using the Wilcoxon signed-rank test.

Results: Patients were equally randomised to the anodal and cathodal arms (n=10 each). Cognitive assessment revealed significant improvement in memory in both groups (immediate Rey auditory verbal learning test: +20%, p<0.05 in the anodal group; +19%, p<0.05 in the cathodal group). A significant improvement in tests for visual memory (paired associative learning test; +6%, p=0.05), visuo-constructive abilities (clock test; +42%, p<0.05) and language comprehension (token test; +9%, p<0.01) was observed only in the anodal group. Conversely, improvement in behavioral symptoms (neuropsychiatric inventory: -36%, p<0.05) was found only in the cathodal group.

Conclusion: These results suggest that anodal tDCS may be more effective than cathodal tDCS in modulating cognition in AD, while cathodal tDCS may have a specific neuromodulator effect over behavior.

EPR2154

Pilot study evaluating the effects of percutaneous tibial nerve stimulation on sexual symptoms in neurological patients reporting overactive bladder

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Background and aims: The aim of this study is to investigate the effect of Percutaneous Tibial Nerve Stimulation (PTNS) on sexual symptoms in neurological patients receiving this treatment for overactive bladder symptoms.

Methods: This was an open-label pretest-posttest study conducted at the Uro-neurology outpatient clinic of a neurology hospital in London between February and September 2017. Sexually active neurological patients referred for PTNS treatment for overactive bladder symptoms were included in the study. ICIQ-LUTS questionnaire was used to evaluate urinary symptoms and ASEX, FSFI, IIEF-5, SQOL-F and SQOL-M questionnaires were used to assess sexual symptoms. The patients were re-assessed after 12 sessions of PTNS treatment.

Results: The mean age of the 12 patients participating in the study was 51.6±13.5 (mean±SD, range 26-70), 66.6% (n=8) female and most (75%) were ambulatory. Patients' ASEX scores decreased from 20 to 17.5 (p=0.05). On the FSFI questionnaire the total score and sub-score scores improved, with a statistically significant improvement in the desire sub-score (p=0.039). Improvement was observed in IIEF-5 scores in males (n=4), and sexual quality of life scores and urinary symptoms improved.

Conclusion: PTNS treatment was shown to improve urinary and sexual symptoms and quality of life in neurological patients reporting overactive bladder. This pilot study has shown that good outcomes can be achieved with the continuation of PTSU treatment, and it is suggested to be done in larger sample groups in future studies.

Keywords: Overactive bladder, percutaneous tibial nerve stimulation, sexual function, urinary symptom,

Disclosure: Nothing to disclose

Peripheral nerve disorders 3

EPR2155

The most sensitive test in the diagnosis of carpal tunnel syndrome

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Background and aims: Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy. In our study, we compared the sensitivity studies of the sensory nerves of the median sensory nerve with those of the first, second, third finger, palm and superficial radial nerves to determine the early diagnosis of CTS

Methods: For the patient group, 282 hands were included, while for the control group 62 limbs were included. Clinical neurophysiologic evaluation was performed according to the criteria determined by the Italian CTS (ITS) Working Group. Motor and sensory conduction velocities, latencies and amplitudes of unilateral or bilateral median, ulnar and radial nerves, were recorded by superficial electrode recording.

Results: 282 symptomatic hands were examined. Mild CTS in 35.1%, moderate CTS in 37.6% and severe CTS in 3,2% were found. 68 hands had normal electrophysiological findings, even though they had symptoms. This group was defined as the electrophysiological negative CTS group. Electrophysiological negative CTS group and control group were compared. There was no statistically significant difference between median and ulnar nerve motor conduction tests. Second finger and palm-wrist segment sensory latencies were longer in the negative electrophysiological CTS group. It was also observed that the velocities of sensory conduction in the second finger-wrist segment of the electrophysiological negative KTS group were decreased.

Conclusion: Routine electrophysiological studies are not enough in the diagnosis of CTS. In this case, palm-wrist segment sensory conduction study may be useful in addition to second finger-wrist segment examination

Disclosure: Nothing to disclose

EPR2156

Restabilisation treatment after IVIG Withdrawal in Chronic Inflammatory Demyelinating Polyneuropathy (CIDP): results from the PATH study

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Background and aims: In patients with chronic inflammatory demyelinating polyneuropathy (CIDP), the dose or frequency of intravenous immunoglobulin (IVIG) administration is recommended to be periodically reduced to assess the need for ongoing therapy. Little is known about the effectiveness of IVIG restabilisation in patients who worsen after IVIG withdrawal.

Methods: In PATH, a randomised, double-blind study of subcutaneous immunoglobulin in CIDP, IVIG therapy was withdrawn before randomisation. Subjects not deteriorating within 12 weeks of IVIG withdrawal discontinued the study as Ig dependency was not confirmed. Upon deterioration (increase in adjusted Inflammatory Neuropathy Cause and Treatment [INCAT] score), subjects received IVIG restabilisation with IgPro10 (Privigen®, CSL Behring): induction dose 2g/kg bw, maintenance doses 1g/kg bw every 3 weeks for up to 13 weeks.

Results: Of 245 subjects in whom IVIG was withdrawn, 28 (11.4%) did not deteriorate within 12 weeks. Another 10 subjects withdrew for other reasons, leaving 207 in the restabilisation phase. Of these 91% improved in at least 1 efficacy measure (improvement: 1 point in adjusted INCAT score, 4 points in RODS score, 8kPa in mean grip strength or 3 points in MRC score). Adjusted INCAT score improved in 72.9% with ~21% of subjects improving beyond their status at study entry. Improvements were seen in all secondary scores (Figure 1). Post-study follow-up of non-improving subjects revealed most subjects had improved.
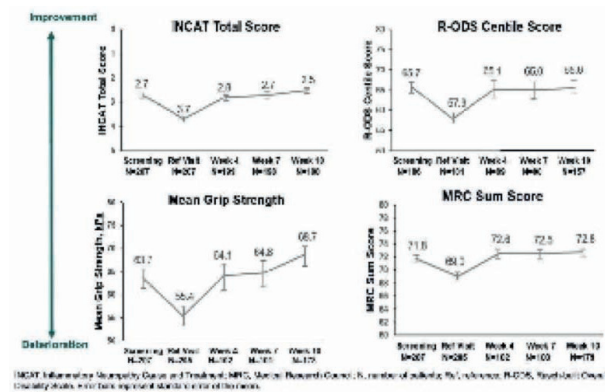
Figure 1. Efficacy of IgPro10 IVIG restabilisation therapy.

Conclusion: IVIG withdrawal was effective in detecting subjects not requiring IVIG therapy. For IVIG-dependent subjects, restabilisation with IgPro10 was effective in reversing observed deteriorations within 12 weeks.

Disclosure: This study is sponsored by CSL Behring

EPR2157

Efficacy and safety of intravenous Immunoglobulin (IVIG) IgPro10 in Chronic Inflammatory Demyelinating Polyneuropathy (CIDP): combined analysis of the PRIMA and PATH studies

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Background and aims: Efficacy and safety of intravenous immunoglobulin IgPro10 (Privigen®, CSL Behring) were investigated in CIDP subjects in two studies: PRIMA and PATH.

Methods: PRIMA was a prospective, open-label, single-arm study in 28 CIDP subjects investigating IgPro10 for induction (2g/kg) and maintenance therapy (1g/kg every 3 weeks for 21 weeks). This regimen was also used in 207 IVIG pretreated subjects during the 10–13 week restabilisation period of PATH (before randomisation to subcutaneous immunoglobulin vs placebo). Both studies investigated response (defined as ≥1 point decrease in adjusted Inflammatory Neuropathy Cause and Treatment [INCAT] score), changes in mean grip strength and Medical Research Council (MRC) score, and safety. We analysed separate and pooled results from both studies.

Results: INCAT response rate at last observation was 76.9% (95% confidence interval [CI]: 49.7–91.8) in PRIMA IVIG pretreated subjects (60.7% in all PRIMA subjects) and 72.9% (95% CI: 66.5–78.5) in PATH (Figure 1). In the pooled cohort (n=235), INCAT response rate was 71.1% (95% CI: 65.0–76.5; Table 1). Most responders improved by week 4; additional responses occurred up to week 13 (Table 1). Change from baseline to last observation in efficacy parameters is shown in Table 2. In the pooled cohort, 271 adverse drug reactions (ADRs) were reported in 105 subjects (44.7%), a rate of 0.144 ADRs per infusion.
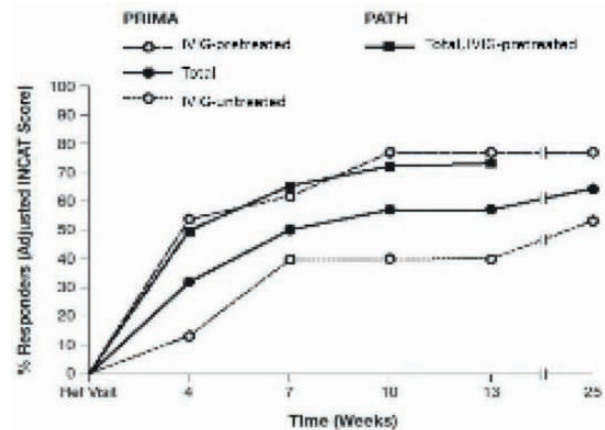
Figure 1. Response rate by INCAT in PRIMA and PATH

Response rate by adjusted INCAT, %	PRIMA IVIG-pretreated (n=13)	PRIMA IVIG-naïve (n=15)	PRIMA total (n=28)	PATH (all pre-treated) (n=207)	PATH and PRIMA pooled (N=235)
	76.9	46.7	60.7	72.9	71.1
Number of responders by adjusted INCAT by week, %					
Week 1	0.0	0.0	0.0	n/a	0.0
Week 4	53.8	13.3	32.1	49.8	47.7
Week 7	61.5	40.0	50.0	65.2	63.4
Week 10	76.9	40.0	57.1	72.0	70.2
Week 13	76.9	40.0	57.1	72.9	71.1
Week 16	76.9	40.0	57.1	n/a	n/a
Week 19	76.9	53.3	64.3	n/a	n/a
Week 22	76.9	53.3	64.3	n/a	n/a
Week 25	76.9	53.3	64.3	n/a	n/a

Table 1. Overall INCAT response rate and response rate by week from PRIMA and PATH as separate and pooled cohorts

	PRIMA IVIG-pretreated (n=13)	PRIMA IVIG-naïve (n=15)	PRIMA total (n=28)	PATH (all pre-treated) (n=207)
Adjusted INCAT score	-2.0	-1.0	-1.0	-1.0
MRC score	5.0	6.0	5.0	3.0
Grip strength, kPa [dominant hand]*	5.0	5.0	5.0	4.4

*Grip strength was assessed using a Jamar dynamometer in PRIMA and a Martin vigorimeter in PATH.

Table 2. Median change from baseline to last observation in efficacy endpoints in PRIMA and PATH

Conclusion: Pooled PRIMA/PATH data showed improvement in disability with IgPro10 in a large cohort of CIDP subjects. Improvement was seen at up to 10–13 weeks, suggesting some subjects may need multiple Ig doses to respond.

Disclosure: This study was sponsored by CSL Behring

EPR2158

Blink R1 latency as a sign of primary demyelination of the peripheral nerves in chronic inflammatory demyelinating polyneuropathy (CIDP)

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Background and aims: CIDP is one of the most common forms of autoimmune disease. Diagnosis of CIDP is based on clinical signs, electromyography (EMG) and biopsy.

Methods: The main group (MG) in our study consisted of 59 patients diagnosed with CIDP (mean age: 58.2 ± 17.2 years) based on neurological examination and EMG that meets international criteria for diagnosis of CIDP (INCAT, 2001). The control group (CG) had 31 individuals without any autoimmune disease. All patients underwent EMG, and a blinking reflex was also studied.

Results: 55 patients (93.22%) of MG had an increase of blink R1 latency (> 13ms). 2 people of CG had the blink R1 latency more than 13ms (6.45%). In the MG, the median of blink R1 latency was 15.1ms [13.9; 16.4]. In the CG, the median of blink R1 latency was 10.7ms [10.2; 11.5]. Statistically significant difference in the duration of blink R1 latency was found between the MG and the CG (Mann-Whitney criterion, $p < 0.001$). Direct correlations between the blink R1 latency and the F-wave of the tibial nerve ($r=0.317$, $p=0.023$) and also the F-wave of the ulnar nerve ($r=0.241$, $p=0.037$) were found.

Conclusion: Blink R1 latency may serve as a marker of demyelinating at CIDP. Thus, at difficult clinical cases with the increased blink R1 latency and the simultaneous sharp decrease or absence of the M-response from the peripheral nerves, it is possible to think about the primary demyelinating process.

Disclosure: Nothing to disclose

EPR2159

Functional disability, fatigue and depression as predictors of quality of life in MGUS polyneuropathy

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Background and aims: Monoclonal gammopathy of undetermined significance related polyneuropathy (MGUS-PNP) is a benign paraproteinemic neuropathy. Despite of being benign in nature, it has a chronic and progressive course, and therefore may highly affect quality of life (QoL). The aim of this study was to show how MGUS-PNP affects patients' QoL.

Methods: Our study included 51 patients diagnosed with MGUS-PNP (23.5% IgM, 66.7% IgG or IgA, 7.8% undetermined, 2.0% light chains). QoL was assessed using the SF-36 questionnaire. The Medical Research Council Sum Score for muscle strength, INCAT disability and sensory scores, Krupp's Fatigue Severity Scale, and Beck's Depression Inventory were also used.

Results: Total SF-36 score was 50.0 ± 21.4. Physical domains were somewhat more affected than mental, although both were significantly influenced by the disease (44.4 ± 21.4 vs. 54.5 ± 20.9, respectively). Following factors showed correlation with the SF-36 total score in a univariate analysis: INCAT disability score, INCAT sensory score, Medical Research Council Sum Score, ataxia, fatigue and depression ($p < 0.01$). Significant predictors of worse SF-36 total score in our MGUS-PNP patients were depression ($\beta = -0.46$, $p < 0.01$), more severe fatigue ($\beta = -0.32$, $p < 0.01$), and worse INCAT disability score ($\beta = -0.27$, $p < 0.01$).

Conclusion: MGUS-PNP patients with more severe functional disability, with presence of severe fatigue and depression need special attention of clinicians since they could be at higher risk to have worse QoL. This should be taken into account when treating MGUS-PNP subjects.

Disclosure: Nothing to disclose

EPR2160

Regenerative medicine approach for treatment of radix compression syndrome caused by herniated intervertebral discs

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Background and aims: In our clinical practice we applied the regenerative medicine methods with use of autologous cultured adipose-derived mesenchymal stromal cells (MSCs) for neurological patients with herniated discs and made the initial assessment of cell therapy safety and effectiveness.

Methods: Complex treatment of fifteen patients with nerve compression syndrome caused by herniated intervertebral discs in the cervical and lumbar spine level. Cultured stem cells were administered via paravertebral injection technique (20 million MSCs). The clinical application of stem cell therapy carried out on a base of patient's informed consent, MC ilaya Bioethics Committee approval, state licenses for medical practice of cells banking. To evaluate the results of treatment we use MRI and clinical methods. Patients received such an experimental treatment when standard drug therapies were ineffective and/or when patients refused of surgery or had somatic contraindications. The observation terms were 10 months.

Results: The use of cell therapy for the treatment of nerve compression syndrome caused by herniated disc resulted in relief of pain symptoms, disc extrusion reduction and complete regression of neurological deficit within 3-4 weeks. Clinical outcome was excellent or good in 86.7% of patients. At 10 months of observation, the hernia size regressed by an average of 5.3 ± 0.4 mm (95%CI 3.9-5.9). We check reduction in visual analog scale scores of pain for 5.3 ± 1.4 point (95% 3.5-6.7).

Before the treatment   In 3 months after cells input   In 10 month
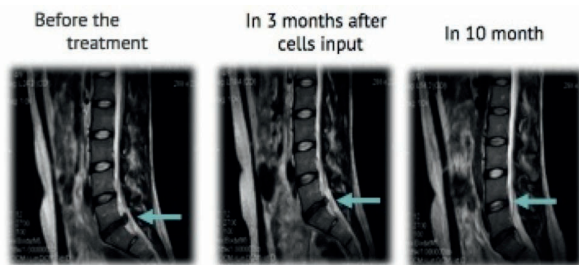
Conclusion: Pilot clinical study on cell therapy methods testing for neurorehabilitation of patients with herniated discs demonstrates the safety and effectiveness of chosen cell-based approach. However, it requires further evaluation within the planned clinical trial.

Disclosure: Nothing to disclose

EPR2161

Psychophysical evaluation of small-fibre function in diabetic patients using brief radiant heat and cold stimulation of skin

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Background and aims: Small-fibre neuropathy (SFN) is a common complication of diabetes mellitus. Yet, SFN is often recognised belatedly because routine techniques to assess small-fiber function are lacking. Our study aims to explore the potential of a novel psychophysical procedure based on brief heat or cold stimulation to assess SFN in diabetic patients.

Methods: Brief (100ms duration) temperature-controlled heat and cold stimuli were applied to the skin of the volar wrist and foot dorsum in 15 patients with diabetes mellitus type 2 (6 females; aged 55±4 years) and 15 age-matched healthy controls. Heat stimuli were delivered using a skin temperature feedback-controlled CO_2 laser (SIFEC, Ferrière, Belgium). Cold stimuli were delivered using a novel device based on micro-Peltier elements (TCS, Strasbourg, France). A Bayesian adaptive algorithm, the PSI method (Kingdom & Prins, 2010), allowed to estimate the threshold and the slope of the psychometric function for heat and cold detection using only 30 trials per run. Conventional electrophysiological tests were performed to assess large-fiber function.

Results: As compared to healthy controls, patients showed on average a significant reduction in detection performance of heat and cold stimuli, particularly in the lower limbs, even in the absence of large-fibre neuropathy. Higher diagnostic performance was achieved with cold than with heat testing.

Conclusion: This study supports the potential usefulness of this novel psychophysical procedure for the assessment of SFN in diabetic patients. Further studies are needed to assess the advantages over conventional methods for the early diagnosis of SFN.

Disclosure: This study was financially supported by an ERC Starting Grant (336130-PROBING-PAIN).

EPR2162

Impact of central nervous system and ocular phenotypes in ATTR V30M patients

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Background and aims: Central nervous system involvement in ATTR V30M is being increasingly recognised and understanding its natural history and impact on patients is fundamental to implement disease oriented treatment strategies. Ocular involvement is also recognised as a highly disabling feature in ATTR V30M patients, but the inter-action between brain and eye have not been addressed in the same cohort.
Methods: We have evaluated a consecutive and prospective series of 107 liver transplanted ATTR V30M patients. We characterised Focal Neurological Episodes (FNE) due to CNS dysfunction, ATTR ocular stage and neuroimaging findings (Focal brain lesions, brain atrophy and white matter damage).
Results: Over a 5-year period 45% of patients presented at least one FNE. Disease duration was the major determinant. Ocular involvement was present in over 90% of the patients. Ocular phenotype preceded CNS involvement in 70% of the patients. Clinical CNS involvement occurred first in 20%. There was no association between a specific ocular disease stage and CNS involvement. Neuroimaging disclosed 6 cases of non-traumatic intracranial brain hemorrhages with different locations (lobar, subarachnoid or cerebellar) as a feature of CNS involvement. White matter damage and brain atrophy were associated to longer disease duration.
Conclusion: Clinical brain and ocular findings are concomitant and are not prevented by liver transplantation. Disease duration is the major determinant of both phenotypes. Neuroimaging findings support that TTR related cerebral amyloid angiopathy contributes to this new clinical phenotype. The hemorrhagic risk of such vasculopathy, hints caution in acute stroke care or in primary stroke prevention of atrial fibrillation.
Disclosure: Nothing to disclose

EPR2163

Central nervous system complications in ATTR Met30 neuropathy, an epidemiological study in the Cypriot cohort of transplanted patients

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Background and aims: ATTRMet30 neuropathy is a lethal autosomal dominant sensorimotor and autonomic neuropathy. Liver transplantation has been the mainstay of treatment for the last 25 years and complications due to brain involvement are causing concern. Transient focal neurological episodes, seizures and brain haemorrhage signify leptomeningeal involvement. The frequency of brain involvement in transplanted patients is largely unknown.
Aims: To assess the prevalence of brain involvment in the Cypriot cohort of transplanted patients.
Methods: Epidemiological data were collected for all ATTRMet30 neuropathy patients at CING since 1992 . CING is the only tertiary neurology centre in Cyprus where all patients are been followed up. Demographic data on all transplanted patients were analysed including brain and ocular manifestations. Neurological complications included: Transient focal neurological episodes (TFNEs), seizures or strokes.
Results: In Cyprus 48 patients have been transplanted since 1992, 26M/22F. 10 patients out of 48 (20%) have developed CNS complications, 1M/9F. 3 have died as a result of a brain hemorrhage (30%), 8 patients had TFNEs Mean time from disease onset to TFNEs is 16 years (11-22) Onset of TFNEs is rarely sudden TFNEs tend to be stereotyped in any given patient duration is variable from minutes to hours All patients had ocular involvement
Conclusion: CNS complications in the Cypriot transplanted ATTRMet30 cohort in the last 25 years shows a minimum prevalence of 20%.
Mortality due to CNS complications is 30% in those that develop them and is due brain haemorrhage.
Disclosure: Nothing to disclose

Peripheral nerve disorders; Muscle and neuromuscular junction diseases

EPR2165

RCT assessing 2mg bumetanide as a therapeutic agent for a focal attack of weakness in Hypokalaemic Periodic Paralysis (HypoPP)

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Background and aims: HypoPP is a genetic disorder characterised by recurrent attacks of weakness in association with low serum potassium levels. Inhibition of the Na-K-2Cl cotransporter using Bumetanide may be a potential therapeutic strategy based on mouse model studies.
Methods: ClinicalTrials.gov Identifier: NCT02582476
An RCT was performed assessing if bumetanide could abort an episode of focal hand weakness in patients with HypoPP. A focal attack of weakness was induced by hand rest following exercise (McManis protocol). Participants received either placebo or 2mg bumetanide on two different occasions at the attack onset defined as 40% decrement in abductor digiti minimi (ADM) compound muscle action potential (CMAP) amplitude from the maximum response. Electrophysiological measurements assessed the severity and the duration of the attack following 4h of IMP intake.
Results: 9 participants completed both trial visits. There was no statistically significant difference in CMAP amplitude between the treatment groups at 1h (p=0.27, primary outcome). Two participants recovered from the attack of weakness (≤35% decrement in ADM CMAP amplitude from the maximum response) within 4 hours following bumetanide intake; none recovered following placebo intake (≥40% decrement). There were no serious adverse events.
Conclusion: 2mg bumetanide was safe but not effective to rescue a focal attack in an immobilised hand in the majority of patients. However, our data supports further studies of this agent. The McManis test used as an objective outcome measure in a clinical trial for the first time was well tolerated.
Disclosure: Nothing to disclose

EPR2166

Oral immunosuppressive treatment of myasthenia gravis in Denmark: a nationwide drug utilisation study, 1996-2013.

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Background and aims: In recent years, several myasthenia management guidelines have been published but population-based studies describing drug utilisation in myasthenia patients are scarce. We aimed in this study to describe the treatment of myasthenia in Denmark in more recent years with emphasis on use of oral immunosuppressant agents.
Methods: Using a validated method, we identified a nationwide cohort of incident myasthenia patients in Denmark in 1996 to 2013 and tracked their use of drugs using data from nationwide registers. Patients with myasthenia were classified according to utilisation of specific immunosuppressants (e.g. prednisolone) as "never user" or "ever user". We used Kaplan-Meier (K-M) and Proportion of Patients Covered (PPC) curves to describe treatment onset and termination.
Results: We identified 928 patients (52% female) with incident myasthenia in the study period. Overall, 638 (69%) were treated with prednisolone and 506 (55%) with azathioprine. Treatment with prednisolone and azathioprine within two years of myasthenia diagnosis was initiated in 462 (56%) and 366 (45%). Only one out of four myasthenia patients (n=231) did not receive oral immunosuppressive treatment at any time in the study period. Prednisolone was stopped in most patients, whereas treatment with azathioprine was often continued throughout follow-up.
Conclusion: Treatment of myasthenia in Denmark in recent years corresponded well to the expected clinical course of myasthenia and was in line with recently published guidelines. Long-term immunosuppressive treatment in the treatment of myasthenia is used extensively in Denmark.
Disclosure: Nothing to disclose

EPR2167

Novel COL6A3 mutation with an autosomal dominant inheritance pattern in a family affected by Bethlem myopathy

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Background and aims: Bethlem myopathy (BM) is one entity of spectrum of collagen VI disorders with autosomal dominant inheritance, which is caused by mutations in the genes COL6A1, COL6A2 and COL6A3. It's characterised by mild fenotype with an early-onset and slowly progressive. We present a family with heterozygous COL6A3 mutation, located in exon 19 c.6360_6322del, not previously reported in collagen VI-related myopathies.

Methods: A 58-year-old male with a history of poliomyelitis without sequels was referred for progressive weakness with difficulty raising his arms above his head, getting up and going up the stairs for 5 years. He needed a unilateral support to walk. Non-consanguineous parents. Neurological examination revealed mild weakness of shoulder girdle and proximal upper limb muscles and slight weakness of hip girdle muscles, mild rigidity of the spine and positive Gower's sign.

Results: Creatine kinase was slightly high. Electromyography showed myopathic pattern (ruled out post-polio syndrome). MRI showed lower limb muscles affectation with peripheral fatty infiltration with sparing of the central part, which is very specific sign of collagen VI-related myopathies. Muscle biopsy without specific pattern. Genetic analysis revealed a heterozygous COL6A3 mutation, located in exon 19 c.6360_6322del not previously reported. Two patient's sisters with clinical manifestations, pathologic neurological examination and MRI presented the heterozygous COL6A3 mutation. One of seven members of next generation presented the same mutation.

Conclusion: This case reports a novel mutation in COL6A3 gene located in exon 19 c.6360_6322del with an autosomal dominant inheritance pattern.

Disclosure: Nothing to disclose

EPR2168

Patient demographics and clinical features of chronic inflammatory demyelinating polyneuropathy – an observational study In Turkey

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Background and aims: Chronic inflammatory demyelinating polyneuropathy (CIDP) is the most common treatable chronic neuropathy worldwide. We present the demographic and clinical features of 65 CIDP patients.

Methods: Patient charts of 139 cases with immune mediated demyelinating neuropathy treated at the Neuromuscular Unit between 1993 and 2017 were reviewed for CIDP retrospectively. Cases with an associated paraprotein were excluded.

Results: We identified 65 patients who fulfilled the 2010 EFNS/PNS diagnostic criteria for definite (n=64) or probable (n=1) CIDP. Among 65 patients (43 male, 22 female), 49% typical CIDP, 31% multifocal acquired demyelinating sensory and motor (MADSAM) neuropathy, 18% distal acquired demyelinating symmetric (DADS) neuropathy, 2% pure sensory CIDP were determined. The mean age of symptom onset was 36.95±18.53 years. Twenty percent had juvenile-onset. Patients who had at least one outpatient clinic visit in the past year (n=43) were evaluated using CIDP disease activity status (CDAS), 9% were cured, 19% were in remission, 42% had active stable disease, 9% were improving and 21% had unstable active disease. The majority of the unstable active disease cases had MADSAM(5/9, 56%). Disability was assessed using inflammatory neuropathy cause and treatment disability score(INCAT). The mean INCAT disability score of MADSAM patients was higher than the others (Mean 1.9).

Conclusion: The mean age of onset was younger then literature however the ratio of patients with childhood-onset was higher. MADSAM, the most common clinical phenotype among atypical variants of CIDP in our cohort was more frequent than the literature. MADSAM patients had higher disability scores and were more likely to have unstable active disease.

Disclosure: Nothing to disclose

EPR2169

The first Portuguese kindred with NEFL-related Charcot-Marie-Tooth type-2 disease: a case report

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Background and aims: Charcot-Marie-Tooth disease (CMT) comprises a heterogeneous group of inherited neuropathies clinically characterised by progressive, distal-predominant weakness, amyotrophy, and sensory loss. NEFL-related CMT is a rare form of inherited neuropathy, accounting for less than 1% of all CMT cases, and obvious genotype-phenotype correlations have not been established so far. We describe the first Portuguese CMT2 patient with c.794A>G NEFL mutation.

Methods: Case report

Results: A 67-year-old woman presented progressive weakness and atrophy of distal limb muscles, with hammer toes and pes cavus, stocking-glove pattern of algic hypoesthesia, absent ankle reflexes, mild positional and vibration sensory loss and sensory ataxia. She also presented a mild cerebellar ataxia and pyramidal signs. These symptoms were first noticed by the age of 42 years. No palpably enlarged hypertrophic peripheral nerves were noted. The nerve conduction studies were compatible with sensory-motor axonal neuropathy. The patient's parents were first-degree cousins, and her mother and daughter presented a similar clinical picture.

Mutation analysis of NEFL gene revealed a c.794A>G mutation in heterozygosity. This missense mutation has previously been reported as likely pathogenic, and therefore we performed a co-segregation analysis in her affected daughter, that was also positive for this mutation.

Conclusion: As far as we know this is the first Portuguese case of CMT2E described. This mutation (c.794A>G) was only previously described in another family, in Australia; this family also presented pyramidal signs, but no cerebellar ataxia. We believe this further widens the phenotypic expression associated with this mutation.

Disclosure: Nothing to disclose

EPR2170

Predictive factors of long-term disability in CIDP

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Background and aims: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a disabling disease and about 10% of patients may become persistently disabled over time. Our aim was to identify clinical prognostic factors of long-term disability in a large series of CIDP patients.

Methods: We collected data from 53 CIDP patients with definite diagnosis according EFNS/PNS criteria and positive response to first-line therapies (immunoglobulin or corticosteroids) including sex, age of onset, phenotype, disease duration, course of disease (monophasic/relapsing-remitting, chronic progressive) and disability at the time of diagnosis assessed using the modified Rankin Scale (baseline mRS). All patients had clinical assessment of disability through mRS within the last 6 months (last mRS). Ordinal logistic regression model was applied to evaluate the relationship among the clinical parameters and last mRS, considered as ordinal outcome (0-6). Anova test for repeated measures was applied to test the overall effects of different course on disability accumulation while t-test was performed to evaluate inter-group differences for parametric variables

Results: We found a significant relationship between last mRS and the course of disease [p<0.000, z=4.05, OR: 14.91]. Disability accumulation was greater in patients with chronic progressive course than those with monophasic/relapsing-remitting course of disease [p=0.04]. Moreover, patients with progressive course were older [p=0.01].

Conclusion: Our data suggest that chronic progressive course of disease may be a major negative prognostic factor for long-term disability in CIDP patients. To note that a chronic progressive course of disease is also associated with an older age from the beginning and a more pronounced worsening over the course of disease.

Disclosure: Nothing to disclose

EPR2171

EFNS/PNS Guidelines for CIDP and MMN: an international audit of perceived value and usefulness amongst clinicians

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Background and aims: Disease management guidelines have unproven uptake and unconfirmed role in real-life clinical practice. We conducted a prospective web-based international audit on the knowledge about and use of European Federation of Neurological Societies/Peripheral Nerve Society Guidelines for chronic inflammatory demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy (MMN) amongst neurologists from a total of nine countries. The project was funded by the EFNS. The global response rate was very low. There was a significantly greater response from by subspecialists in the field. Awareness of the guidelines was higher amongst subspecialists. Although felt helpful, the guidelines did not appear to influence diagnostic and therapeutic management decisions for the majority of subspecialist responders. The guidelines were considered by most to be a useful teaching and training tool and were felt by the majority to represent the most adequate set of criteria and recommendations available for these disorders. We conclude that the clinical value of guidelines for rare disorders such as CIDP and MMN may be limited in general neurological practice. Clinical uptake and usefulness remains incomplete for subspecialists. Further work and research is needed to determine ways of optimising uptake and increasing use as well as interest in the wider neurological community, for future revisions. EFNS/PNS Guidelines are the best known and most used in CIDP and MMN and are of important educational value.

Disclosure: References: EFNS/PNSguideline on management of chronic inflammatorydemyelinating polyradiculoneuropathy: report of a jointTF of the EFNS and the PNS - first revision. Van den Bergh PY, Hadden RD, Bouche P, Cornblath DR, Hahn A, Illa I, Koski CL, Léger JM, Nobile-Orazio E, Pollard J, Sommer C, van Doorn PA, van Schaik IN; EFNS; PNS. EJON. 2010 Mar;17(3):356-63. EFNS/PNS guideline on management of multifocal motor neuropathy. Report of a joint TF of the EFNS and the PNS--first revision. JointTF of the EFNS and thePNS J Peripher Nerv Syst. 2010 Dec;15(4):295-301.

Monday, June 18 2018

Ageing and dementia 3

EPR1155

Event-related cerebral dynamics during mirror movement of hand closing

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Background and aims: Upper extremity mirror rehabilitation is recently used to let a stroke patient induce the movement of affected arm by parallel watching the mirrored movement of unaffected arm. The mirror training has been demonstrated useful in motor improvement but the corresponding neuromuscular processing is less investigated. In this study, event-related cerebral dynamics and corticomuscular coherences during simulated mirror hand movement is investigated.

Methods: 16 healthy adults were included for a movement experiment of right-hand closing then opening but left-hand keeping still under mirror feedback of right-hand movement (MF condition) or watching right-hand movement (non-MF condition). 32-channel electroencephalograms and electromyograms of flexor digitorum profundus and extensor digitorum were parallel recorded.

Results: MF caused significant alpha-band (8-12 Hz) event-related synchronization at CP4 and P4 prior to hand closing than non-MF did and significant weakened beta-band (13-30 Hz) event-related desynchronization at C4, CP4 and P4 compared to their contralateral sites during hand closing. This implies that the MF evoked more somatosensory processing prior to motor execution and reduced cerebral demands during hand closing in the right hemisphere. In addition, MF yielded significant higher peak corticomuscular coherence of F4 and FC4 versus right flexor than non-MF did. The MF may enhance the corresponding association between muscular activity of right-hand closing and right frontal-central operation.

Conclusion: MF is shown to induce a significant enhancement of somatosensory processing and corticomuscular link.

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EPR3001

Executive dysfunction is a predictive factor of cognitive decline in early onset Alzheimer's Disease

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Background and aims: Alzheimer's disease (AD) is the most common cause of dementia under 65 years. In the absence of curative treatment, the current strategy remains to slow the progression of the disease.

The aim of our study was to identify predictive factors of rapid cognitive in Early Onset Alzheimer's Disease (EOAD).

Methods: We included the first 84 consecutive patients younger than 60 years old at the time of the first symptoms of a probable or certain AD according Mckhann's et al 2011 criteria, with a Mini Mental State Examination (MMSE) greater than 10, included at Lille hospital in the COMAJ cohort between July 2009 and February 2015. For each patient, we reported its clinical, biological, radiological characteristics, the results of the first cognitive screening tests, and their cognitive treatment. Cognitive decline was measured by the difference between MMSE at inclusion and after 2 years of follow-up. We identified three groups of patients declining according to the progression: slow, intermediate or fast.

Results: After 2 years of follow-up, 6 points was the median cognitive decline on the MMSE. After a logistic regression, a low score at the Rapid Battery of Frontal Efficiency at inclusion in the cohort was the only predictor of rapid cognitive decline ($p < 0.02$).

Conclusion: In conclusion, severe alteration of executive functions may predict a poor prognosis at 2 years.

Disclosure: Nothing to disclose

EPR3002

Diagnosing frontotemporal dementia: clinico-pathological correlations in the Dutch population

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Background and aims: Over the past years a tremendous growth of knowledge in FTD pathology has occurred, including the identification of novel TDP-43 molecular pathological subgroups. In addition, the diagnostic criteria for clinical subgroups of behavioural-variant FTD and primary progressive aphasia have been updated, providing a more accurate diagnostic framework for clinicians. However, due to the overlap in clinical symptoms with other dementia's and with psychiatric disorders, diagnosing FTD in sporadic patients remains challenging. Here, we aim to assess the agreement between clinical and pathological diagnoses over the past ten years, and explore clinical symptoms that concur within a pathological subgroup.
Methods: Donors with a clinical primary FTD diagnosis, or FTD diagnosis during their disease duration, were selected from the Netherlands Brain Bank Cohort (n=108). Extensive clinical information was available from all donors. Psychiatric and diagnostic clinical features were retrospectively scored, and pathological molecular subgroup was determined. Comparisons between pathological subgroups were made with chi-square test.
Results: The overall clinical-pathological agreement was 71%. Since the introduction of the new criteria diagnostic accuracy has improved (from 68% to 88%). Within our cohort 43 donors had FTD-TDP pathology and 30 FTD-Tau pathology. We found that hallucinations were more prevalent in donors with FTD-TDP pathology (p<0,05).
Conclusion: The current diagnostic criteria have improved the agreement between clinical and pathological diagnosis. In addition, in our cohort hallucinations were more frequent in FTD-TDP compared to FTD-tau , which suggests it can be used as a tool to differentiate pathological subgroups in patients with FTD.
Disclosure: Nothing to disclose

EPR3003

Peripapillary retinal nerve fiber layer thickness and macular ganglion cell layer volume are reduced in Alzheimer's disease

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Background and aims: Alzheimer's disease (AD) represents a great medical challenge in the Third Millennium. Great efforts have been produced to develop disease-modifying drugs. Reproducible, easy to handle progression markers are needed to monitor the response to treatment. Since AD pathological hallmarks were found in retinas of AD patients, OCT might reliably detect pathological changes occurring in AD retinas
Methods: 145 subjects were involved in this study (49 with AD, 39 with Mild Cognitive Impairment, MCI and 57 healthy controls, HC), receiving an OCT scan acquisition at baseline. CSF AD biomarkers (Aβ42, t-tau and p-tau) and neuropsychological assessment were available, as well. 19 AD and 23 MCI underwent a follow-up OCT scan
Results: At baseline, peripapillary RNFL, both global and in superior quadrant, was significantly thinner in AD and MCI patients than in HC (global: AD: 91.56±10.5, MCI: 93.26±9.8, HC: 98.44±8.36μm; superior: AD: 108±17.8, MCI: 113.96±14.8, HC: 124.3±12.99μm, p<0.05). Macular GCL volume was significantly reduced in AD (AD: 0.95±0.9; MCI: 1.03±0.87; HC: 1.05±0.68mm³, p<0.05). Over time, AD patients showed a significantly higher decay in global RNFL thickness than MCI subjects (-2.28±2.99 vs. -0.72±1.94μm/year). RNFL, GCL and IPL thinning over time was positively associated with worsening in cognition
Conclusion: OCT might reflect the current disease stage in which patients are and seems to correlate with worsening in cognition. Therefore, OCT might be considered as a possible disease progression marker
Disclosure: Nothing to disclose

EPR3004

Cognitive impairment in patients with Parkinson's disease dementia and dementia with Lewy bodies in Slovenia (2010–2015)

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Background and aims: There is a considerable overlap in clinical presentation of Parkinson's disease dementia (PDD) and dementia with Lewy bodies (DLB) suggesting common disease spectrum. We aimed to describe and compare cognitive impairment (CI) and management in PDD vs DLB.

Methods: We reviewed the medical records of PDD and DLB patients who attended the movement disorders clinic at the UMC Ljubljana, Slovenia, in the period between 2010–2015, using a retrospective cross-sectional study design. Assessment of CI was based on Mini-Mental State Exam (MMSE) score. Demographic characteristics and risk factors for cognitive impairment were analysed.

Results: 204 PDD and 50 DLB patients were included in the study. Mean age for PDD was 77.9±7.9 years, DLB 78.1±6.3 years, disease duration: PD 12.2±6.1 years and 6.6±3.8 years for DLB. Duration of CI in PDD was 4.8±2.9 years, DLB 6.0±4.0 years. The first recorded MMSE score was 25.0±3.6 in PDD vs. 22.3±3.9 for DLB and the mean two years rate of cognitive decline for PDD was -1.2±3.9 points vs. -3.8±3.3 points for DLB. Acetylcholinesterase inhibitors were used in 86% of PDD and 92% of DLB patients. Antidepressants were used equally in 44% and antipsychotics in 44% of PDD vs 60% of DLB patients.

Conclusion: Patients with DLB have more rapid cognitive decline and are more commonly treated with antipsychotics than PDD patients. This was the first study to describe and compare the characteristics and management of cognitive decline in PDD and DLB patients in Slovenia.

Disclosure: Nothing to disclose

EPR3006

Retina changes in Alzheimer's disease: potential biomarker for dementia

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Background and aims: A relatively new concept in neurodegenerative diseases claims that the retina can be used as a window to look into the brain. Structural retinal imaging biomarkers are important for early recognition and monitoring of neurodegeneration in Alzheimer's disease (AD). With the introduction of Optical Coherence Tomography (OCT), a non-invasive approach, supervised segmentation of retinal layers is possible. We aim to investigate which retinal layers show atrophy associated with neurodegeneration in AD and the correlation with disease variants and other biomarkers.

Methods: Patients with diagnosis of mild AD, between 55 and 75 years, without ophthalmologic pathology, were selected. The protocol included: clinical assessment, neuroftalmologic evaluation (retinal and optic nerve structures evaluated by OCT), neuropsychological assessment, CSF biomarkers, C11 PiB-PET and alipoprotein E.

Results: We included 20 patients, mean age 66 years, 9 years of education. All patients were positive for amyloid deposits in C11-PiB-PET. Patients that recently converted to AD presented higher total retinal thickness than those with a longer evolution time, as well as in the IPL-OD, OPL-OD, ONL layers. There was no relationship between neuropsychological tests, apoE4 allel and retinal thickness. However, considering clinical subtypes, the visual forms presented Outer Segment thicker than mnesic forms. Regarding CSF biomarkers, higher p-tau correlated with smaller OPL thickness (p<0.001).

Conclusion: Retinal atrophy seems to be related with evolution time of AD. The mnesic variants showed a greater atrophy compared to visual forms of the disease, especially in the Outer Segment layer. OPL atrophy layer correlated with a greater evidence of CSF degeneration biomarkers.

Disclosure: Nothing to disclose

EPR3007

Clinical variability in Gerstmann-Sträussler-Scheinker syndrome with the P102L mutation - a study of 6 cases and retrospective analysis of 80 cases reported in the literature

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Background and aims: P102L Gerstmann-Sträussler-Scheinker syndrome (P102L-GSS) is a rare genetic prion disease caused mutation at codon 102 in the prion protein gene. Clinical presentation includes early ataxia with gait disturbance, sensory symptoms in lower extremities and late cognitive decline, but clinical presentation is highly variable.

Methods: We compared data from six Czech patients with neuropathologically confirmed P102L-GSS and retrospective data from 80 published P102L-GSS cases. We focused on gender, onset of disease, duration of disease, onset of dementia (in the first 2 years of disease, late, none), duration of cognitive impairment, ataxia (early, late, none), MRI brain abnormalities (basal ganglia, cortex, and cerebellum), polymorphism in codon 129 and 219, changes in deep tendon reflexes and sensory symptoms. We used descriptive statistics; Wilcoxon-Mann-Whitney parametric hypothesis test, principle component analysis, Mardia multivariate analysis of normality a DBscan cluster analysis to define typical phenotypes of GSS syndrome.

Results: GSS is probably far more common than previously estimated and cluster analysis of our patients and data from previously published cases suggest the existence of three GSS clinical phenotypes ("classical GSS", "GSS with areflexia and paresthesia" and "GSS with dominant dementia") with distinct disease duration and clinical manifestation.
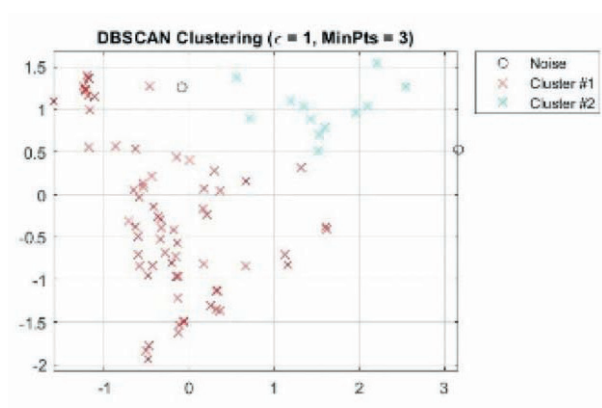
Figure 1. DBscan analysis of 3 PCA components, epsilon=1
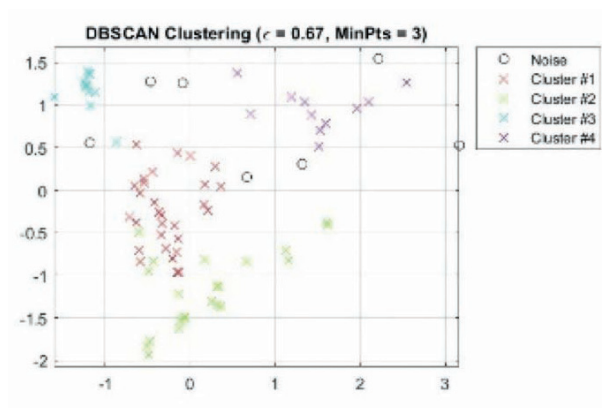
Figure 2. DBscan analysis of 3 PCA components, epsilon=0,67

Conclusion: GSS is a rare genetic disease with probably higher prevalence that previously estimated and despite its clinical variability, different phenotypical groups may be identified. Supported by program Progress Q27/LF1 (Charles University, Prague, Czech Republic)

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Autonomic nervous system

EPR3008

Adrenergic hyperactivity: a missing link between multiple sclerosis and cardiovascular comorbidities?

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Background and aims: Impaired autonomic control of cardiovascular function has been reported in a large proportion of patients with Multiple Sclerosis (pwMS). The implications of this may be numerous, especially due to an increased risk of ischemic heart disease and congestive heart failure in pwMS. The aim of his study was to investigate differences in non-standard adrenergic baroreflex sensitivity (BRS) indices in patients with different phenotypes of pwMS and healthy controls (HC).

Methods: Retrospective analysis of types of systolic blood pressure (BP) curves during Valsalva maneuver (VM) (balanced (BAR), augmented (AAR) and suppressed (SAR) autonomic responses) and adrenergic baroreflex sensitivity measured with BRSa1, α-BRSa and β-BRSa in patients with clinically isolated syndrome (CIS), relapsing remitting Multiple Sclerosis (RRMS), progressive multiple sclerosis (PMS) and HC. We also investigated correlations between BRSa1, α-BRSa, β-BRSa and resting catecholamines levels.

Results: pwMS had higher α-BRSa compared to HC (p=0.02). There was no difference in BRSa1, α-BRSa and β-BRSa between patients with CIS, RRMS and PMS. There was no association between pwMS and HC and the type of sBP curve ($\chi(2)$=4.332, p=0.114). pwMS and BAR or AAR had higher supine systolic and diastolic BP compared pwMS and SAR. There was a significant correlation between α-BRSa and upright systolic BP (rp =0.194, p=0.017) (Fugure 1), α-BRSa and norepinephrine (rs =0.228, p= 0.021) (Figure 2) and BRSa1 and epinephrine (rs =0.226, p=0.040).
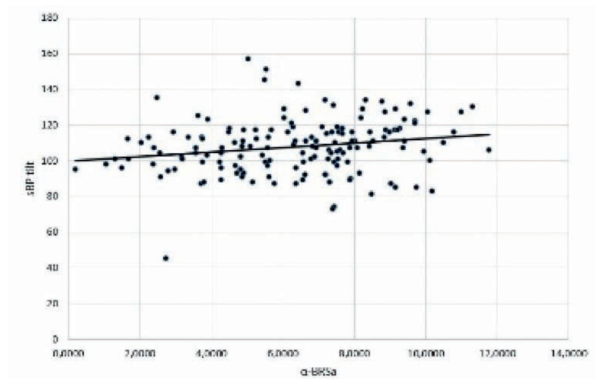
Correlation between α-BRSa and systolic BP in the tilted position.
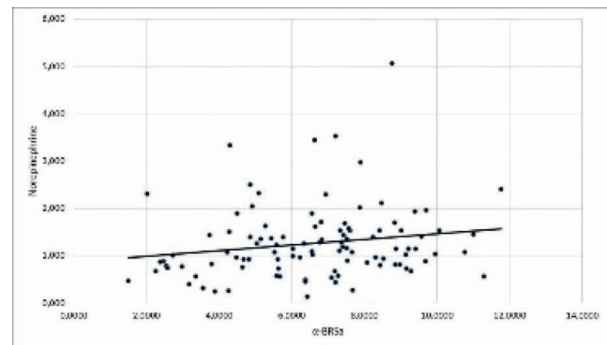
Correlations between α-BRSa and norepinephrine.

Conclusion: pwMS and HC exhibit different alpha-adrenergic response to Valsalva maneuver. These results may explain the connection between MS and increased cardiovascular risk.

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EPR3009

Joint hypermobility is related to pathological finding on tilt table testing

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Background and aims: Aim of this study was to evaluate the association of generalized joint hypermobility, expressed by Beighton score (BS), and pathological findings on head-up tilt table test (HUTT).

Methods: Prospective study that included consecutive patients referred for the HUTT. Generalised joint hypermobility was evaluated according to the BS system. Clinically significant BS was considered if ≥4.

Results: 115 patients met the inclusion criteria (91 females, mean age 34.35±14.11). BS was 0 in 65 (56.5%) and ≥1 in 50 (43.5%) patients. HUTT was normal in 58 (50.4%) patients, 15 (13.0%) patients fulfilled criteria for OH, 30 (26,1%) for syncope and 21 (18,3%) for POTS. Patients with pathological findings on HUTT had significantly higher BS compared to patients with normal HUTT (median 1 vs. 0, p=0.001). The same finding was observed for patients with OH, POTS and syncope (Table 1). We found significant association between participants with BS ≥4 and pathological HUTT and also with each type of pathology (Table 2). A multivariate logistic regression was performed in order to examine the influence of gender, age and BS on the likelihood that patients have HUTT pathology ($\chi2(3)$=18.009, p<0.001) and it correctly classified 71.3% of cases. Increase in the BS was associated with increased likelihood of HUTT pathology (Exp(B) 1.44, 95%CI 1.084 – 1.922, p=0.012), while increase in age was associate with lower risk of HUTT pathology (Exp(B) 0.968, 95%CI 0.939 – 0.998, p=0.036).

HUTT		BS				
		Median	Range	Mean Rank	Sum of Ranks	p
HUTT pathology	No	0	0-5	49.10	2848.00	0.001
	Yes	1	0-9	67.05	3822.00	
OH	No	0	0-5	33.45	1940.00	0.001
	Yes	2	0-8	50.73	761.00	
POTS	No	0	0-5	36.95	2143.00	0.023
	Yes	1	0-5	18.43	1017.00	
Syncope	No	0	0-5	40.22	2332.50	0.012
	Yes	1	0-9	52.78	1583.50	

Table 1. Difference in the Beighton score regarding the HUTT pathology. HUTT – head-up tilt table test. BS – Beighton score. OH – orthostatic hypotension. POTS – postural orthostatic tachycardia syndrome.

		BS 0	BS ≥4	p
HUTT pathology	No	55	3	0.011
	Yes	45	12	
OH	No	55	3	0.012
	Yes	11	4	
POTS	No	55	3	0.015
	Yes	16	5	
Syncope	No	55	3	0.030
	Yes	24	6	

Table 2. Association between participants with BS ≥4 and HUTT pathology. BS – Beighton score. HUTT – head-up tilt table test. OH – orthostatic hypotension. POTS – postural orthostatic tachycardia syndrome.

Conclusion: Results of this study demonstrate an association of joint hypermobility features and pathological findings on HUTT.

Disclosure: Nothing to disclose

EPR3010

Evolution of dysautonomia in people with clinically isolated syndrome over two-year follow-up

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Background and aims: The Composite Autonomic Scoring Scale (CASS) has been validated for assessment of dysauotnomia in people with clinically isolated syndrome (pwCIS). Dysautonomia in pwCIS is restricted to sympathetic nervous system involvement. The aim of this study was to investigate the evolution of dysautonomia in pwCIS over two-year follow-up.

Methods: In 59 pwCIS (45 females, mean age 31.88±9.12) CASS was performed during the CIS diagnosis and 24 months later. Baseline Expanded Disability Status Scale (EDSS) and Multiple Sclerosis Functional Composite were performed at baseline and month 24 visit.

Results: Baseline median CASS was 1 (0-4) (adrenergic 0 (0-3), cardiovagal 0 (0-1) and sudomotor 0 (0-2)). At M24, median CASS was 1 (0-5) (adrenergic 0 (0-3), cardiovagal 0 (0-1) and sudomotor 0 (0-3)). Out of 47 patients with all data available for analysis, increase in CASS was identified in 22 (47%), improvement in 15 (32%) and 10 patients (21%) had no change in CASS. Baseline median EDSS was 2 (0-3.5) and median MSFC was 0.057 (-2.089-1.343). There was no difference in baseline EDSS in patient with and without progression of dysautonomia measured with CASS. However, those patients who progressed in CASS had higher EDSS at M24 (2 vs 1, p=0.012). Furthermore, patients who had progressed in CASS, had worse baseline MSFC (0.458 vs. -0.246, p=0.004). According to binary logistic regression model, baseline MSFC is statistically significant predictor for worsening in dysautonomica measured with CASS (Exp(B)=0.343, p=0.023).

Conclusion: Substantial proportion of pwCIS experience worsening of CASS over 24 months of follow-up.

Disclosure: Funded by the Installation Research project HRZZ UIP-11-2013-2622 of the Croatian Science Foundation.

EPR3011

Autonomic nervous system involvement in patients with neuromyelitis optica spectrum disorders

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Background and aims: Autonomic dysfunction (AD) occur in patients with multiple sclerosis (MS), and until now, it has not been investigated in patients with neuromyelitis optica spectrum disorders (NMOSD). Therefore, the aim of our study was to analyse its presence in patients with NMOSD.

Methods: 20 NMOSD (16 females, mean age 47.2±10.7 years, median EDSS 2.5, median disease duration 88.5 months, and 14 NMO-IgG positive) patients from two University hospital centers were enrolled. Dysautonomia was evaluated subjectively with the Composite Autonomic Symptom Score (COMPASS 31), and additionally, objectively, with the following autonomic tests: heart rate and blood pressure responses to the Valsalva maneuver, heart rate response to deep breathing (RSA), blood pressure response to passive tilt. All tests were interpreted in the form of the adrenergic and cardiovagal indices, parts of the Composite Autonomic Scoring Scale (CASS).

Results: All participants had COMPASS 31 score >0. Median value of the total score was 12.2 (orthostatic intolerance 2.0, vasomotor 0, secretomotor 1.1, gastrointestinal 3.6, bladder 1.1, pupillomotor 1.3). Pathological adrenergic and cardiovagal indices of the CASS were present in 8 (42.1%) and 10 (50.0%) patients, respectively. Median (range) of the adrenergic and cardiovagal indices was 0 (0-3) and 0.5 (0-1), respectively. There was no correlation between disease duration and EDSS with neither the COMPASS, nor the CASS variables. There was significant correlation between adrenergic index and bladder domain of the COMPASS 31 (r=0.559, p=0.015).

Conclusion: AD is frequent in patients with NMOSD and shows different pattern compared to patients with MS.

Disclosure: Nothing to disclose

EPR3012

Frequency of the invalidity of tachicardia pick in patients with peripheral sensory diabetic polyneuropatie

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Background and aims: Tachycardia at rest is often the first symptom of cardiovascular autonomic neuropathy and therefore has high diagnostic value in the early detection of serious cardiac dysregulation, including sudden death syndrome in type-2 diabetes mellitus (DM 2).

Methods: Surveyed 83 patients with type-2 diabetes (52 women and 31 men) aged 43 to 65 years (53,8±7.96 years) with an average duration of diabetes in the range of 7.04±3.73 years. All patients had various symptoms of peripheral sensory diabetic polyneuropathy (DPN) without active complaints of the cardiovascular system (CVS)

Results: The main sensory complaints were pain and burning sensation in the feet - in 56% of patients, numbness of the toes - in 47%, fast fatigue with minor physical exertion - in 58%. In a physical examination, tachycardia at rest (> 90 beats/min) was detected in 43% of patients with type-2 diabetes with sensory DPN without active cardiac complaints. Asymptomatic tachycardia at rest without cardiac arrhythmias was registered in 67% of patients. Such a high frequency of occurrence of diabetic autonomic neuropathy (DAN) in patients with sensory DPN is due to the failure of the small unmyelinated sensory sympathetic and parasympathetic fibers under the influence of chronic hyperglycemia

Conclusion: Thus, in patients with diabetes mellitus with sensory DPN, it is advisable to actively detect signs of autonomic cardiac dysfunction during routine clinical monitoring, as well as to conduct instrumental studies for early detection and intensive correction of cardiovascular risk factors to prevent fatal complications of type-2 diabetes.

Disclosure: Nothing to disclose

EPR3014

Hemodynamic changes during tilt table test: neurogenic orthostatic hypotension or vasovagal syncope? Towards improved hemodynamic criteria to distinguish between neurogenic orthostatic hypotension and vasovagal syncope during tilt-table testing

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Background and aims: Current criteria may not distinguish sufficiently well between neurogenic orthostatic hypotension (nOH) and vasovagal syncope (VVS) in tilt table tests (TTT). We explored additional criteria.

Methods: TTT data were gathered from our tertiary Syncope Unit. Inclusion criteria for VVS were a history of VVS and symptoms, complaint recognition, blood pressure (BP) drop and EEG changes during TTT. Inclusion criteria for nOH were a history of nOH and a BP decrease following the 2011 consensus. Clinical diagnoses were established prior to TTT. Exclusion criteria were incomplete data, age<16 years, concurrent nOH and VVS and additional diagnoses. We defined (1) the overall shape of systolic BP (i.e. whether the BP drop accelerated –convex- or decelerated –concave-; (2) when half the BP drop was reached, relative to tilt-up and tilt-back; (3) the direction of HR change at the BP nadir (up or down).

Results: We included 43 VVS and 42 nOH cases. For nOH, 83% had a concave BP pattern and for VVS 95% had a convex pattern (p<0.0001). Half the BP drop was reached shortly after tilt-up for nOH, but just before syncope/tilt-down in VVS (p <0.001). HR in nOH increased or remained unaltered in 88%, whereas HR dropped in 95% in VVS (p <0.0001).

Conclusion: Three criteria help differentiate nOH and VVS: the shape of BP decline (convex for VVS, concave for nOH; the rate of drop (late in VVS, early in nOH); the HR response to BP drop (down in VVS, up or no change in nOH).

Disclosure: Nothing to disclose

Cerebrovascular diseases 5

EPR3016

Lung function, sleep-disordered breathing and incidence of stroke: a community-based longitudinal cohort study

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Background and aims: Impaired lung function is regarded as a risk factor for stroke in patients with chronic obstructive pulmonary disease. However, the association between reduced lung function and incident stroke in a community-based population with sleep-disordered breathing (SDB) remains unknown.

Methods: We performed a prospective study within the Sleep Heart Health Study cohort. Full montage home sleep testing and spirometry data on 2082 and 2072 individuals with and without SDB, respectively, were analysed. Cox proportional hazards regression models were used to estimate the association between lung function and incident stroke.

Results: During a median (interquartile range) follow-up of 11.7 (10.8–12.5) years, 183 cases of stroke were identified in participants without pre-existing cardiovascular diseases, including 112 and 71 with and without SDB, respectively. In the entire population, after all covariate adjustments, lung function was inversely associated with incident stroke (hazard ratio, HR: 0.913 [95% confidence interval (CI): 0.839–0.994] for every 10% increase in percentage of predicted forced vital capacity, FVCPP). In subgroup analysis, the association of lung function with incident stroke became stronger in individuals with SDB (HR: 0.899 [0.822–0.984] for every 10% increase in percentage of predicted forced expiratory volume in one second; HR: 0.881 [0.787–0.987] for every 10% increase in FVCPP) but not in individuals without SDB.

Conclusion: Lung function may serve as a risk factor for incident stroke in a community-based population, especially in those with SDB. Spirometry may improve the risk management for primary care in community-based populations.

Disclosure: Nothing to disclose

EPR3017

Correlation between occurrence of cerebral microembolic signals and characteristics of carotid plaques, inflammatory biomarkers, and lipid profile

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Background and aims: Microembolic signals (MES) are only detectable via transcranial doppler (TCD), and can occur in individuals with embolic origin of cerebral ischemia. Role of lipids and systemic inflammation in appearance of cerebral MES is not fully understood. Aim of our study is to investigate the correlation between occurrence of cerebral MES and characteristics of carotid plaques, inflammatory biomarkers, and lipid profile.

Methods: Retrospective study included 107 individuals, treated at Neurology Clinic CCS in Belgrade. MES were detected by TCD, whilst morphological and hemodynamic parameters were obtained via a carotid artery ultrasound (intima–media complex thickness; presence and character of carotid plaques; degree of stenosis). The erythrocyte sedimentation rate; C-reactive protein; fibrinogen; leukocytes; total cholesterol; HDL, LDL; and triglyceride were measured by appropriate tests.

Results: Out of entire sample, 54 were females and 53 males, with an average age of 52.96±14.25. A comparison was made between 34 MES positive and 73 MES negative individuals. Highly statistically significant MES positive individuals were those with migraines and/ tension headaches, whilst significantly higher frequency of plaques (p=0.002; p=0.001, left and right sides respectively) was noted in MES negative patients, who also had higher average value of right side carotid stenosis. MES positive patients depicted presence of more frequent statistically significant unstable left side plaques.

Conclusion: Detection of MES with carotid artery ultrasound, as well as adequate monitoring of specific biomarkers in the blood, can help in prevention of initial as well as recurrent cerebral ischemic events.

Disclosure: Nothing to disclose

EPR3018

Hospital management of acute ischemic stroke in dementia: a cohort study from the Swedish Dementia and Stroke Registries

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Background and aims: 10% of strokes occur in persons with pre-existing dementia. The aim of the study was to compare hospital management of acute ischemic stroke in patients with and without dementia.

Methods: Observational cohort study combining Swedish national registries SveDem, the Swedish dementia registry, and Riksstroke, the Swedish stroke registry. Patients with dementia and an acute ischemic stroke 2010–2014 (n=1356) were compared with matched non-dementia acute ischemic stroke patients (n=6755). Outcomes included length of stay in a stroke unit, total length of hospitalisation, and utilisation of diagnostic tests and assessments.

Results: Dementia patients were equally likely to be directly admitted to a stroke unit as their non-dementia counterparts, however, their stroke unit and total hospitalisation length were shorter (10.5 vs. 11.2 days and 11.6 vs. 13.5 respectively, p<0.001). Dementia patients were less likely to undergo assessments by the interdisciplinary team members (physiotherapists, speech therapists, occupational therapists; p<0.05 for all adjusted models). On the other hand, a similar proportion of patients received a swallowing assessment (90.7% vs. 91.8%, p=0.218) and CT imaging (97.4% vs. 98.6%, p<0.001).

Conclusion: Patients with dementia and acute ischemic stroke have equal access but shorter stay in a stroke unit, shorter hospitalisation, and are less likely to receive specific diagnostic tests and assessments by the interdisciplinary stroke team compared to non-dementia counterparts. In most aspects of stroke care (e.g. CT, swallowing assessment, longitudinal ECG) we found no or small differences. Diagnosis of dementia should not be the reason to exclude them from post-stroke investigations and rehabilitation.

EPR3019

Erythrocytes deformability in acute ischemic stroke and cerebral small vessel disease

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Background and aims: Erythrocyte deformability is rheological parameter that measures the ability of blood cells to change their shape in capillary tube. The pathogenesis of acute and chronic ischemia of the brain consist of a violation of cerebral circulation, associated with hemodynamic and rheological disturbantes, leading to diffuse and focal changes in brain tissue. The aim of study is observation of erythrocytes deformability in acute ischemic stroke (AIS) and small vessel disease (SVD).

Methods: The study included 47 patients with AIS, age 62 [53; 69] years, 48 patients with SVD, age 60 [53;65] years, and 20 control patients, age 55 [54,59] years. Erythrocyte deformability measured by laser diffraction in shear rates 90, 180, 360 and 890 s-1. Erythrocyte deformability was been measured in patients with SVD one time and with AIS - 3 times (in the first 12 hours, in 3-5 and 18 - 20 days).

Results: Erythrocyte deformability was significantly reduced in SVD: the index of deformability at shear rates 90-360 s-1 was been low, compared with the AIS and control group (Fig. 1). Was been found a significant deterioration of erythrocyte deformability during the acute phase of ischemic stroke in the measurement from the first hours after stroke to 18-20 days of the disease (Fig. 2). Erythrocyte deformability in patients with AIS in 18-20 days after onset was significantly lower than in the control group.

Figure 2. Erythrocyte deformability at different shear rates in patients with ischemic stroke in 12 hours, 3-5 days and 18-20 days

Conclusion: Persistent changes in erythrocyte deformability is important pathogenetic mechanism at the level of microcirculation in patients with chronic and acute cerebrovascular ischemic disorders.

Disclosure: Nothing to disclose

Figure 1. . Erythrocyte deformability at different shear rates in patients with ischemic stroke, small vessel disease and control group

EPR3020

Treatment of acute ischemic stroke classified as lacunar with i.v. rtPA - systematic review and meta-analysis

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Background and aims: Small-vessel and large-vessel ischemic strokes are characterised by different structure of aetiologies and pathogenesis. Large clinical trials on intravenous thrombolysis (iv-rtPA) combined these groups in effect analyses. Thrombolysis in lacunar stroke (LS) is safe although it is unclear how large is the benefit from this therapy. We reviewed all original studies to determine the efficacy of iv-rtPA in LS.

Methods: Two of the authors have independently reviewed scientific databases using the search code ("lacunar"[Title/Abstract]OR"small vessel"[Title/Abstract]OR"small artery"[Title/Abstract]OR"minor stroke"[Title/Abstract]) AND("thrombolysis"[Title]OR"rtPA"[Title] OR"actilyse"[Title]OR"alteplase"[Title] OR"fibrinolysis"[Title]) for PubMed, and analogical for Scopus. They selected papers towards original comparative trials investigating the efficacy of iv-rtPA administration (vs placebo) in OCSP or TOAST or neuroimaging defined LS, covering as a minimum data on modified Rankin Scale (mRS) at discharge or 90-day. All search and analytical procedures have been based on PRISMA.

Results: Amongst 89 (Pubmed) and 97 (Scopus) initially identified studies, 6 fulfilled the criteria (three defining LS according to OCSP, two –TOAST, one –neuroimaging), and included five observational plus one randomised trial. The meta-analyses did not reveal any significant differences in mRS between thrombolysis and placebo. mRS 0-2 was more frequent in thrombolysed patients (RR=1.10, 95% CI:0.92-1.32, I^2:81%; Figure 1), similar effect was found for mRS 0-1 (RR=1.13, 95% CI:0.94-1.35, I^2:63%; Figure 2).
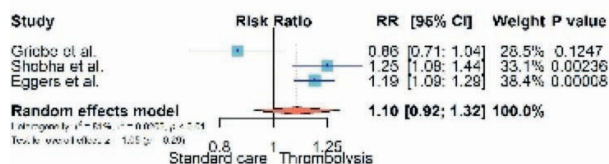
Forest plot of pooled risk ratio for mRS 0-2
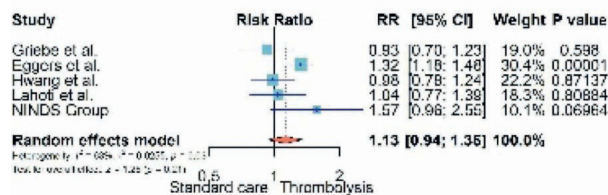
Forest plot of pooled risk ratio for mRS 0-1

Conclusion: There are few trials showing the effects of iv-rtPA in LS. mRS is not an optimal measure of the outcome in these patients as many show initially only mild neurological deficit. Management of LS demands separate analyses and different therapeutic designs in future studies.

Disclosure: Nothing to disclose

EPR3021

Ten years of Stroke code: a retrospective review of diagnostic performance at a comprehensive stroke centre

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Background and aims: Stroke is one of the leading causes of morbidity and mortality in Portugal. Rapid recognition of stroke and timely therapy are the cornerstone of current treatment. The Portuguese stroke code program ensures a fast track for stroke patients recognised by emergency medical services (EMS) using the face-arm-speech criteria (FAST), or at triage using broader criteria (e.g. vision loss, altered consciousness). Our goal was to evaluate the diagnostic performance of both systems over 10 years at a single centre.

Methods: All stroke code activations from 2007-2016 were included. Demographic and diagnostic variables were analysed using descriptive statistics and compared using the chi-squared test.

Results: There were 5028 stroke code activations, of which 63.2% were strokes (83.8% ischaemic). A third (23.5% triage; 42% EMS p<0.001) of ischaemic strokes underwent thrombolysis and 12.7% had an endovascular procedure (2015-16). Activations progressively decreased until 2014 (range: 356-722). In 2015-16, there was a marked increase of activations (453 and 712, respectively) likely due to the introduction of mechanical thrombectomy (treatment window up to 6h or if onset unknown). Yearly false positive rates (stroke mimics) were significantly higher with broader triage criteria (EMS: 27.5%-41%, triage: 45-72.5% p<0.001). Functional neurological disorders, seizures, syncope and migraine accounted for 55% of total mimics.

Conclusion: Stroke code allowed timely treatment of a good proportion of stroke patients while maintaining a reasonable false positive rate. As expected, broader criteria correlate with higher false positive rates.

Disclosure: Nothing to disclose

EPR3022

Mild encephalitis/encephalopathy with reversible splenial lesion (MERS) in adults-a case report and literature review

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Background and aims: Mild encephalitis/encephalopathy with reversible splenial lesion (MERS) is a rare clinico-radiological entity characterised by the magnetic resonance imaging (MRI) finding of a reversible lesion in the corpus callosum, sometimes involved the symmetrical white matters. Many cases of child-onset MERS with various causes have been reported. However, adult-onset MERS is relatively rare. The clinical characteristics and pathophysiologiccal mechanisms of adult-onset MERS are not well understood. We reviewed the literature on adult-onset MERS in order to describe the characteristics of MERS in adults and to provide experiences for clinician.

Methods: We reported a case of adult-onset MERS with acute urinary retension and performed literature search from PubMed and web of science databases to identify other adult-onset MERS reports from Januarary 2004 to March 2016. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline was followed on selection process. And then we summarized the clinico-radiological features of adult-onset MERS.

Results: 29 adult-onset MERS cases were reviewed from available literature including the case we have. 86.2% of the cases (25/29) were reported in Asia, especially in Japan. Ages varied between 18 and 59 years old with a 12:17 female-to-male ratio. The major cause was infection by virus or bacteria. Fever and headache were the most common clinical manifestation, and acute urinary retention was observed in 6 patients. All patients recovered completely within a month.

Conclusion: Adult-onset MERS is an entity with a broad clinico-radiological spectrum because of the various diseases and conditions. There are similar characteristics between MERS in adults and children, also some differences

Disclosure: Nothing to disclose

EPR3023

Cerebrospinal fluid analysis in acute stroke patients of noninflammatory etiology

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Background and aims: Cerebrospinal fluid (CSF) assessment is rarely performed in ischemic stroke, unless inflammatory etiology is suspected. Ischemic stroke initiates inflammatory response. CSF cellular response is reported in variable extent ranging from normal to pleocytosis. Consequently, there is often uncertainty in identifying stroke mimics or underlying inflammatory etiology. The aim was to assess CSF in acute ischemic stroke of noninflammatory etiology.

Methods: Retrospective monocentric analysis of ischemic stroke patients with CSF analysis. Inclusion criteria were complete evaluation of etiology, lumbar puncture in the first 30 days and acute infarction on CT/MR. Exclusion criteria were vasculitis, inflammatory vasculopathy or traumatic puncture.

Results: 127 patients out of 547 screened were included, 81 (63.8%) men, age 59.9 (22-89) years. Mean time of lumbar puncture was 8.0 (SD 5.7) days poststroke. Etiology was in 40 (31.5%) cardioembolic, 26 (20.5%) large vessel atherosclerosis, 11 (8.7%) small vessel disease, 39 (30.7%) undetermined and 11 (8.7%) other. Infarct on imaging was territorial in 22 (17.3%), lacunar 38 (29.9%), cortico-subcortical subterritorial 35 (27.7%) or peripheral emboli 28 (22.0%). Mean CSF leucocyte count was 1.56 (0-30, SD 2.98)/mm^3, erythrocyte 56.56 (0-1000, SD 151.04)/mm^3, total protein was 533.6 (230-1310, SD 217.6) mg/l. We have not found any significant differences depending on infarct size, etiology, age or delay of CSF analysis.

Conclusion: Noninflammatory ischemic stroke should have normal CSF values irrespective of etiology or size. Abnormal CSF should prompt further search for other etiology or stroke mimics.

Cognitive neurology/neuropsychology 2

EPR3024

Post-stroke cognitive impairment in patients with metabolic syndrome

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Background and aims: Post-stroke cognitive impairment (PSCI) significantly influences professional, social adaptation, retards patient rehabilitation.

Methods: There were 100 patients after ischemic stroke (IS) in the anterior circulation area enrolled into the study. Cognitive functions 3 and 6 months after IS were evaluated, depending on the presence of metabolic syndrome (MS) and localisation of the ischemic lesion. Patients were divided into 2 groups: with MS (n=62) and without (n=38) and into 3 age subgroups: middle, elderly, senile age. Clinical and neuropsychological examinations, laboratory tests, MRI of the brain were done. Exclusion criteria were aphasia and severe paresis.

Results: The incidence of post-stroke dementia was significantly higher in patients with MS 3 months after IS (p<0.05), comparing with patients without MS. There was significant augmentation of PSCI severity with age in patients with and without MS. Comparing data of neuropsychological tests in patients without MS 3 and 6 months after IS we found significant improvement of immediate and delayed associated memory on the Paired Associates Learning Test, increasing of information processing speed on the Stroop Color-Word Interference Test, increase in the rate of psychomotor reactions on the Shulte tables (p<0.05), especially in patients with left hemisphere IS. In patients with MS we did not find significant improvement of cognitive functions comparing results of neuropsychological tests 3 and 6 months after IS in both hemisperes of the brain.

Conclusion: Patients with MS had significantly severe PSCI. Presence of MS worsened recovery of cognitive functions in patients with PSCI.

Disclosure: Nothing to disclose

EPR3025

Deficits in cognitive theory of mind are associated with self-perceived lack of social support in Parkinson's disease

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Background and aims: Theory of Mind (ToM) is defined as the ability to infer about other person's state of mind. It has been reported that patients with Parkinson's disease (PD) experience ToM deficits which may result in malfunctioning in day-to-day social relationships. The aim of the current study was to find out if deficits in cognitive ToM performance are associated with impaired social support quality of life (QoL).

Methods: We enrolled 51 non-demented patients with idiopathic PD according to UK Brain Bank Criteria (32 male, age 62.49±10.2, disease duration 6.28±4.78). ToM abilities were assessed using Comic Strip Task which challenges cognitive component of ToM. To assess the health-related QoL 39-item Parkinson's disease Questionnaire (PDQ-39) was used. For further analyses, it was divided into standard subdimensions (mobility, activities of daily living, emotional well-being, stigma, social support, cognition, communication and bodily discomfort). Non-parametric Spearman correlation was used to assess the relationships between the variables.

Results: The performance in Comic Strip Task did not correlate with the total score of PDQ-39. We found a negative correlation between Comic Strip Task and subscore reflecting social support (rs=-0.339, p=0.022).

Conclusion: Patients with worse performance in cognitive ToM task reported more significant lack of social support. Deficits in ToM could be one of the underlying mechanisms of self-perceived lack of social support.

Disclosure: This study was supported by APVV grant nr. 15-055.

EPR3026

Epidemiology of functional cognitive disorders: prospective memory clinic study

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Background and aims: A previous retrospective study suggested functional cognitive disorders (FCD) account for >50% of referrals to a dedicated cognitive disorders clinic; age, referral source, and attended alone sign were suggestive of FCD.

Methods: A prospective study to examine clinical features which distinguish functional cognitive disorders (FCD) from traditional cognitive disorders was initiated.

Results: Initial data on 29 patients, seen November-December 2017, were analysed. 20 (69%) were diagnosed with FCD. Compared to patients with other cognitive disorders, a higher percentage of FCD patients was found to be younger (≤65 years: 75% vs 22%), attended alone (50% vs 11%), manifested la maladie du petit papier (15% vs 0%), had positive family history of dementia (40% vs 11%), and had markers of disturbed mood (two question screener for depression, 74% vs 44%) and sleep (dichotomised Jenkins Sleep Questionnaire, 74% vs 44%), but there was no difference in referral source (70% vs 77% from primary care). None of the comparisons reached statistical significance (chi-square test), unsurprisingly in view of the small patient numbers recruited thus far.

Conclusion: FCD are commonly encountered in dedicated cognitive disorders clinics. A positive diagnosis of FCD, rather than a diagnosis of exclusion, may be possible based on relatively simple, dichotomised, clinical observations.

Disclosure: Nothing to disclose

EPR3027

Structural and functional abnormalities underlying cognitive impairment in benign MS

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Background and aims: The definition of benign Multiple Sclerosis (BMS) does not take into consideration cognitive deficits. We investigated whether cognitive impairment in BMS patients is associated with specific patterns of structural and functional abnormalities using advanced MRI techniques.

Methods: High-resolution 3D-T1-weighted, diffusion tensor (DT), dual-echo, and resting state (RS) functional MRI were acquired from 38 BMS patients (EDSS score<3.0 and disease duration >15 years) and 50 matched healthy controls (HC). All patients underwent neuropsychological assessment. Regional GM atrophy was estimated using a voxel-based-morphometry analysis, WM microstructural abnormalities were investigated with tract-based-spatial-statistical analysis, and RS functional connectivity (FC) was assessed using independent-component analysis.

Results: 16 (42%) BMS were classified as cognitively impaired (CI). Compared to HC, cognitive preserved (CP) BMS patients had GM atrophy of thalami, left precuneus and left middle cingulum. In CI-BMS patients, GM atrophy in the anterior/posterior cingulate gyrus, left caudate nucleus, and right precentral gyrus was also found. Compared to HC, CP and CI-BMS patients had decreased fractional anisotropy of supratentorial/infratentorial WM tracts and increased mean (MD), axial and radial (RD) diffusivity of the main supratentorial WM tracts. CI-BMS patients had additional increased MD and RD of several infratentorial regions located in the cerebellum and brainstem. Compared to the other two groups, CI-BMS patients showed a widespread increase of RS-FC in fronto-temporo-parietal regions of the attention and executive functions networks.

Conclusion: Distinct patterns of structural and functional abnormalities relevant for cognitive processing are associated with CI in MS patients with a benign course.

Disclosure: Partially supported by Fondazione Italiana Sclerosi Multiple (FISM2013/S/1).

EPR3028

Divergent thinking and cognitive reserve in mild cognitive impairment

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Background and aims: In the last years, creativity and its potential role in terms of diagnosis and rehabilitation for patients with Alzheimer's disease (AD) has attracted the scientific interest. Research has demonstrated that divergent thinking (DT) usually begin early to decrease in non-artist AD patients but less is known about patients affected by Mild Cognitive Impairment (MCI). The present study aimed to preliminary evaluate the relationships between DT, cognitive reserve (CR) and neuro/psychological conditions in MCI patients.

Methods: 32 subjects, 12 MCI patients and 20 controls, has been recruited in this observational study. The main measures were general cognitive functioning (Mini Mental State Examination – MMSE; Montreal Cognitive Assessment -MOCA), CR index (CRIq), divergent thinking (Abbreviated Torrance Test for Adults - ATTA) and psychological conditions scales (i.e. perceived quality of life, depression, anxiety and apathy).

Results: MCI patients performed worse at MOCA (p=0.05). A significant positive correlation between ATTA total score and CRIq total score (p=0.05) and a negative correlation between AES (Aphaty Evaluation Scale) and ATTA total score (p=0.01) were found in the whole sample.

Conclusion: Despite the small sample of patients, our preliminary results showed that, in line with the current literature, there was a significant positive correlation between DT and CR. These results allowed us to hypotize that an early cognitive intervention focused on divergent thinking could enhance CR and subsequently slow down the cognitive decline of MCI patients. Our results suggested also the necessity for further investigations about the relationship between apathy and creativity.

Disclosure: Nothing to disclose

EPR3029

The effect of early-stage Alzheimer's disease on right-left discrimination and mental rotation

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Background and aims: Alzheimer's disease (AD) is associated with gradual cognitive decline that may result in spatial disorientation. We aimed to evaluate two spatial abilities – right-left discrimination and mental rotation in early clinical stages of AD.

Methods: 152 participants – amnestic mild cognitive impairment (aMCI) due to AD (n=62), mild AD dementia (n=37) and cognitively normal (CN) older adults (n=53) underwent clinical and neuropsychological evaluation, MRI brain scan and Standardized Road-Map test of Direction Sense (RMTDS). In the RMTDS, the participants followed a pathway on a city map indicating a direction of turning (left or right) at each intersection. Group and gender differences in a total score (the higher the better) and three subscores – A) left-right discrimination without rotation, B) half-, and C) full- mental rotation were evaluated using non-parametric tests with Holm-Bonferroni correction.

Different turn types
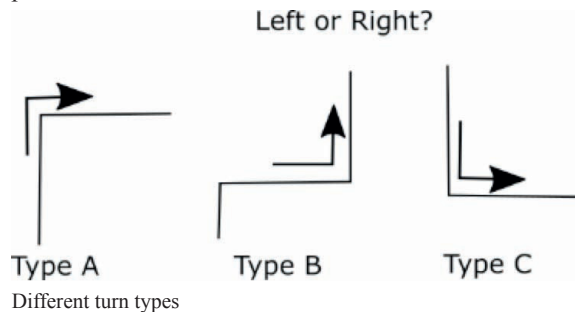
Results: Both AD groups had lower RMTDS total score, B and C subscores than the CN group (p<0.001). AD dementia group had lower subscore A than the CN group (p<0.001). Men reached higher scores than women across all groups (p<0.001). The between-group differences were more pronounced among the women (p≤0.003).

Conclusion: Patients in the early clinical stages of AD including aMCI due to AD and mild AD dementia were impaired in mental rotation, while right-left discrimination was impaired only in mild AD dementia. Gender differences in the RMTDS favoring men may be taken into account when evaluating the test. RMTDS may be a useful test to detect spatial cognition decline in the early stages of AD.

Disclosure: Nothing to disclose

EPR3030

Predictors of cognitive impairment in untreated Multiple Sclerosis: preliminary findings

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Background and aims: Cognitive impairment is frequent in Multiple Sclerosis (MS), but its natural history has still to be completely elucidated. This is partly due to the early treatment approach, which is able to modify neurodegeneration and brain volume, likely deflecting the natural trajectory of cognitive decline. On this background, the aim of our study is to assess the cognitive performance of MS patients who did not undergo early disease modifying treatment (DMT) and to correlate findings with well established clinical and imaging prognostic measures collected at disease onset.

Methods: Complete neuropsychological testing (T1) was administered at last follow-up consult (in 2017) to all MS patients who did not receive DMT over the first five years of disease. So far, we enrolled 22 patients, who were defined as cognitively healthy or impaired. We retrospectively collected clinical (sex, age, type and recovery from first attack, relapse-rate) and MRI (lesion load rated: ≤10 or >10) data at onset.

Results: Clinical features are presented in Table 1. We found a statistically significant association between current cognitive state and MRI lesion load at onset (chi-square=5.59, p=0.018). Conversely, we found no other statistically association with other prognostic factors (gender, severity or onset type, relapse-rate). Noteworthy, we found a trend of association with older age at onset (≥35year-old, p=0.09).

Demographic data and MS history N=22	
Female (N, %)	15 (68%)
Age at onset, years (mean value ± SD).	37 ± 10,6
Age at T1, years (mean value ± SD).	54 ± 8,6
Functional system at onset. N (%):	
-pyramidal	8 (36,3%)
-sensory	2 (9,1%)
-cerebellar	2 (9,1%)
-brainstem	2 (9,1%)
-visual	2 (9,1%)
-sphinteric	6 (27,3%)
Relapse-rate in the first 5years of disease. N (%)*:	
-high relapse-rate (>0,5)	10/20 (50%)
-low relapse-rate (<0,5)	10/20 (50%)
*2PPMS were excluded	
Lesion load MRI at onset. N (%):	
- <=10 lesions	13 (59%)
->10 lesions	9 (41%)
MS type at T1. N (%):	
-RR	17 (77,3%)
-SP	3 (13,6%)
-PP	2 (9,1%)
Disease duration at T1, years (mean value ± SD).	16,7 ± 7,2

Table 1

Conclusion: Lesion load at onset may predict cognitive changes over time in MS patients who underwent delayed or no DMT. We plan to increase our sample size and collect MRI data on atrophy and grey matter lesions to strengthen our results.

Disclosure: Nothing to disclose

Epilepsy 3

EPR3031

Detection of motor seizures using wearable multi modal sensors

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Background and aims: This study aims to evaluate the detection of motor seizures using physiological parameters such as ictal movements, heart rate and audio signal with wearable multi-modal sensors that are available with smart watches.

Methods: 35 seizures (13 automotor seizures, 11 tonic-clonic seizures, and 11 hypermotor seizures) of 12 patients (5 F, 7 M, mean age 26±9.7) who were underwent continuous EEG-video-monitoring were included. Seizure detection included analysis of limb movements via four accelerometer (ACM) (418 hours of data), heart rate (HR) and audio data. One class non parametric probability density function classifier was used to identify seizures.

Results: Hypermotor seizures were detected with a sensitivity of 100%, a positive predictive value (PPV) of 76.8%, specifity of 99.5% and a false detection rate (FDR) of 0.025 per hour. Automotor seizures were detected with a sensitivity of 96%, PPV of 65.8%, specifity of 98.9% and a FDR of 0.088. Tonic-clonic seizures were detected with a sensitivity of 100%, PPV of 80.5%, specifity of 99.6% and a FDR of 0.025. Adding audio and HR data to movement data improved the sensitivity and PPV by 12%. Using four ACM sensors did not improve the seizure detection performance significantly compared to one sensor.

Conclusion: Motor seizures in epilepsy patients can be reliably identified using currently available wearable multimodal sensors such as smart watches.

Disclosure: Nothing to disclose

EPR3032

The therapeutic effect of repetitive transcranial magnetic stimulation (rTMS) combined with neuronavigation systems on non-lesional focal epilepsy

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Background and aims: Repetitive transcranial magnetic stimulation(rTMS) is a non-invasive technique that changes excitability of different cortical areas. Our aim is to evaluate the number and duration of seizures in patients with focal epilepsy during and after 0.5Hz-rTMS.

Methods: Three patients with focal epilepsy were studied whose electrical sources of paroxysmal activity in neocortical regions were determined. They received standard pharmacological treatment without modification from at least 1-month before study.

rTMS was carried out at baseline, intervention, follow-up periods. The baseline period duration was 4-weeks and intervention with rTMS for 2-weeks, follow-up period for 8-weeks.

A high-resolution 120ch-EEG was used. The epileptic focus was determined with current source analysis of paroxysmal activity by sLORETA. Current sources are restricted to brain parenchyma by the use of a mask that prohibits solutions where the mask is zero, i.e., in the CSF (Figure1). rTMS session at 0.5Hz was carried out on the epileptogenic zone with total of 900pulses delivered at 100% intensity of the resting motor threshold (RMT) during 2-weeks. Using neuronavigation system improved the targeting of the epileptic foci (Figure1).
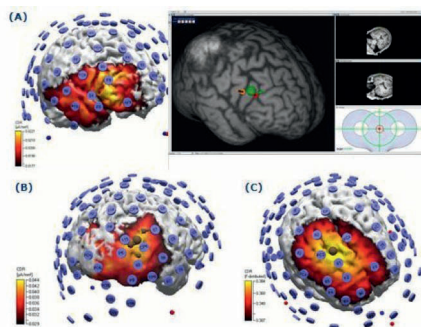
Localisation of the epileptic focus using sLORETA (A)Rt. inferior frontal region of patient No.1. A precise localisation of the epileptic focus combined with neuronavigation systems to place the coil over the head improved targeting of the epileptic foci (B)Rt. parietal region of patient No.2 (C)Rt. superior frontal region of patient No.3

Results: Seizure reduction
During the baseline, three patients had seizures, 7.25,3.25,4times/week. In patient 2&3, this frequency decreased during the intervention to 1,0.5/week respectively, which means 69%, 87% reduction. During follow-up period, this decreased to 2.13,1.13/week, corresponding to 34%, 72%(Figure2).

Patient	Gender	Years of evaluation	Age	Focus localization with sLORETA
1	M	21	24	Rt Inf. Frontal
2	F	10	26	Rt Parietal
3	F	13	28	Rt sup. Frontal

Clinical data of patients with focal epilepsy
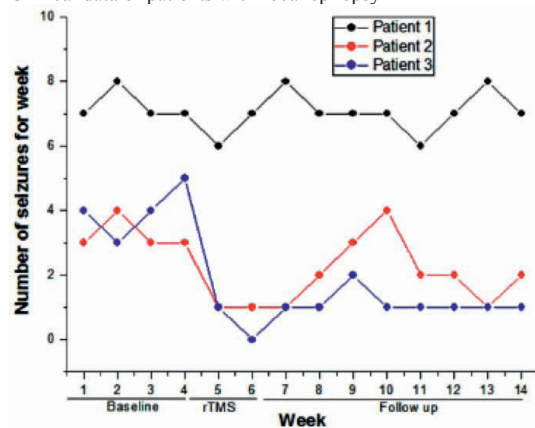
Mean number of seizures per week during, baseline, rTMS and follow-up period.

Conclusion: We think that 0.5Hz rTMS over epileptic focus decrease the number of seizures in patients with focal epilepsy. rTMS for non-lesional focal epilepsy may be an alternative treatment for pharmoco-resistant patients, who have the identifiable seizure foci.

Disclosure: Nothing to disclose

EPR3034

Single-center long-term results of vagal nerve stimulation for epilepsy: a 10–17 year follow-up study

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Background and aims: We present a long-term follow-up study of VNS patients, analysing seizure outcome, the role of medication changes, and surgical aspects.

Methods: The study followed 74 adult patients with VNS for 10 to 17 years. The patients were evaluated yearly as: non-responder – NR (seizure frequency reduction<50%), responder – R (seizure frequency reduction ≥ 50% and<90%), and 90% responder – 90R (seizure frequency reduction ≥ 90%). Patients with delayed response (≥ 4 years after surgery) and patients with battery replacement or complete system replacement were identified.

Results: A markedly increasing R rate was evident up to study year 4, and the 90R rate rose to year 6; both then remained stable until the end of the study. During the study period, antiepileptic therapy was changed in 62 patients (87.9%). There were 11 delayed responders (categorised as R at or after study year 4) with associated antiepileptic medication changes in 9. There were four delayed 90R (categorized as 90R at or after study year 4) with associated antiepileptic treatment changes in three. At least one battery replacement was performed in 51 patients (68.9%), 49 of which were categorised as R or 90R. A complete system replacement was needed in seven patients (9.5%). The VNS system was explanted in seven NR (9.5%).

Conclusion: The study provides data on VNS patients over a long-term, complex follow-up period. After an initial steady increase for at least four years, the rate of R and 90R remained high and stable.

Disclosure: Nothing to disclose

EPR3035

Individual prediction of post-operative verbal memory decline in temporal lobe epilepsy: the contribution of post-ictal memory testing

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Background and aims: The prediction of verbal memory decline after temporal lobe epilepsy surgery remains difficult at individual level. We evaluated the prognostic value of post-ictal memory testing in predicting the post-operative verbal memory decline.

Methods: 74 consecutive patients were included, who underwent temporal lobe epilepsy (TLE) surgery in our center with preoperative interictal/post-ictal and post-operative memory testing. Verbal memory was evaluated using Rey's auditory-verbal learning task. Sensitivity (Sn), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV) and area under the curve (AUC) were calculated to find the best threshold to predict a clinically significant post-operative verbal memory decline (20%). The analysis was performed for all TLE patients and for the subgroup with hippocampal sclerosis (HS).

Results: The L-TLE patients (n=39) had lower verbal memory scores than R-TLE at 3 months (59 vs 79%) and 12 months (54 vs 79%) after surgery. The interictal scores correlated with the post-operative decline (CC=0.415, p<0.001). The post-ictal verbal memory predictive value was not significant in the whole group (p=0.25). In HS patients, the post-ictal verbal memory predicted the post-operative VDR decline (p=0.03, AUC=0.694, CI [0.493-0.895]). The 40% posti-ctal decline had Sn of 46%, Sp of 90%, PPV of 63%, NPV of 82% and an AUC of 0.677 to predict a significant post-operative memory decline in patients with HS.

Conclusion: Post-ictal memory testing is a non-invasive bedside measure that can help predict the post-operative verbal memory decline in patients with HS with an overall accuracy of 78%.

Disclosure: Nothing to disclose

EPR3036

Is automated interictal epileptiform discharge detection sufficient to diagnose epilepsy from overnight EEG?

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Background and aims: In clinical practice, the detection of interictal epileptiform discharges (IED) in overnight EEG is the hallmark to diagnose epilepsy. Nevertheless, visual analysis to identify the IEDs in the EEG is a labor-intensive, objective and time consuming task. In this study, we investigate the usefulness of automated IED detection to diagnose epilepsy.

Methods: 38 patients had an overnight EEG recording at the University Hospital of Geneva, Switzerland. Epilepsy diagnosis based on visual inspection of the EEG, performed by expert electrophysiologist (MS), was compared to diagnosis made by a second blinded expert electrophysiologist (SV) based on the automatically detected IEDs that were summarised in a concise report (Epilog NV, Belgium). The blinded reviewer did not receive any clinical information about the patient.

Results: Visual interpretation of the overnight EEG led to a diagnosis of epilepsy in 12 of the 38 admitted patients had IEDs present in the overnight EEG. The diagnosis based on the report corresponded with the visual analysis in 33 of the 38 patients. The sensitivity of epileptic diagnosis was 75%, the specificity 92%, positive predictive value 82% and negative predictive value 89%, which corresponds to a diagnostic odds ratio of 36.

Conclusion: We showed that automated IED detection can help in the diagnosis of epilepsy from overnight EEG. It can help neurologists decrease the time spent for visual analysis of the EEG, but for now the achieved sensitivity should be augmented before using it in standard clinical practice. This could be achieved by adding clinical details about the patient to the reports.

Disclosure: Pieter van Mierlo is co-founder and shareholder of Epilog NV, Belgium.

EPR3037

Remodeling of morphology in temporal lobe epilepsy

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Background and aims: Medial temporal lobe epilepsy (TLE) is one of the most widespread neurological network disorders. Computational anatomy MRI studies demonstrate a robust pattern of cortical volume loss. The majority of statistical analyses provide information about localisation of significant focal differences in a segregationist way. Multivariate Bayesian modeling provides a framework allowing causal inferences about interregional dependencies. We adopt this approach to answer following questions: Which structures within a pattern of dynamic epilepsy-associated brain anatomy reorganisation best predict TLE pathology and do these structures differ between TLE subtypes?

Methods: 128 TLE patients were characterised dependent on laterality of epileptogenic focus and on MRI detected pre-/absence of mesial temporal lobe sclerosis (MTS/MRI-) and compared to 120 healthy volunteers.

Building upon classical inferences on mass univariate analysis of MRI data, we observed a pattern of structural reorganisation in TLE patients. Using MVB, we set the detected partitioned cortical regions as distinct regional models to estimate their predictive power for disease and TLE subtypes using Bayesian model selection.

Results: Corresponding ranking of predictive structures demonstrated that volume estimates in ipsilateral medial temporal lobe regions best predict disease-related cortical differences between TLE and healthy controls, independent of laterality and TLE subtype. Consequent ranking positions were located in ventromedial PFC for left TLE and bilaterally thalamic and ipsilateral temporal polar for right TLE.

Conclusion: Para-/hippocampal regions are the most predictive ones for disease-related remodeling whereas beyond medial temporal lobes, focal weightings are highly dependent on laterality of the epileptogenic focus and mesial temporal lobe pathology.

Disclosure: BD and ER are supported by the Swiss National Science Foundation (NCCR Synapsy, project grant Nr 320030_135679 and SPUM 33CM30_140332/1), Foundation Parkinson Switzerland and Foundation Synapsis. The research leading to these results has received funding from the European Union Seventh Framework Programme (FP7/2007-2013) under grant agreement no. 604102 (Human Brain Project).

EPR3038

Efficacy and safety of different antiepileptic drugs in post-stroke epilepsy

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Background and aims: The proper choice of antiepileptic therapy is of a major importance for patients with post-stroke epilepsy (PSE). Interactions with cardiovascular therapy, attenuation of post-stroke depression or vascular cognitive impairment are possible side effects of antiepileptic drugs (AEDs). Data on efficacy and safety of AEDs in PSE are limited. The aim was to compare different AEDs in the treatment of PSE in terms of an observational study.

Methods: Data on patients with PSE on antiepileptic monotherapy were collected and analysed in terms of the Mainz Epilepsy Register (MAINZ-EPIREG) and the Marburger Stroke Register (MARSTREG).

Results: Overall, 88 patients with PSE on antiepileptic monotherapy were recruited. In this cohort, 25% of patients (N=22) were treated with levetiracetam(LEV), 22.7%(N=20) with eslicarbazepine (ESL), 22.7%(N=20) with lacosamide(LCS), 15.9%(N=14) with lamotrigine(LTG), 13.6%(N=12) with valproate. The mean annual seizure frequency was 2±4 on LCS, 2±3 on ESL, 3±5 on LEV, 4±8 on LTG and 5±7 on VPA. Among side effects, the most frequent were vertigo (25%), tiredness (15.9%) and headache (13.2%). Post-stroke depression was attenuated in 31.8% of patients on LEV. Other AEDs did not show association with depression. Insomnia was reported by 42.9% of patients on LTG. Weight gain was observed in 41.7% of patients on VPA.

Conclusion: Our analyses show the best efficacy and the most desirable safety profile for ESL and LCS in the monotherapy of PSE. One can speculate that AEDs facilitating slow inactivation of sodium channels have most favourable properties for the treatment of PSE. Farther studies with larger patient groups should replicated these findings.

Disclosure: Nothing to disclose

EPR3039

Cost savings and improved patient outcomes from best management of epilepsy

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Background and aims: Variability in access to epilepsy care results in delayed diagnosis and access to treatments. This results in poorer clinical outcomes and has economic consequences. As part of the European Brain Councils Value of Treatment programme we modelled the costs of 'better' management versus 'current' management, using the UK as an example.

Methods: Using the NICE-guidelines as the reference for better management, we constructed an economic model that considered patient pathways from first seizure through to epilepsy surgery, with a time horizon of 70 years. Costs and quality adjusted life years (QALYs) were considered from the perspective of the UK National Health Service and discounted at an annual rate of 3.5%. The model pathways, and the assumptions underpinning the model, were determined through consultation with EU clinical experts, reviews of the literature, and data from the SANAD study.

Results: For better compared to standard care, we estimate an incremental cost-effectiveness ratio (ICER) of £6,848 per QALY gained for people aged 20 with epilepsy. 97.6% of the monetary savings resulted from preventing seizures and hence complications and admissions. The overall incremental cost per person associated with better management was £7,321 with an incremental QALY gain of 1.069 per person.

Conclusion: Failure to provide good accessible epilepsy care results in poorer clinical outcomes. Our results indicate that it would be cost effective invest in services, with ICERs per QALY much lower than those typically estimated for new treatments and technologies. Our open access model is available in the public domain.

Disclosure: This case study on epilepsy is part of a series of case studies covering nine neurological and psychiatric conditions, conducted within the "Value of Treatment for Brain Disorders" research project of the European Brain Council and was supported by Livanova and UCB.

Headache and pain 3

EPR3040

Utilisation of acute neurological service during the European refugee crisis in Salzburg, Austria 2014-2016: high rate of chronic pain and psychiatric comorbidity

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Background: Between 2014 and 2016, the European Union experienced an unprecedented influx of refugees. Little is known about neurological emergencies during the arduous journey, which would be valuable to prepare health care providers for upcoming challenges.
Aim of the study: To analyse acute neurological health service utilisation among refugees and asylum seekers in a gateway city along the refugee route.
Material and methods: Retrospective chart review of refugees and asylum seekers treated at the neurological emergency ward of a tertiary care in Salzburg, Austria between 2014-2016. Demographics and diagnosis on discharge were extracted and compared with findings in consecutive non-refugee patients utilizing acute neurological service between Jan-Apr 2015.
Results: The refugee group consisted of 134 patients (77.6% men) with a median age of 30.2 years (range 15-70). The most frequent countries of origin were Afghanistan, Syria and Iraq (total 86.6%). Diagnosis on discharge were most frequently headache and back pain (47.8 and 38.1%, respectively), followed by psychiatric disorders (33.6%).
The patients in the non-refugee group (679 patients, 51.7% men) were significantly older (median 67.9 years, range 11-101, P<0.0001). Diagnoses at discharge in this cohort were headed by cerebrovascular disease (50.8%) and seizures (18.1%).
Discussion: Both demographics of patients and conditions leading to acute neurological consultations differ for refugees and asylum seekers. Health care provides need to take the high rate of pain syndromes and psychiatric disorders for future provision of adequate medical service into account.
Disclosure: Nothing to disclose

EPR3041

Comparing effectiveness of electrocatheter-mediated pulsed radiofrequency to epidural adhesiolysis for chronic lumbosacral radicular pain with neuropathic features: a randomised controlled study

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Background and aims: Objective of this study is to investigate the effectiveness of electro-catheter-mediated pulsed radiofrequency and epidurolysis (P+E) in comparison with epidurolysis alone (E) in chronic lumbosacral radicular pain with neuropathic features.
Methods: We evaluated 31 adult patients suffering from an unresponsive single leg-radiating neuropathic pain lasting for>6 months. 19 subjects were randomly assigned to P+E whereas 14 subjects underwent E. Mean changes in numeric rating scale (NRS), Italian Pain Questionnaire, Oswestry Disability Index (ODI) and DN4 questionnaire at pre-treatment, one and six months post-treatment. P values<0.05 were considered statistically significant.
Results: At one and six months respectively, a significant reduction in mean NRS (p=0.01, p=0.01), ODI (p=0.03, p=0.01) and DN4 score (p=0.03, p=0.02) was observed in the P+E compared to E group. The 58% and 53% in P+E but only the 29% and 21% of patients in the E group showed a radicular pain reduction in NRS>30% at one and six month respectively.
Conclusion: P + E appears to be more effective than E in the treatment of chronic lumbosacral radicular pain with neuropathic features.
Disclosure: Nothing to disclose

EPR3042

Evaluation of peripheral vascular alteration in migraine patients by using video capillaroscopy

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Background and aims: The aim of this study is to examine the nailbed capillaries of migraine patients with video capillaroscopy and to show the extracranial vascular changes.

Methods: 45 migraine patients and 50 control were included. Demographic data, migraine disability scale and numeric pain rating scale were noticed. Nailbed assessment was made on total of 8 fingers of both hands excluding the thumbs. Capillary architecture, tortuosity, avascular fields, hemorrhage, the presence of giant capillaries were evaluated. The largest diameters of apical capillaries, capillaries, veins and arteries detected in the measurements of all fingers were recorded and the average of the largest three measurements was accepted as the overall value of the patient.

Results: Capillary tortuosity and giant capillaries were seen more frequently in migraine patients (p<0.05). The apical diameter of the patient group was found to be significantly larger (p= 0.045). The severity of the headache was directly proportional with the incidence of giant capillaries (p=0.015). The severity of the headaches increased with the diameter of the capillaries (p=0.024).The effect of the length of headache history by means of years on the capillaroscopic findings was investigated. Migraine incidence was found to be directly proportional with the apical diameter (p=0.005).

Conclusion: Vascular pathology can be determine objectively by using video capillaroscopy.Increased tortuosity is a sign of tissue hypoxia. Increased tortuosity and giant capillaries were seen more frequently in migraine patients and migraine patients with old headache history also. These findings will be guide for understanding migraine pathophysiology.

Disclosure: Nothing to disclose

EPR3043

Headache intensity is associated with increased white matter lesion burden in CADASIL patients

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Background and aims: CADASIL (Cerebral Autosomal Dominant Arteriopathy With Subcortical Infarcts and Leukoencephalopathy) is the most common hereditary cause of vascular dementia in adults. Migraine is a major symptom of the disease.

Aim: To identify variables associated with increased cerebral lesion burden in a cohort of Portuguese CADASIL patients.

Methods: Cross-sectional study of CADASIL patients. Demographics data, vascular risk factors and headache characteristics were collected through a structured questionnaire. MRI (3-Tesla) was used to determine white matter hyperintensities burden - in terms of volume (WMH-V) and number (WMH-N).

Results: We included 32 patients with CADASIL. WMH-V was significantly associated with age (β=1.266, 95%CI=[0.805, 1.726], p<0.001), headache intensity (β=5.143, 95%CI=[2.362, 7.924], p=0.001) and female sex (β=19.727, 95%CI=[8.750, 30.075], p=0.001). WMH-N is best predicted by age, obesity and history of migraine, although not statistically significant.

Conclusion: Age, female sex and headache intensity are associated with increased white matter lesion burden in CADASIL.

Disclosure: Nothing to disclose

EPR3044

Gene expression of the endocannabinoid system components in peripheral blood mononuclear cells of subjects with migraine

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Background: Among the mediators involved in the modulation of the trigeminovascular system, the endocannabinoid system (ES) has recently attracted considerable attention. The ES interacts with the serotonergic system, NO synthesis and neuropeptides release, all of which are involved in migraine pain. Increasing experimental and clinical evidence suggests a link between dysregulation of this system and migraine.

Aim: To further investigate the possible changes in ES tone in episodic and chronic migraine.

Methods: The gene expression of cannabinoid receptors CB1 and CB2, and of two enzymes involved in the metabolism/catabolism of endocannabinoids - N-Acyl Phosphatidylethanolamine Phospholipase D (NAPE-PLD) and FAAH) - was evaluated by means of rtPCR in peripheral blood mononuclear cells (PBMCs) of patients with episodic or chronic migraine and age-matched healthy controls.

Results: We detected an increase in cannabinoid2 (CB2) gene expression in PBMCs of migraine subjects, compared to controls. The increase was more markerd in subjects with chronic migraine when compared to either episodic migraine and controls. CB1 and NAPE-PLD gene expression increased only in chronic migraine patients. A significant decrease in FAAH gene expression was found in all migraineurs compared to controls, with significantly lower levels in chronic migraine patients.

Conclusion: The present findings show significant transcriptional changes in ES components in PBMCs of patients suffering from migraine. These changes are more marked in the chronic subtype of migraine and, for their characteristics, they are likely to reflect ongoing compensatory mechanisms aimed at maintaining AEA levels.

Disclosure: Nothing to disclose

EPR3045

Role of the transient receptor potential ankyrin type-1 (TRPA1) channel in migraine pain: evaluation in an animal model

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Background and aims: To date, the pharmacological treatment of migraine remains somewhat unsatisfactory, partly because the pathophysiology of this disabling disease is still poorly understood. Clinical and experimental studies have pointed to the possible involvement of the transient receptor potential ankyrin type-1 (TRPA1) channels in migraine pain.

The aim of this study is to further investigate the role of TRPA1 in the pathophysiology of migraine pain in an animal model using a novel TRPA1 antagonist (ADM_12) as a probe.

Methods: The effects of ADM_12 on nitroglycerin-induced hyperalgesia at the trigeminal level were investigated in male rats using the quantification of nocifensive behavior in the orofacial formalin test. The expression levels of the genes coding for c-Fos, TRPA1, calcitonin gene-related peptide (CGRP) and substance P (SP) was evaluated in peripheral and central neuronal areas relevant for migraine pain.

Results: The findings show that ADM_12 inhibited the hyperalgesia induced by nitroglycerin treatment, in the second phase of the orofacial formalin test. This effect was associated to a significant inhibition of nitroglycerin-induced increase in c-Fos, TRPA1 and neuropeptides mRNA levels in medulla-pons area, cervical spinal cord and in the trigeminal ganglion.

Conclusion: The present findings support a critical involvement of TRPA1 channels in the pathophysiology of migraine, and show their active role in counteracting hyperalgesia at the trigeminal level.

Disclosure: Nothing to disclose

EPR3046

The efficacy of ergotamine-based combination antimigraine drug compared to sumatriptan in the treatment of migraine without aura

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Background and aims: The aim of the study was to investigate the efficacy of ergotamine tartrate + mecloxamine ciitrate + camylofine hydrochloride + caffeine + propyphenazone (Nomigren®) compared to Sumatriptan in the treatment of migraine without aura.

Methods: The study was designed as double-blind with double placebo (double dummy), parallel, randomised, multicentric. The study included patients aged 18-64 years with a diagnosis of migraine without aura according to the International Headache Society Criteria (ICHD-3 Beta). There were 201 respondents in four clinical centers (98 in the Nomigren® group and 103 in the Sumatriptan group). The efficacy was assessed on the basis of a complete cessation of pain two hours after administration of the drug and the need for additional analgesic therapy (diclofenac).

Results: The use of Nomigren® resulted in the complete cessation of pain in 51% of reported migraine headaches without aura (91/178), while Sumatriptan administration resulted in complete cessation of pain in 34% of migraine attacks (62/184) (p=0.0015). The use of additional analgesic therapy with diclofenac was observed in 21% of migraine attacks in the Nomigren® group and 35% in the Sumatriptan group (p=0.004). A complete failure of therapy was observed in 2 subjects in the Nomigren® group and in 9 subjects in the Sumatriptan group (p=0.0006). Approximately the same number of patients in both groups (70%) were willing to continue the therapy.

Conclusion: The study showed better effectiveness of Nomigren® in the complete cessation of migraine pain compared to Sumatriptan in the treatment of migraine without aura.

Disclosure: Nothing to disclose

EPR3047

Are clinical features of nummular headache different when precipitated by head trauma? Analysis of a series of 225 patients

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Background and aims: Nummular Headache (NH) is located in a sharply contoured rounded area of the scalp. Head trauma as a precipitating event has been described. We aimed to compare characteristics of idiopathic and post-traumatic NH.

Methods: Patients diagnosed of NH in a Headache Unit in a tertiary hospital (January 2008-January 2018), accordingly to ICHD criteria. We prospectively considered clinical and epidemiological data, comparing idiopathic cases with those triggered by a cranial trauma.

Results: We included 225 patients (145 women, 80 men) with NH. Among them 29 (23 women, 6 men) described a head trauma related to beginning of pain. In 27 there was a background pain of oppressive or burning character and rated as 5±1.9 (2-10) on a verbal analogical scale (VAS), and in 12 stabbing superimposed exacerbations rated as 6.6±1.3 (4-8) on VAS. In 15 post-traumatic patients, an oral preventative was considered necessary, usually gabapentin, achieving at least a partial relief in most cases. When comparing groups with or without previous trauma, age of onset was higher among post-traumatic patients (59.9±17.4 vs 48.1±18 years, p:0.002). Allodynia upon palpation was encountered more frequently in trauma triggered painful areas (53.3% vs. 32.7%, p:0.04). There was no difference between both groups regarding characteristics of pain, location of painful areas or requirement of preventatives and their efficacy.

Conclusion: Cranial trauma is not an uncommon trigger in our series of Nummular Headache. Patients with post-traumatic forms are older and the presence of allodynia is more frequent.

Disclosure: Nothing to disclose

EPR3048

Efficacy of erenumab for the treatment of patients with episodic migraine with aura

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Background and aims: Erenumab is a fully human monoclonal antibody that inhibits the calcitonin gene-related peptide (CGRP) receptor. In a Phase III study (NCT02456740), erenumab demonstrated a significant reduction in the mean monthly migraine days (MMD) compared with placebo. Here, we report a subgroup analysis assessing the efficacy of erenumab in episodic migraine patients with/without history of aura (self-reported).

Methods: Patients were randomised 1:1:1 to erenumab 70mg, 140mg or placebo monthly for 6 months. This subgroup analysis assessed changes in MMD, acute migraine-specific medication days (MSMD), and proportion of patients achieving ≥50% reduction in MMD averaged over months 4-6. Nominal p-values were presented without multiplicity adjustment and were not used for pre-planned hypothesis testing.

Results: Of 955 patients randomised, 52% had a history of aura. Baseline characteristics were similar among the groups. Compared with placebo, erenumab induced greater reductions in MMD in both the subgroups. In patients without history of aura, least-squares mean (SE) changes from baseline were −1.5 (0.3) for placebo vs −2.7 (0.3) for 70mg (p=0.002) and −3.8 (0.3) for 140mg (p<0.001). In patients with history of aura, changes were −2.1 (0.3) for placebo vs −3.8 (0.2) for 70mg (p<0.001) and −3.5 (0.3) for 140mg (p<0.001). In both the subgroups, treatment with erenumab 70 and 140mg resulted in more patients achieving ≥50% reduction in MMD and fewer acute migraine-specific medication days than with placebo (Table).

Conclusion: Erenumab was efficacious in migraine patients with and without history of aura.

Disclosure: This study was supported by Amgen Inc. USA

EPR3175

Pericranial nerve block for the short-term preventive treatment of refractory chronic migraine: a randomized, double-blinded, placebo-controlled study

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Background and aims: This study aims to investigate the efficiency of a single and repeated the greater occipital nerve (GON), the supraorbital (SON) and the auriculotemporal nerve (ATN) block using lidocaine in the treatment of refractory chronic migraine.

Methods: Patients between 18 and 60 years old with chronic migraine (modified ICHD-II as patients with > 10 days with consumption of acute medications were permitted into the study) were randomized to receive either 5 ml 1% lidocaine plus 5mg dexamethasone over pericranial nerve block application or 6 ml normal saline(placebo). Patients completed a one-month headache diary prior to and after the double-blind injection. The primary outcome measure was defined as a 50% or greater reduction in the frequency of days with moderate or severe migraine headache in the four-week post-injection compared to the four-week pre-injection baseline period.

Results: 50 patients received active and 50 patients received placebo treatment. In the active and placebo groups respectively, the mean frequency of at least moderate (mean 6.2 versus 9.5) and severe (2.6 versus 4.3) migraine days and acute medication days (5 versus 10.0) were statistically significant difference between the groups after treatment (p>0.05). The percentage of patients with at least a 50% reduction in the frequency of moderate or severe headache days was 45% for pericranial nerve block group.

Conclusion: These results show that repeated pericranial nerve blocks with local anesthetic can be an effective alternative treatment in migraine patients who are unresponsive to medical prophylaxis or who do not prefer to use medical prophylaxis.

Disclosure: Nothing to disclose

Miscellaneous

EPR3049

TK2-deficiency masquerading as critical illness neuromyopathy in an adult

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Background and aims: Critical illness polyneuropathy (CIP) and critical illness myopathy (CIM) are common complications in patients undergoing intensive care treatment. They are usually diagnosed on clinical grounds and by neurophysiological findings.

Methods: A 37-year-old patient sustained hypoxic brain damage after resuscitation from cardiac arrest and required prolonged artificial ventilation. After developing a severe flaccid tetraparesis with bilateral ptosis, a diagnosis of CIP/CIM was made based on the neurophysiological findings of severe neuropathy and myopathy. A 53-year-old patient developed peritonitis with sepsis which necessitated long-term artificial ventilation. She developed a severe neuromyopathy with tetraparesis and cranial nerve involvement, and a diagnosis of CIP/CIM was assumed. In both patients, muscle biopsy was performed to confirm CIP/CIM. Mitochondrial DNA deletions were analysed by long-range PCR; sequencing of thymidine kinase 2 (TK2) was performed.

Results: In patient 1, muscle histology findings did not support CIM, instead ragged blue fibres were identified. Long-range PCR analysis revealed multiple deletions in mtDNA and sequencing of the TK2 gene revealed a known pathogenic homozygous mutation. In patient 2, muscle histology was in keeping with CIM, but also showed some multiple deletions of mtDNA. Sequencing of TK2 revealed a novel heterozygous mutation, which was predicted to be pathogenic.

Conclusion: Both patients were noted to have clinical features unusual for CIP/CIM (ptosis, cranial nerve involvement). Further testing eventually showed pathogenic mutations in TK2, expanding the phenotype of TK2 deficiency. Investigation for multiple mtDNA deletions and TK2 deficiency is warranted in patients who present with apparent CIP/CIM and unexplained additional clinical features.

Disclosure: Nothing to disclose

EPR3050

The PSH-AM is a valuable tool in diagnosing autonomic dysregulation: a cohort study and review.

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Background and aims: This study aimed to determine the clinical expression of autonomic dysregulation in patients with diffuse axonal injury (DAI) after traumatic brain injury (TBI) in comparison with the literature.

Methods: Patients clinically diagnosed with autonomic dysregulation were selected from a cohort study involving 116 patients with DAI. We studied the incidence, autonomic features, treatment, and outcome, and performed a systematic review.

Results: In 16.4% (n=19) patients autonomic dysregulation was diagnosed. In 58% (n=11) of these patients was a probable PSH scored according to the PSH-AM, only 5% (n=1) scored unlikely. Autonomic dysregulation was associated with age (OR 0.95), DAI grade (OR 7.2), and an unfavourable outcome (OR 5.6). Patients with autonomic dysregulation had a significantly longer ICU and hospital stay.

The review yielded 30 articles. The incidence of autonomic dysregulation after TBI varied from 7.7-32.6% (mean 13.5%). TBI patients with autonomic dysregulation had a longer ICU stay and poorer outcome.

Conclusion: Patients with DAI and autonomic dysregulation had a longer ICU stay and a poorer outcome compared to patients without autonomic dysregulation. The number of autonomic features is no prerequisite for diagnosing PSH. The PSH-AM is a valuable tool to determine the likelihood of autonomic dysregulation.

Disclosure: This work resulted from the TopCare Experiment which is supported by a grant of the Dutch organization for health research and care innovation (ZonMw, grant number 842004002), the authors alone are responsible for the content and writing of the article.

EPR3051

The use of continuous EEG-monitoring in intensive care units in Europe: an international survey

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Background and aims: For unclear reasons, there is variation in the use of continuous electroencephalographic monitoring (cEEG) between medical centers. In this study, we aim to describe the current practice of cEEG monitoring among European physicians.

Methods: An online survey was sent to 23 European national clinical neurophysiology societies for distribution amongst their members.

Results: The survey was completed by 62 physicians from 11 countries, corresponding to a response rate of 48%. More than half of respondents use cEEG (57%). The duration of cEEG monitoring is <24h (17%), 24 to 48h (45%), 49 to 74h (24%) and >74h (14%). Nonconvulsive seizures (NCS) or nonconvulsive status epilepticus (NCSE) detection is the most common indication for cEEG (42%). The majority of respondents do not comply to (inter)national guidelines to determine the indications and duration for cEEG (59%). There is general agreement on the impact of cEEG monitoring on clinical decison-making. Almost all participants refraining from cEEG use, perform routine 30 minutes EEG if NCS or NCSE is suspected. Limited technical and financial resources besides limited qualified personal are the most common obstacles for introducing or expanding cEEG.

Conclusion: More than half of respondents to this international European survey use cEEG. The primary indication for applying cEEG is NCS(E) detection. However, due to lack of consensus, significant variation exists among physicians who currently use cEEG at their institutions. Also, implementation of cEEG is hampered by technical, financial and personnel issues.   Further multicenter prospective studies are needed to advance uniformity of cEEG utilisation.

Disclosure: Nothing to disclose

EPR3052

Lower limb neurological examination and interpretation by medical trainees

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Background and aims: Neurological symptoms account for one-fifth of admissions to the emergency department, yet the neurological examination is thought to be the hardest examination to learn by doctors.

Methods: We studied medical trainees attending a revision course in London for the clinical part of the Membership of the Royal College of Physicians examination. Candidates were observed during the lower limb neurological examination of people with four different neurological diseases including spastic paraparesis and peripheral neuropathy.

Results: One examiner observed 245 trainees over 3 years. Gait was assessed by 233 (95%) doctors, with tandem gait checked by 39 (25%) and Romberg's test by 100 (41%). Tone, power and reflexes were assessed fully by over 80% of candidates. Plantar response was checked by 86% of candidates. When reflexes were absent, 123 of 180 (68%) candidates attempted reinforcement manoeuvres. For sensation, 63% chose to use cotton wool first, 32% chose pinprick first, and 4% chose a tuning fork or tested proprioception first.

When presenting their findings, the proportion of candidates who correctly identified signs were: 54% for gait, 91% for tone, 66% for pattern of weakness, 59% for reflexes and 69% for plantar response. 64 out of 245 (26%) candidates correctly diagnosed the subjects.

Conclusion: This is the first study, to our knowledge, to observe neurological examination technique, detection of abnormal signs and interpretation of findings in a controlled setting. Trainees find certain parts of the neurological examination difficult and the majority of trainees have difficulty interpreting their findings and diagnosing conditions.

Disclosure: Nothing to disclose

EPR3053

A new form of martyrdom?

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Background and aims: Organ donation after euthanasia has been practiced in Belgium in some 25 patients. Transplant surgeons testify that organ donation often leads to a new sense of identity and meaning. The case presentation illustrates a problem confounding the decision-making process on euthanasia followed by organ donation.

Methods: A 34-year-old woman was being treated for a long-standing depression. As an adolescent, she had already made several suicide attempts. At one point in her life, she had promised her parents that she would not make another attempt. Now that both parents were deceased she requested euthanasia.

Results: The doctor who received her euthanasia request immediately presented organ donation as a possibility. A documentary film was made before her death, in which she stated that her 'suicide' provided a new meaning and sense of identity for her because she felt that she would be living on thanks to her organ donation. She claimed to have the right to self-determination in connection with others up to and beyond death.

Conclusion: Candidates for organ donation after euthanasia often suffer from neuropsychiatric disease. Patient's motivation in living altruistic organ donation has been thoroughly debated. No act is unmotivated and gratuitous and in patients with severe neurodegenerative disease the renewed sense of identity involved in organ donation would be acceptable. In patients with primary psychiatric diseases such as long-standing depression and intense death wish, the increased significance that is attached to the life-ending-act should be viewed with extreme caution. Dying for someone else seems to be a new form of martyrdom.

Disclosure: Nothing to disclose

EPR3054

What can mythology of Portuguese river Lima and ancient Greek and Roman goddesses Lethe and Mnemosyne tell us about ancient knowledge of memory and memory loss?

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Background and aims: Greek and Roman goddesses and rivers of memory (Mnemosyne) and oblivion (Lethe) may give us some insight into the common knowledge about memory and memory loss in the ancient times. The Portuguese river Lima was believed to be the mythological river of forgetfulness – Lethe.

Picture 1: Mnemosine enhancing the retrieval with her touch. Hatay Archaeology Museum, Turkey. Mnemosyne's symbol was luscious hair, representing many thoughts coming out the head. "If you had no memory you could not even remember that you ever did enjoy pleasure, and no recollection whatever of present pleasure could remain with you."(Plato)

Methods: We searched texts on ancient Roman and Greek mythology and artworks for symbols and descriptions of Menmosyne and Lethe and put them into the context of modern neurocientific knowledge.

Picture 2: The nine Muses - Roman sarcophagus, Louvre, Paris. Mnemosyne was mother of nine muses, that are personifications of different aspects of memory, from implcit to semantic. In culture based on oral tradition, people heavily depended on memory when passing knowledge through generation (muses represent music, law, dance, poetry, etc.)

Results: Knowledge on different memory stages (from imprinting to retrieving) could be identified. For example: "This is the gift of Mnemosyne...Whenever we wish to remember anything, we hold this wax under the perceptions and thoughts and imprint them upon it. Whatever is imprinted we remember and know as long as its image lasts, but whatever is rubbed out or cannot be imprinted we forget

and do not know."(Plato,Theaetetus 191d). Mnemosyne touch on a forehead, was believed to enhance memory retrieval (Picture 1).

Mnemosyne was also believed to be responsible for language processes, for invention of meanings of all the things (semantic memory) and controlling episodic and autobiographical memory (Picture 1).

As goddess, Lethe was also a mythological river, causing symptoms now closely associated with dementia. Drinking from Lethe induced symptoms such as fading of existing memories, daytime sleepiness and poor orientation in space (Picture 3).

Picture 3: Photography of Ponte de Lima. Legend says, Roman army was afraid to cross the Lima river, believing it is the mythological river Lethe: ''Romans believed that Lima River produced forgetfulness, and they feared to cross it, in doing so, they thought that they would forget Rome and remain in the area forever'' (Augusto Pino Lehal).

Conclusion: We found evidence on ancient awareness of different types of memory, memory stages and symptoms of memory loss. There was public awareness of dementia even 2500 years ago

Disclosure: Nothing to disclose

EPR3055

Patients with diffuse axonal injury can recover to a favourable long-term functional and quality of life outcome

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Background and aims: Functional outcome and quality of life are difficult to predict in patients with diffuse axonal injury (DAI) after traumatic brain injury (TBI). Primary aim of this cross-sectional cohort study was to assess long-term functional outcome in patients with DAI and to identify prognostic factors. Secondly health-related quality of life (HRQL) at long-term follow-up was assessed.

Methods: Patients aged ≥16 with TBI and DAI (admitted 2008-2014) were included. Clinical and imaging data were collected. The primary outcome parameter was the Glasgow Coma Scale Extended (GOSE) at long-term follow-up. Secondly HRQL was assessed with the Quality Of Life after Brain Injury (Qolibri) questionnaire.

Results: DAI was diagnosed in 185 patients. Long-term functional outcome was obtained in 134 patients (72%), median follow-up 54 months (range 14-100). 51% had a favourable outcome (GOSE 6-8). Independent prognostic factors were age, pupillary reaction, Hb, DAI grading, and return of consciousness ≤7 days. Sixty-two percent had a good HRQL, median follow-up 57 months (range 14-100) with age as an independent prognostic factor.

Conclusion: More than half of patients with DAI had a favourable functional outcome and a good HRQL at long-term follow-up. Also in patients with a DAI grade 3 a favourable outcome was seen. HRQL is a clinically relevant outcome measure since it reflects perceived outcome by patients. Independent prognostic variables for the functional outcome were factors obtained in the acute phase after injury whereas age was an independent prognostic factor for HRQL.

Motor neurone diseases 2

EPR3056

Oligogenic and discordant inheritance: a population based genomic study of Irish kindreds carrying the C9orf72 repeat expansion

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Background and aims: The C9orf72 repeat expansion is the most commonly identified genetic cause of ALS in Ireland and has known pleiotropic effects evidenced, in part, by higher rates of neuropsychiatric conditions in family members. In addition, oligogenic inheritance of C9orf72 with other risk variants e.g. knockdown of SUPT4H1 gene, may modify expression and thus perceived penetrance of the repeat expansion.

Methods: 151 individuals with familial ALS, identified through the Irish ALS Register, were screened for the presence of the pathogenic GGGGCC hexanucleotide repeat expansion by repeat-primed PCR.

Results: 47 patients with ALS from 40 families carried the C9orf72 repeat expansion. By analysing inheritance, we observed definite co-segregation in 2 of the 40 families. However, in 7 families co-segregation was absent. 8 C9orf72 positive patients carried one or more additional known or putative ALS risk variants: SETX (2), TBK1 (2), ATXN2 (2), TAF15 (1), SPG11 (1), NEK1 (1) and UNC13A (1).

Conclusion: Our findings demonstrate that the presence of a family history does not necessarily infer the presence of a common disease aetiology. Genetic pleiotropy, oligogenic inheritance, age dependent penetrance, variable tissue expression and the potential for laboratory error all have implications for counselling of patients and asymptomatic relatives.

Disclosure: Nothing to disclose

EPR3057

CSF Tau as survival biomarker in Amyotrophic Lateral Sclerosis

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Background and aims: Amyotrophic lateral sclerosis is a fatal neurodegenerative disease that still lacks of reliable diagnostic biomarkers. Aim of the study is to test the diagnostic and prognostic potential of CSF protein Tau, p-Tau and p-Tau/Tau ratio in ALS compared to other neurodegenerative and non-neurodegenerative diseases.

Methods: We included 66 incident patients with possible, probable and definite ALS. Control groups included 126 patients with Alzheimer's disease (AD) and 49 patients with other non-neurodegenerative diseases (ONND) (mainly polyneuropathies and some migraines). Patients were enrolled in a period from March 2009 to April 2016 and followed up till April 2017. Comparisons between groups were performed with Mann-Whitney test while correlations were evaluated with Spearman rank correlation test. Kaplan-Meier estimator was used for the analysis of survival.

Results: ALS patients had higher CSF Tau and pTau/tau than ONND, whereas AD patients had the highest levels of both the biomarkers. ROC analysis revealed a sensitivity of 80.3% and a specificity of 61.2% of CSF Tau in discriminating ALS patient from ONND. No relations were found between CSF Tau and p-Tau and clinical features. Survival analysis showed a shorter survival in ALS with higher CSF tau ($p=0.03$).

Conclusion: The increased levels of CSF Tau and p-Tau in comparison to ONND confirms the existing process of neurodegeneration in ALS. Nevertheless, the low specificity of CSF Tau makes it as an unreliable diagnostic tool for ALS. However, the shorter survival observed in patients with high levels of CSF Tau makes this biomarker a potential biomarker of survival.

Disclosure: Nothing to disclose

EPR3058

Microstructural correlates of Edinburgh Cognitive and Behavioural ALS (ECAS)

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Background and aims: ECAS has been designed for testing patients with amyotrophic lateral sclerosis (ALS) including tests sensitive to impairment of cognitive domains specifically involved in ALS (Language, Fluency, Executive functions), and an assessment of ALS non-specific functions (Memory, Visuospatial functions). Using whole-brain tract-based spatial statistics (TBSS) diffusion tensor imaging (DTI) we aim to explore the potential association between brain microstructural damage and ECAS scores.

Methods: 40 ALS patients (King's clinical stages 1 or 2), cognitively assessed by ECAS, and 35 healthy controls underwent 3T-MRI. DTI TBSS analysis was performed to measure fractional anisotropy (FA) and axial, radial and mean diffusivities (AD, RD, MD) for between-groups comparisons and correlations between DTI metrics and ECAS scores.

Results: ALS patients exhibited a decreased FA ($p < 0.05$, corrected) in bilateral cortico-spinal tracts, corpus callosum (CC) and superior longitudinal fasciculi and an increased RD in the rostral part of the right cortico-spinal tract and in the midbody of CC. ECAS total score were significantly related to measures of FA, MD and RD ($p < 0.05$, corrected). Regard ALS-specific scores, verbal fluency was significantly associated to RD in the splenium of CC. The total score from all ALS non-specific tests was significantly related to FA decrease in the right cortico-spinal tract, the body of CC, the fornix, the left inferior fronto-occipital fasciculus and bilateral superior longitudinal fasciculi, extended also to bilateral superior longitudinal fasciculi, considering the memory subscore alone.

Conclusion: Results point towards an early microstructural degeneration of brain areas, with significant relationships between DTI metrics and ALS-specific and non-specific ECAS scores.

Disclosure: Nothing to disclose

EPR3059

Molecular biomarkers associated with respiratory insufficiency in Amyotrophic Lateral Sclerosis

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Background and aims: Amyotrophic Lateral Sclerosis (ALS) is a devastating and fatal neurodegenerative disorder. Death typically occurs within 3–5 years after disease onset. ALS patients die mainly from respiratory failure (RF). No effective treatment is available and no molecular biomarker related to respiratory outcome and to early ventilatory dysfunction was described. The club-cell protein (CC-16) is a biomarker associated with respiratory distress and lung inflammation. We aim to explore CC-16 as a candidate biomarker for respiratory failure in ALS. Additionally, we intend to identify morphological and viscoelastic changes of the erythrocyte membrane and associate them with the clinical features.

Methods: Patients were compared with a control group of healthy blood subjects. CC-16 was quantified by ELISA. Morphological and viscoelastic properties of the erythrocytes were analysed by Atomic Force Microscopy (AFM).

Results: CC-16 was significantly higher in ALS patients and predictive of non-invasive ventilation within 3 months and death in the 18 months. It was observed higher erythrocyte maximum height, area and volume, decreased erythrocyte membrane roughness, increased membrane stiffness and fluidity, and lower membrane negativity (zeta potential), in the ALS population. This set of findings indicates abnormal erythrocyte the membrane structure and changed lipid composition.

Conclusion: Overall, our preliminary results are in favor of an increased lung inflammatory response related to respiratory distress. Moreover, erythrocyte abnormalities can enhance risk of tissue hypoxia. These results should prompt a larger study to confirm our preliminary results, since we urge to find biomarkers of respiratory dysfunction and tissue hypoxia in ALS.

Disclosure: Nothing to disclose

EPR3060

Do ALS motor phenotypes develop stochastically?

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Background and aims: Amyotrophic lateral sclerosis manifests with various motor phenotypes. Our aim was to assess whether these phenotypes are determined by detectable factors.

Methods: ALS incident patients (N=2,702) included in the PARALS (an Italian regional registry of ALS) from 1995 to 2014 were enrolled. Six motor phenotypes were considered: classic, prevalent upper motor neuron, flail arm, flail leg, respiratory, classic bulbar, prevalent upper motor neuron bulbar (Chiò, JNNP 2011). Logistic regression analysis was performed, adjusting for gender and age (ten-year age classes). The outcome was represented by dummy variables: spinal vs bulbar phenotypes as macro-categories; each spinal phenotype (classic, flail arm, flail leg, prevalent upper motor neuron, respiratory) vs bulbar phenotypes; each bulbar phenotype (classic and prevalent upper motor neuron) vs spinal phenotypes.

Results: Males showed a probability of developing a spinal form 72% higher than females (OR=1.72; p=0.000). Among patients over 60 years, the spinal onset was less frequent than the bulbar one (test for trend in subsequent ten-year age classes: p<0.0001). This finding was particularly strong in females, with ORs between 5.40 (60-69 years) and 9.10 (over 80 years). Respiratory and flail arm phenotypes were more common in males, with a probability more than ten-fold and more than two-fold than females respectively (OR=11.72 and OR=3.39). The likelihood of the pyramidal bulbar phenotype resulted more than two-fold in females compared to males (OR=2.20; p=0.0001), without differences among age classes.

Conclusion: ALS motor phenotypes seem to arise from a combination of patients' gender and age.

Disclosure: Nothing to disclose

EPR3061

Assessment and diagnostic utility of the upper motor neuron involvement in amyotrophic lateral sclerosis by 3T-MRI

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Background and aims: Clinical signs of upper motor neuron (UMN) involvement are important for amyotrophic lateral sclerosis (ALS) diagnosis, although often difficult to appreciate. Conventional MRI can identify abnormalities associated with UMN involvement, especially with high field scanners. We evaluated the diagnostic contribution of 3T-MRI in ALS patients.

Methods: We retrospectively evaluated MRI from 93 ALS patients (55 men, mean age 62.8±10.1) and 89 controls (56 men, mean age 60.2±9.5). All subjects performed 3T-MRI study including 3D-FSPGR-T1, FSE-T2, GRE-T2*, FLAIR-T2 and SWI sequences, visually assessed by two blinded neuroradiologists. A third rater resolved disagreements. Features of interest were cortico-spinal tract T2/FLAIR hyperintensity, motor cortex T2*/SWI/FLAIR hypointensity and selective motor cortex atrophy. Agreement was tested using Cohen's k statistics and differences between groups using χ2 test (p<0.05 corrected). Sensitivity, specificity, PPV, NPV, and accuracy of ALS diagnosis by MRI were calculated using clinical diagnosis as gold standard.

Results: Raters agreement was 83%-91% (kappa=0.53-0.75, p<0.001). All MRI features were significantly more prevalent in ALS patients, mainly cortico-spinal tract FLAIR hyperintensity (75% vs 32%; p<0.0001) and motor cortex SWI hypointensity (76% vs 39%; p=0.001). Diagnostic accuracy was 60%-72% considering single features. The highest accuracy was reached combining cortico-spinal tract FLAIR hyperintensity and motor cortex SWI hypointensity (sensitivity: 70%; specificity: 81%; PPV: 90%; NPV: 51% and accuracy: 73%).

Conclusion: 3T-MRI is able to detect specific changes related to UMN involvement with good accuracy and can be useful to support the clinical diagnosis of ASL.

Disclosure: Nothing to disclose

EPR3062

The natural course of dysphagia in ALS is different between patients with bulbar and spinal onset

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Background and aims: We aimed at evaluating the relationship between dysphagia and site of onset in amyotrophic lateral sclerosis (ALS) in terms of progression rate.

Methods: We enrolled 871 incident ALS patients (580 with spinal onset, 291 with bulbar onset), resident in Piemonte and Valle d'Aosta, Italy, from 2007 to 2013. Based on ALSFRS-R item 3, dysphagia was classified as "severe" (0-1), "moderate" (2-3), "absent" (4). The progression of dysphagia was considered as time-dependent variable and was reassessed at each visit. Progression rate of dysphagia was calculated separately among patients with bulbar and spinal onset (N=642). Time intervals ended with the date when dysphagia became severe. The starting date was the date of onset for bulbar patients (N=279) and the date of first bulbar symptoms (considering ALSFRS-R items 1 and 3<4) for spinal patients (N=363). 217 patients did not develop dysphagia during the follow-up.

Results: ALS patients showed moderate dysphagia after a median of 24.4 months (IQR=13.5-44.7) from the onset. Dysphagia became severe after additional 17.7 months (IQR=9.5-29.8); death/tracheostomy occurred after additional 6.9 months (IQR=2.6-14.7). The progression rate showed a median time interval of 17.4 months (IQR=8.9-29.5) between the first bulbar symptom and severe dysphagia. These time intervals were shorter in patients with spinal onset (median 11.9 months; IQR=5.5-24.1) than in cases with bulbar onset (22.9 months; IQR=16.0-31.8) (Wilcoxon test p=0.000).

Conclusion: The progression rate of dysphagia significantly differs between ALS patients with bulbar and spinal onset.

Disclosure: Nothing to disclose

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EPR3063

Changes in resting state cerebellar connectivity in cervical dystonia induced by botulinum toxin

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Background and aims: Administration of botulinum neurotoxin A (BoNT) injections is currently the preferred treatment of focal dystonia. The clinical effect of BoNT is assumed to be mediated by dynamic changes at multiple levels of the sensorimotor system. Recently, the role of the cerebellum in the pathophysiology of dystonia has been discussed. The aim of our study was to compare the connectivity between large-scale resting state networks and the cerebellum before and after treatment initiation.

Methods: 12 patients with cervical dystonia indicated for treatment with BoNT were enrolled (11 female, aged 50.8 ± 8.1 years, range 38-61 years). Clinical and functional MRI examinations were carried out immediately before and 4 weeks after BoNT injection. Clinical severity of dystonia was evaluated using the TWSTRS. The functional imaging data were acquired using a 1.5 Tesla MRI scanner during an 8-minute rest. Pre-processed data from both sessions were decomposed into 30 group-wise independent components (IC's) using MELODIC from the FSL toolbox. Treatment-related changes in connectivity between the cerebellum and the whole-brain components were evaluated using dual regression analysis and non-parametric permutation testing. Results were thresholded at the corrected $p < 0.05$.

Results: Clinical scoring demonstrated satisfactory clinical effect of BoNT. The only significant difference was detected in the left-sided fronto-parietal component (IC 7, Figure 1), which demonstrated a decrease of functional connectivity after the treatment in the left cerebellar lobule VIIIa (coordinates [x,y,z]: -34, -54, -56).
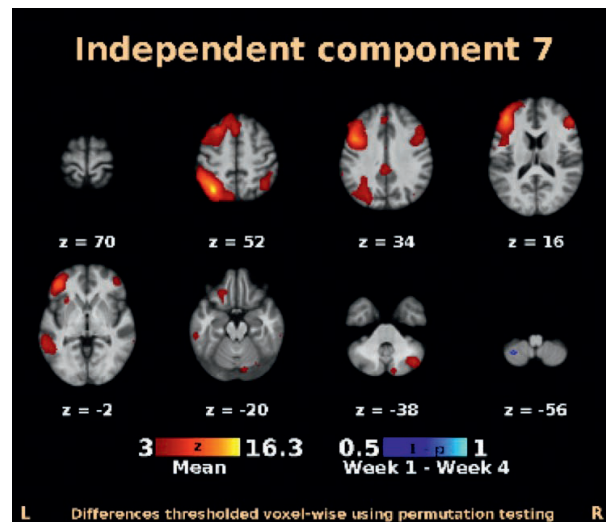
Independent component 7 and treatment-related difference. The red-yellow overlay shows the spatial representation of the IC 7. The blue overlay shows the significant connectivity decrease at Week 4.

Conclusion: Our data provide evidence for abnormal resting state connectivity between large-scale cortical networks and the cerebellum.

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EPR3064

Mutations of the VPS35 (PARK17) and FBXO7 (PARK15) genes associated with pathological finding of Lewy body pathology

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Background and aims: A 83-year-old man with positive family history of parkinsonism suffered from atypical parkinsonism with a clinical picture phenotypically correlated with PSP-P from his 66 years. Mutations associated with parkinsonism in this family have been identified in VPS35 (PARK17) and FBXO7 (PARK15) genes. The aim of this study was a description of a neuropathological finding associated with these PARK genes mutations.

Methods: Post-mortem histopathological examinations (formalin-fixed, paraffin –embedded blocks from the temporal, frontal, parietal and occipital cortex, hippocampus and parahippocampal regions, basal ganglia, thalamus, subthalamic nucleus, brain stem, substantia nigra and cerebellum) were performed by using H-E, Luxol blue, impregnation of silver salts, immunohistochemistry with monoclonal antibodies against: phospho-PHF-tau AT8, anti-tau 3-repeat isoform RD3, anti-tau 4-repeat isoform RD4, α-synuclein, b-amyloid, and antiphospho- TDP-43.

Results: The macroscopic finding was characterized by diffuse cerebral atrophy. The immunohistochemical examination confirmed the diagnosis of Parkinson's disease, Braak stage VI, neocortical type by McKeith. Lewy body pathology was also present in periaqueductal gray matter, in the rostral interstitial nucleus of the medial longitudinal fasciculus, interstitial nucleus of Cajal and nucleus Darschewitsch which are involved in the supranuclear control of gaze. Together with Lewy body pathology, low level Alzheimer's disease neuropathologic changes (A1B1CO) according to the ABC scoring system was present. Concomitant tauopathy and TDP-43 proteinopathy were excluded.

Conclusion: This case provides the first description of neuropathological correlation of Parkinson's disease associated with VPS35 (PARK17) and FBXO7 (PARK15) genes mutations. The clinical picture resembled PSP-P due to involment of the structures involved in eye movement control.

Disclosure: This work was supported by grans: AZV-Ministry of Health of the Czech Republic Nr. 15-32715A, IGA-LF-2017-023 and MH CZ – DRO (FNOL 00098892) – 2017.

EPR3065

Pharmacokinetic and safety characterisation of carbidopa/levodopa subcutaneous infusion (ND0612): Phase I studies in healthy volunteers and patients with fluctuating Parkinson's disease

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Background and aims: Improving the continuity of carbidopa/levodopa (CD/LD) delivery is desirable in Parkinson's disease (PD) patients experiencing motor fluctuations. As an alternative to oral LD formulations with pulsatile pharmacokinetics, ND0612 is under development as a drug-device combination to provide continuous delivery of CD/LD (without the need for surgical gastrostomy tube implantation for drug infusion).

Methods: Study 001 was a dose-escalating study conducted in healthy volunteers (n=54). Study 002 was a randomised, cross-over study in 8 PD patients experiencing motor fluctuations; both treatments (placebo/ND0612) were given with 2 doses of Stalevo® 100. CD/LD plasma concentrations at steady-state were assessed following continuous ND0612 subcutaneous delivery over 24 hours. Systemic and local skin safety were evaluated.

Results: Study 001: LD and CD plasma concentrations increased proportionally as a function of ND0612 infusion rate during testing of low (night-rate of 80μl/h) and a high (day-rate of 240 μl/h) delivery. Study 002: In PD patients, ND0612 demonstrated plasma concentrations that were markedly increased in the therapeutic range and steady-state plasma LD concentrations with substantially reduced (10-fold) fluctuations in LD plasma concentrations. In both studies, ND0612 showed good systemic tolerability. For some subjects, small, transient nodules were palpable at infusion sites.

Conclusion: Subcutaneous delivery of ND0612 in PD patients can achieve continuous therapeutic LD plasma concentrations, offering the potential for fewer motor fluctuations.

Disclosure: Funded by NeuroDerm

EPR3066

ND0612 infusion in fluctuating Parkinson's disease: a randomised, double-blind, placebo-controlled study

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Background and aims: ND0612 is being developed as the first non-surgical drug-device combination that provides continuous delivery of levodopa-carbidopa (LD-CD) to patients with fluctuating Parkinson's disease (PD).

Methods: iNDiGO is a multicenter, randomised, double blind, placebo-controlled clinical study. PD patients (Hoehn and Yahr ≤3) on ≥4 doses/day of LD-CD therapy, experiencing motor fluctuations (≥2h OFF time per waking day) that cannot be further improved with oral PD medications will be randomised equally to 4 treatment arms (Figure). Study treatment is added to standard-of-care oral LD-CD. Oral immediate-release LD-CD may be used as rescue therapy. The primary endpoint is change from Baseline to Week 16 in the mean percentage of OFF time during waking hours, based on patient home diary assessments on 3 consecutive days before the visit. The mean percentage of ON time without troublesome dyskinesia during waking hours will be assessed as the key secondary endpoint. Statistical analyses will use the combination of both placebo arms.

Results: The goal is to conduct the study at 85 sites internationally.

Conclusion: This will be the first Phase III trial of two dosing regimens (low and high) of ND0612 for establishing efficacy and safety of continuous subcutaneous levodopa delivery in patients with PD who experience motor fluctuations that are not satisfactorily controlled on conventional oral PD medications. Patients who complete the study will be offered open-label ND0612 for an extension period of additional 48 weeks of treatment.

Disclosure: Funded by NeuroDerm

EPR3067

Decreased amyloid-beta in patients with idiopathic Parkinson's disease and white matter hyperintensities

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Background and aims: Parkinson's disease (PD) is the fastest growing neurological disorder, surpassing Alzheimer's disease, and its incidence increases sharply with age. Cardiovascular disease and associated risk factors, including cerebral white matter hyperintensities (WMH), are also common among the elderly, and their association with PD has been debated. The aim of this study is to investigate the clinical and biochemical profile of patients with PD with and without WMH.

Methods: 91 patients were included in this pilot project. All participants had given written consent to recruitment in an academic study, at the movement disorders clinic in the Department of Neurology, Karolinska University Hospital Huddinge. WMH were assessed by a neuroradiologist according to Fazekas. Patients were divided in those with no or light WMH (Fazekas 0 or 1; n=66), and with moderate or severe WMH (Fazekas 2 or 3; n=25).

Results: Patients with light WMH were younger than those with severe WMH (median age 64.5 vs. 74; p<0.0001), had less often hypertension (29% vs. 56%, p=0.02), and had less severe motor symptoms assessed with MDS-UPDRS part 3 (22 vs 29 points, p=0.03). Glucose and HbA1c levels did not differ between the two groups. Amyloid-beta in cerebrospinal fluid was lower in patients with severe WMH compared to those with light WMH (558ng/L vs 994ng/L; p=0.009).

Conclusion: Lower amyloid-beta levels were observed in cerebrospinal fluid of patients with PD and severe WMH compared to patients with PD and light WMH. Further investigation of the impact of this association on development of dementia and all-cause mortality is ongoing.

Disclosure: Travel grant with application number 1057/17 has been awarded by Parkinsonfonden, for the presentation of this abstract in EAN Congress 2018.

EPR3068

A cross-sectional evaluation of health resource use in patients with functional neurological disorders referred to a tertiary neuroscience centre

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Background: Patients with Functional Neurological Disorder (FND) constitute approximately 30% of referrals to general neurology clinics. Analysis of this cohort's resource use is required for service reform and more efficient NHS planning.
Aim: To evaluate the health and social care costs over the preceding 6 months of FND patients attending a tertiary FND clinic.
Methods: Method: Health and social care resource use, in the 6 months preceding their consultation, were assessed through a modified version of the Client Service Receipt Inventory (CSRI) in the form of a postal questionnaire. The total cost was estimated by combining the number and frequency of health resource use with recognized sources of national unit costs.
Results: Results: 41.6% of the 77 participants returned the CSRI, 94% of which were sufficiently completed. Of the 30 CSRI respondents, the mean cost of NHS resource use was £2686.60 (±£4821.63) in the six-month period, with 16.67% of respondents costing over £7500 predominantly due to in-patient admission. Of the cohort's total outpatient costs, General practitioner appointments represented 51.87%, with a mean cost of £237.27 (±£272.49) per patient. The longer the duration of the patient's FND before diagnosis the greater the NHS costs in the previous 6 months (p=0.028, r=0.372).
Conclusion: Discussion: Patients with FND present significant costs to the NHS. The longer the duration of their disease, the greater their cost in the preceding 6 months. Adequate reform of the patient pathway and re-organization of NHS services to make diagnoses and initiate treatment more quickly would reduce direct NHS costs.
Disclosure: Nothing to disclose

EPR3069

Management of dyskinesia in COMT-naïve patients starting adjunctive therapy with opicapone: the BIPARK-I double-blind experience

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Background and aims: Elucidate which levodopa-treated COMT-naïve Parkinson's disease (PD) patients were at higher risk for developing dyskinesia when starting opicapone (OPC) 50mg or entacapone (ENT).
Methods: Double-blind, 14 to 15-week, placebo- and active-controlled study. In the emergence of dopaminergic adverse-events (AE) during the first 3-weeks of treatment, investigators could titrate the levodopa daily-dose. Dopamine-agonists (DA) and MAO-B inhibitors (MAO-Bi) for the treatment of PD were allowed provided their stable regimen for 4-weeks before and throughout the study. Dyskinesia-related AEs were defined as new or worsening of baseline dyskinesia. This subgroup analysis investigated the association of dyskinesia with a daily-dose of levodopa (<700mg; ≥700mg) as well as concurrent use of DA/MAO-Bi.
Results: 359 patients were randomised to placebo (PLC, n=121), OPC-50mg (n=116) or ENT (n=122). Patients taking OPC-50mg presented more frequently with dyskinesia (16%) compared to ENT (8%) and PLC (4%). Patients with concurrent use of DA and taking levodopa ≥700mg at baseline appeared to be at higher risk of developing dyskinesia. About 64% of all patients with dyskinesia-related AEs had a levodopa daily-dose reduction by ~25%. No new dyskinesia-related AEs were reported during maintenance period for patients on OPC-50mg who reduced their levodopa daily-dose during adjustment period.
Conclusion: High levodopa daily-dose and DA concomitant use were associated with a higher risk of developing treatment-emerging dyskinesia. Patients who develop dyskinesia after starting OPC may benefit from a reduction of their daily-dose of levodopa. An early follow-up during the first weeks of treatment may be warranted, particularly in patients taking high levodopa daily-dose (≥700mg) and DA concomitant.
Disclosure: Nothing to disclose

EPR3070

Electrocortical connectivity and non-linear quantitative analysis of EEG signal in PD-MCI

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Background and aims: To analyse electrocortical networks related with cognitive decline in Parkinson's disease (PD) patients with mild cognitive impairment (PD-MCI) compared to PD patients with normal cognition (PD-NC).

Methods: From the PaCoS (Parkinson's disease Cognitive Study) cohort of 659 PD patients, a sample of 102 subjects (46 PD-MCI and 56 PD-NC) was selected based on the presence of a comprehensive neuropsychological assessment and at least one artifact-free EEG recording. Diagnosis of PD-MCI was made according to the definition by Litvan et al. EEG signal epochs were analysed using Independent Component Analysis LORETA. The Power Spectral Density (PSD) of site-specific signal epochs was also obtained together with the power law exponent β to estimate fractal-like behavior of site-specific signal.

Results: LORETA analysis revealed significant differences in PD-MCI patients as compared to PD-NC, with a reduced network involving alpha activity over the occipital lobe, an increased network involving beta activity over the frontal lobe associated with a reduction over the parietal lobe, an increased network involving theta and delta activity over the frontal lobe and a reduction of networks involving theta and delta activity in the parietal lobe. Quantitative EEG analysis showed a significant decrease of alpha PSD over the occipital regions and an increase of delta PSD over the left temporal region, with a significant β increase over the frontal regions in PD-MCI as compared to PD-NC.

Conclusion: Results suggest reduced occipital resting-state alpha rhythms and enhanced frontal low-frequency electrocortical networks associated with non-stationary EEG signals in PD-MCI as compared to PD-NC.

Disclosure: Nothing to disclose

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EPR3071

Asymmetric neurostimulation to improve freezing of gate: a case report

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Background and aims: Freezing of gate (FOG) is usually one of the most disabling symptoms for patients with Parkinson's disease (PD) and may appear or persists after subthalamic nucleus (STN) deep brain stimulation (DBS). Recent studies suggest the use of low-frequency stimulation to improve FOG. We report a 68-year-old male with Parkinson's disease (PD) with asymmetric freezing of gate (FOG) who showed an improvement after reduce frequency stimulation asymmetrically.

Methods: We report a 68-year-old male who was diagnosed with PD 15 years ago. In the last year, he developed severe motor fluctuations, dyskinesias and gate disorders despite medical treatment. NST-DBS was considered and levodopa test was performed, obtaining a motor benefit of 63%.

Results: During the months following surgery, an asymmetric adjustment of the intensity stimulation was required and patient showed an improvement of parkinsonian syndrome but persistence of FOG. We observed the freezing disorder was more evident when patient turned to his left than to his right. In addition, it was decided to reduce frequency stimulation asymmetrically, 66 Hz in right STN and 79 Hz in left STN, and FOG improved considerably.

Conclusion: Low-frequency stimulation of NST seems to be useful in improving FOG in PD patients. It would be interesting to consider the use of different frequencies in patients with asymmetric freezing.

Disclosure: Nothing to disclose

EPR3072

Non-motor symptoms (NMS) improvement is positively correlated with baseline NMS burden and improved quality of life in advanced Parkinson's disease patients treated with levodopa-carbidopa intestinal gel: a post-hoc analysis from the GLORIA registry

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Background and aims: To evaluate the relationship between baseline (BL) NMS burden and NMS improvement in advanced Parkinson's disease (APD) patients treated with levodopa-carbidopa intestinal gel (LCIG, also known as Carbidopa/Levodopa Enteral Suspension) over 24 months (M).
LCIG, delivered via percutaneous gastrojejunostomy, significantly improved NMS and QoL in the GLORIA registry at 24M.

Methods: LCIG was administered over 24M to APD patients in routine clinical care (Gloria Registry). NMS were measured with the NMS Scale (NMSS); QoL was measured with the 8-item PD Questionnaire (PDQ-8). The relationships between BL NMS burden and NMSS total score improvement (TSI) at M24 and NMSS TSI at M24 and QoL were assessed (Pearson correlation coefficients). NMS responder rates with different changes from BL in NMSS total score were calculated at M24.

Results: BL NMS burden correlated significantly with NMSS TSI at M24 of LCIG treatment (r=0.565; P<0.0001) [Figure1]. Median NMSS total score improved by 35% (M24) compared to BL (median change from BL=-18.0; n=170/233). 47% (n=42/89) of patients with severe NMS burden at BL (> 80 BL NMSS total score) had NMSS TSI's ≥30 points (M24); as a group, these patients exhibited 42% improvement in median NMSS total score compared to BL (median change from BL=-45.0; n=64/89). NMSS TSI correlated significantly with PDQ-8 TSI at M24 (r=0.464, P<0.0001). Observed patient tolerability was consistent with established LCIG safety profile.

Figure 1. Correlation between baseline NMS burden and NMSS total score improvement at M24
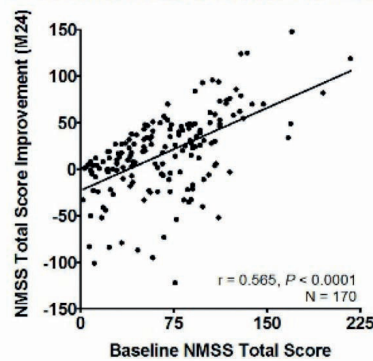
M = month, NMSS = Non-Motor Symptom Scale

Conclusion: At M24, NMS improvement correlated strongly with BL NMS burden and associated with improved QoL and nearly half of patients with the highest BL NMS burden exhibited ≥30 points NMSS TSI.

Disclosure: Funding: This work was funded by AbbVie Inc. AbbVie participated in the study design, research, data collection, analysis and interpretation of data, writing, reviewing, and approving the publication.

EPR3073

Applying "5-2-1" diagnosing criteria for advanced Parkinson's disease to an observational study population treated with Levodopa-carbidopa intestinal gel

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Background and aims: 5- (times oral levodopa tablet intake/day) 2- (hours of OFF time/day) 1 (hour/day of troublesome dyskinesia [TSD]) criteria have recently been proposed by a Delphi expert consensus panel for diagnosing advanced Parkinson's disease (APD).

Methods: In this initial application of "5-2-1" criteria, patients were analysed post-hoc as subgroups meeting single or any or all criteria. ADEQUA was a 6-month, observational study assessing the effect of LCIG on quality of life (QoL) of Spanish patients. Assessments included the frequency of daily levodopa intake, hours of OFF time and TSD per day, and total scores of 39-item Parkinson's Disease Quality of Life Questionnaire (PDQ-39) and Non-motor Symptom Scale (NMSS).

Results: Of the 59 study patients, 93% met ≥1 of the "5-2-1" criteria, 15% met all. More patients had ≥5 times oral levodopa intake/day (56%) or ≥2 hours OFF/day (88%); whereas fewer patients had ≥1 hour TSD/day (31%). All subgroups with n>5 experienced significant (P<0.05) improvements in PDQ-39 and NMSS Total Scores from baseline to month 6 (Figures 1 and 2). The only significant difference between subgroups was on the NMSS Total Score between patients with <1 hour TSD/day (significantly greater reduction) and ≥1 hour TSD/day (p=0.039, Figure 2).
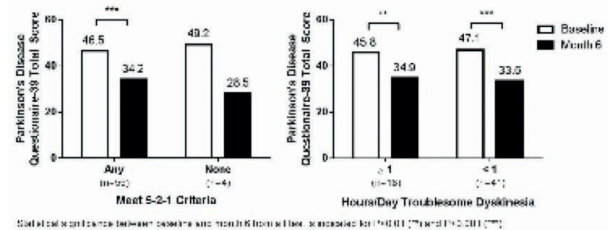
Figure 1: Parkinson's Disease Questionnaire-39 Total Score at Baseline and Month 6 for APD Patients in the Troublesome Dyskinesia and Any Vs. None Criteria Subgroups
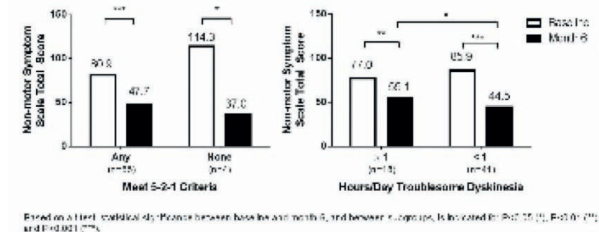
Figure 2: Non-motor Symptom Scale Total Score at Baseline and Month 6 for APD Patients in the Troublesome Dyskinesia and Any Vs. None Criteria Subgroups

Conclusion: In this first application of the "5-2-1" APD diagnosis criteria to an observational LCIG study population, most patients fulfilled ≥1 criterion and experienced QoL improvements, suggesting usefulness as a screening tool for APD and consideration of device-aided therapies.

1Antonini, A. et al., Movement Disorders. 2015;30:S1186

Disclosure: This work was funded by AbbVie Inc. AbbVie participated in the study design, research, data collection, analysis and interpretation of data, writing, reviewing, and approving the publication.

EPR3075

Brainstem volumetry for separating progressive supranuclear palsy from other parkinsonian disorders

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Background and aims: Separating progressive supranuclear palsy (PSP) from Parkinson's disease (PD) and multiple system atrophy (MSA) is often challenging. An early diagnosis is important for prognostics and management. We aimed to retrospectively evaluate automatic volumetric brainstem measurements in distinguishing PSP from PD and MSA.

Methods: Clinical 3D T1-weighted magnetic resonance images were obtained from 30 patients with PSP, 28 with MSA and 146 with PD. At the time of MRI, 18 were probable and 12 possible PSP. All but one possible PSP converted to probable later on. Midbrain, pons, medulla oblongata and superior cerebellar peduncles were segmented using FreeSurfer. Metrics from these analyses were evaluated as biomarkers for disease using receiver operating characteristic curves. We calculated a brainstem index analogous to the midbrain-pons area ratio by dividing the midbrain volume by the pons volume.
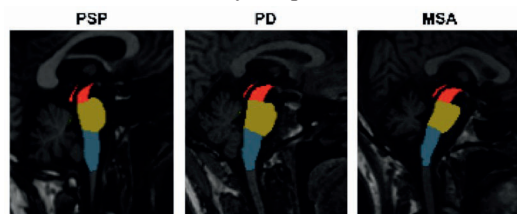
Figure 1. Visualisation of the segmentation process showing representative images from a 63 year old woman with PSP, a 45 year old man with PD and a 55 year old woman with MSA. Red=midbrain; yellow=pons; blue=medulla oblongata; green=superior cerebellar peduncles.

Results: We found that midbrain volume was most effective in diagnostically separating PSP from PD, with a sensitivity of 87% and a specificity of 79%. For separation between PSP and MSA, best results were seen with our brainstem index, with a sensitivity of 70% and a specificity of 71%. Discriminant analysis using all brainstem regions improved diagnostic separation PSP vs. MSA to sensitivity 83% and specificity 71% while separation PSP vs. PD was stationary.
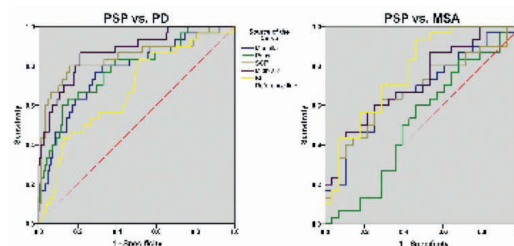
Figure 2. Receiver operating characteristic (ROC) curves depicting diagnostic separation PSP vs. PD and PSP vs. MSA. SCP=superior cerebellar peduncle; BI=brainstem index.

Conclusion: Automatic brainstem segmentation using FreeSurfer shows a promising diagnostic performance for separating PSP from PD and MSA. If further developed, automatic brainstem volumetrics could play a role in diagnosing PSP. A correct diagnosis is important in management and when considering treatment trials.

Disclosure: The study was funded by the Stockholm County Council through an ALF grant.

EPR3076

Longitudinal assessment of autonomic dysfunction in early Parkinson's disease

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Background and aims: Profile and clinical correlates of dysautonomia in early Parkinson's disease (PD) have been addressed in a cross-sectional way in previous studies.

Methods: We report longitudinal assessment of autonomic dysfunction in a cohort of early PD patients (Hoehn and Yahr stage 1 and disease duration <2 years at baseline) over 3-year follow-up. Autonomic dysfunction was assessed using SCOPA-AUT.

Results: A total of 112 PD patients and 79 healthy controls at baseline and 83 PD patients during longitudinal phase were included. PD patients had more overall symptoms of dysautonomia compared to controls. At least one dysautonomia symptom was present in 72% of PD patients at the baseline and in 93% of patients after three years. Nocturia was the most commonly reported symptom both at baseline and year 3. All gastrointestinal symptoms tended to worse during follow-up, except for dysphagia. Urinary dysfunction including urgency, increased frequency and incontinence, as well as lightheadedness, hyperhydrosis, cold intolerance, erection and ejaculation problems progressed over time. Age, depression, anxiety and apathy, but not motor impairment contributed to the autonomic dysfunction. Higher doses of dopaminergic medications and cognitive impairment were significant predictors of cardiovascular autonomic dysfunction over time.

Conclusion: Autonomic dysfunction affects the majority of patients with PD within the first 3 years from disease onset. Dysautonomia symptoms are usually mild, and progress independently from motor impairment.

Disclosure: This study was supported by a grant from the Ministry of Education and Science, Republic of Serbia (project No. ON175090).

EPR3077

Can a smartphone camera 'see' different tremor types?

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Background and aims: Computer vision refers to the processing of camera images or video to automatically extract useful information. The technology can recognise and track the human body from simple video, and this is used in multiple commercial applications. It has the potential to provide objective and automatic measurement of neurological signs, which currently rely on subjective visual estimation by a doctor. Crucially, no special hardware is required. Cameras and computers are ubiquitous and inexpensive (e.g. smartphones). There have been relatively few attempts to apply computer vision to neurology, but we report early findings using a smartphone camera applied to limb tremor.

Methods: Smartphone video of the upper limbs was recorded from healthy controls and also patients with three types of tremor disorder: Parkinson's, Essential Tremor, and Functional Tremor. The computing technique of Eulerian magnification was applied to these videos, to amplify small pixel movements. We then applied a computing method termed 'optical flow', to track and measure hand movement.

Results: We present striking videos that reveal hitherto invisible tremor in upper limbs (which could not be seen on the original video). Examples of this revealed tremor suggest the clinical appearance may differ across groups. Furthermore, we describe computer vision metrics derived from the tremor, such as motion vector distribution, which begin to allow characterisation of tremor types.

Conclusion: Our early findings (and remarkable videos) suggest that a simple smartphone camera may be able to detect and characterise tremor, including tremor that cannot be seen with the human eye alone.

Disclosure: Nothing to disclose

EPR3078

Sarcopenia and frailty in Parkinson's disease: a case-control study

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Background and aims: Sarcopenia and frailty are found in up to 1/4 of the general elderly and associated with major adverse health outcomes. Data on the frequency of both syndromes in Parkinson's disease (PD) is very limited. Thus, we aimed to screen for sarcopenia and frailty in PD patients and to assess potential demographic and clinical associations and the impact on QoL.

Methods: In this case-control study, we included 104 PD patients from a tertiary center and 330 non-PD controls from a population-based cohort aged >65 years. All groups were screened using the SARC-F score and the Clinical Frailty Scale of the Canadian Study of Health and Aging. Moreover, Prevalences were assessed in 18 PD patients from a population-based cohort. PD patients from the tertiary center were evaluated for motor and non-motor symptoms, QoL, and their level of dependency.

Results: Prevalence of sarcopenia was 55.8% (46.1–65.5%) in PD patients from the tertiary center and 8.2% (5.2–11.2%; p<0.01) in non-PD controls. Frailty was detected in 35.6% (26.2–44.9%), and 5.2% (2.8–7.6%; p<0.02). Prevalences for sarcopenia and frailty were 33.3% (9.2–57.5%; p<0.01) and 22.2% (1.0–43.5%; p<0.02) in the community based PD sample. Sarcopenia and frailty were significantly associated with longer disease duration, higher MDS-UPDRS-III scores, higher Hoehn and Yahr stages, decreased QoL, higher frequency of falls, higher non-motor symptom burden, and institutionalisation in PD patients compared to not affected PD patients (all p<0.034).

Conclusion: Sarcopenia and frailty are common in PD patients and are associated with a more adverse course of the disease.

Disclosure: Nothing to disclose

Movement disorders 9

EPR3080

Walking in orthostatic tremor – effects on tremor frequency, intensity and gait stability

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Background and aims: Primary orthostatic tremor (OT) is characterised by high-frequency lower-limb muscle contractions and a disabling sense of unsteadiness while standing. Patients consistently report a relief of symptoms when starting to ambulate. The objectives of this study were to systematically examine and link tremor and gait characteristics in patients with OT while walking.

Methods: Tremor and spatiotemporal gait features were examined in 9 patients with OT on a pressure-sensitive treadmill for one minute of continuous walking framed by two 1-minute periods of standing. Tremor characteristics (frequency, intensity, and coherence) were assessed by frequency domain and continuous time-frequency analysis of surface EMG-recordings from 4 leg muscles (tibialis anterior, gastrocnemius, biceps femoris, vastus medialis).

Results: All patients exhibited a coherent high-frequency tremor during standing (mean frequency: 15.29±0.17Hz). This tremor persisted during walking but was consistently reset to a higher frequency (mean frequency: 16.34±0.25Hz; p<0.001). Tremor intensity during walking was phase-dependently modulated, being predominantly observable during the stance phase of the gait cycle (p<0.001). Tremor intensity levels scaled with the force levels applied during stepping (p<0.001) and were linked to specific gait alterations, i.e., wide base walking (p=0.019) and increased stride-to-stride fluctuations (p=0.002).

Conclusion: Tremor activity in OT during walking persists but undergoes specific alterations indicating the influence of supraspinal centers (with respect to tremor frequency reset) and peripheral sources (with respect to tremor intensity modulations). High-frequency muscle contractions during walking are linked to gait alterations resembling a cerebellar and/or a sensory ataxic gait disorder.

Disclosure: Nothing to disclose

EPR3081

Unveiling the relationship between motor impairment, vascular burden and cognition in Parkinson's disease

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Background and aims: To determine frequency and type of cognitive disorders in cross-sectional analysis of a Parkinson's disease (PD) cohort, and explore its relations to motor symptoms, vascular risk factors and white matter lesions (WML) volume.

Methods: In a group of 133 PD patients, mild cognitive impairment (PD-MCI) and dementia (PDD) were diagnosed according to Movement Disorders Society task force criteria (level 2 for PD-MCI). Detailed motor measurements were applied, including rigidity, axial, bradykinesia, tremor and postural instability gait disorders (PIGD) scores. Vascular risk was estimated by the Framingham General Cardiovascular Disease risk-scoring algorithm and WML volume was measured for whole brain and frontal lobe.

Results: 61 (46.9%) patients fulfilled criteria for PD-MCI, and 23 (17.7%) for PDD. Non-amnestic multiple domain MCI was most frequent (52% of PD-MCI patients). Motor scores were significantly higher in cognitively impaired patients, but only axial score discriminated between MCI and dementia. High vascular risk was related to impaired cognition, bradykinesia, axial, PIGD and FOG score, while whole brain WML volume was associated with PDD, freezing of gait and attention deficits. Furthermore, high vascular risk was identified as a potential predictor of both MCI and dementia in PD. Additionally, age and bradykinesia score were independently associated with PD-MCI and age, axial score and whole brain WML volume with PDD.

Conclusion: Cognitive disorders in PD are associated with more severe motor deficits and probably aggravated by elevated vascular risk, thus opening an avenue for possible preventive strategies in PD.

Disclosure: This study was partially funded by a grant from the Ministry of Education and Science, Republic of Serbia (project 175090).

EPR3082

Are there two different forms of functional dystonia? A multimodal brain structural imaging study

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Background and aims: To investigate brain structural alterations in two diverse clinical forms of functional (psychogenic) dystonia (FD) – typical phenotype of fixed dystonia (FixFD) and recently recognized new phenotype "mobile" dystonia (MobFD) compared with controls.
Methods: 43 FD patients (13 FixFD, 30 MobFD) and 42 controls were recruited. All subjects underwent three-dimensional T1-wighted and diffusion tensor (DT) magnetic resonance imaging (MRI). We assessed cortical thickness with surface-based morphometry, subcortical volumes using FIRST, and DT MRI metrics using TBSS.
Results: Normal cortical volumes in both FD patient groups compared to age-matched controls were found. However, when compared with FixFD, MobFD patients showed cortical thinning of the left orbitofrontal cortex, and medial and lateral parietal and cingulate regions bilaterally. Compared with both controls and MobFD cases, FixFD patients showed a severe disruption of white matter (WM) tract architecture along the corpus callous, corticospinal tract, anterior thalamic radiations, and major long-range WM tracts. Additionally, compared to controls, MobFD patients showed reduced volumes of the left nucleus accumbens, putamen, thalamus, and bilateral caudate nuclei, while MobFD patients compared to FixFD demonstrated atrophy of the right hippocampus and globus pallidus.
Conclusion: These data showed different morphology patterns in two variants of FD. FixFD group was related to a global WM disconnection affecting main sensorimotor and emotional control circuits. On the other hand, MobFD had alterations in grey matter structures important for sensorimotor processing, emotional, and cognitive control. These findings may have important implications in understanding the neural substrates underlying different phenotypic expressions.

EPR3083

Brain structural changes in focal dystonia – what about task specificity? A multimodal imaging study

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Background and aims: Brain abnormalities in the basal ganglia, thalamus, cerebellum and sensorimotor cortices were identified as common features of focal dystonia with heterogeneus phenotypic expression. However, task-specificity present in some forms of dystonia is still a poorly understood phenomenon. This study investigated grey and white matter alterations in patients with task-specific (TSD) and non-task-specific dystonia (NTSD), and defined common and group-specific brain changes.
Methods: 36 patients with TSD (spasmodic dysphonia and writer's cramp), 61 patients with NTSD (blepharospasm and cervical dystonia), and 83 healthy controls were included in the study. Participants underwent 3D T1-weighted and diffusion tensor MRI to study cortical thickness, basal ganglia volume, and WM tract damage.
Results: Compared to healthy controls, TSD patients had widespread, bilateral WM tracts damage including superior and inferior longitudinal fasciculi, cingulate bundle, anterior thalamic radiations, and corticospinal tracts. NTSD patients compared to healthy controls had more focal and right lateralised damage. Vertex analysis of cortical thickness showed cortical thinning in the right pars triangularis in NTSD group.
Conclusion: TSD is characterised by disruption of the main subcortical motor and cognitive controlling networks suggesting complex pathophysiology of task-specificity of dystonia.

EPR3084

The occurrence of dopamine-responsive and dopamine-resistant resting tremor in Parkinson's disease

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Background and aims: To investigate individual differences in the dopamine-responsiveness of Parkinson's resting tremor.

Parkinson's resting tremor has a variable clinical response to levodopa that can differ considerably between patients. However, it is unclear whether there are two distinct tremor phenotypes (dopamine-responsive and dopamine-resistant) or whether these groups are two ends of a normal distribution. Furthermore, it is unclear to what extent the dopamine response of resting tremor is different from that of bradykinesia.

Methods: We performed a standardised L-Dopa challenge in 76 tremulous Parkinson patients. Clinical scores (MDS-UPDRS part III) were collected OFF and ON 200/50mg levodopa-benserazide. In both sessions, resting tremor intensity was quantified during REST and during cognitive co-activation, using accelerometry. We calculated the distribution of dopamine-responsiveness for resting tremor and for bradykinesia.

Results: The dopamine response of bradykinesia, assessed clinically and using finger tapping speed, showed a unimodal (i.e. normal) distribution. In contrast, the dopamine response of resting tremor, assessed clinically and using accelerometry, significantly departed from a unimodal distribution and best fitted a bimodal distribution. This effect was present both at rest and during cognitive-stress. Comparison of the extreme groups revealed that the dopamine-responsive group schowed higher prevalence of women, a higher levodopa-equivalent-dose, and a higher prevalence of dyskinesia.

Conclusion: Our findings indicate that there are two partially overlapping tremor phenotypes, i.e. Parkinson patients with a dopamine-responsive and a dopamine-resistant tremor. This pattern sets tremor apart from bradykinesia, the core motor symptom of Parkinson's disease. Female gender and the presence of dyskinesia are associated with a better dopamine-response of resting tremor.

Disclosure: Nothing to disclose

EPR3085

Identification of a prospective rapid motor progression cluster of Parkinson's disease: data from the PPMI study

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Aim: The aim of our study is to phenotype PD motor progression, and to detect whether serum, cerebrospinal fluid (CSF), neuroimaging biomarkers and neuropsychological measures characterise PD motor progression phenotypes.

Methods: We defined motor progression as a difference of at least one point in the H&Y (H&Y) scale between the baseline (Visit 0, V0), 12 months (Visit 04, V04) and 36 months (Visit 08, V08) of the Progression Markers Initiative (PPMI) study. H&Y progression events were recorded at each milestone in order to be used as cluster analysis variables that would produce progression phenotypes. Subsequently, cross-cluster comparisons prior to and following (pairwise) propensity score matching were performed ito assess phenotype – defining characteristics.

Results: Four progression clusters where identified: SPPD: Secondarily Progressive PD, H&Y progression between V04 – V08; EPPD: Early Progressive PD. H&Y progression between V0 – V04; NPPD: Non Progressive PD, no H&Y progression; MIPD: Minimally Improving PD, i.e. Minimal H&Y improvement H&Y progression between V04 – V08;. Independent Samples Mann Whitney U tests determined CSF aSyn (p=0.006, adj p-value=0.036) and Semantic Animal fluency T-score (SFT, p=0.003, adjusted p-value=0.016.) as statistically significant cross-cluster characteristics. Following PSM, SFT, Hopkins Verbal Learning Test (Retention / Recall), Serum IGF1, CSF aSyn and DaT-SPECT binding ratios (SBRs) and the Benton Judgement of Line Orientation Test (BJLOT) were determined as statistically significant predictors of cluster differentiation (p<0.05).

Discussion: SFT, Serum IGF1, CSF aSyn and DaT-SPECT, basal ganglia SBRs warrant further investigation as possible motor progression biomarkers.

Disclosure: Nothing to disclose

EPR3086

Long-term course of progression of clinical ocular motor signs in progressive supranuclear palsy

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Background and aims: To investigate the natural course of progression of ocular motor signs in patients with progressive supranuclear palsy (PSP).

Methods: 114 patients with a possible or probable PSP following NINDS-SPSP criteria were included in this retrospective study. All patients underwent structured neuro-ophthalmological testing at initial diagnostic evaluation, 35 patients several times during their course of disease. The following ocular motor signs were analysed: Saccadic slowing/paresis in vertical/horizontal direction, up-/downward/horizontal ocular motility, square wave jerks, VOR-function. Ocular motor signs were investigated in relation to disease duration.

Results: In the whole group of PSP patients saccadic abnormalities showed the following distribution over time: at 1y of disease duration 10% showed only saccadic slowing on upgaze, 40% on up- and downgaze, 21% saccadic paresis on upgaze and 29% complete vertical saccade paresis; at 2y the proportion of vertical saccade paresis was 32%, at 3y 65% and at 4y 82%. Progression of horizontal saccade paresis was slower (1y: 6%, 2y: 9%, 3y: 21%, 4y: 41%). The subgroup of patients with longitudinal follow-up showed a similar tendency. Ocular motility in this group decrease by a mean of 1.5mm/y on upgaze, 1.6mm/y on downgaze and 1.4mm/y on horizontal gaze. The degree of motility loss on up-/downgaze over time showed a good correlation ($R2=0.71$).

Conclusion: Ocular motor examination can be used as a robust marker of disease progression. Variability between patients however is considerable. Prospective clinical and apparative quantification of ocular motor markers in well-characterized cohorts of PSP patients is needed.

Disclosure: Nothing to disclose

MS and related disorders 7

EPR3087

Durable suppression of MRI disease activity and slowing of brain volume loss in alemtuzumab-treated patients with active RRMS: 7-year follow-up of CARE-MS I (TOPAZ Study)

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Background and aims: In CARE-MS I (NCT00530348), alemtuzumab (12mg/day, baseline: 5 days; 12 months later: 3 days) demonstrated significant improvements in MRI outcomes, and reduced brain volume loss (BVL) versus SC IFNB-1a over 2 years (y). Alemtuzumab efficacy was durable in a 4-y extension (NCT00930553; 95% of CARE-MS I patients enrolled, 92% completed Y6), in which patients could receive alemtuzumab retreatment as needed for relapse/MRI activity or receive other DMTs per investigator's discretion. Further evaluation is ongoing (TOPAZ; NCT02255656). We present MRI lesion/BVL outcomes over 7 y (2 y core study plus 4 y extension, and TOPAZ Y1) in alemtuzumab-treated CARE-MS I patients.

Methods: Assessments: Annual MRI for disease activity (scored as new Gd-enhancing lesions; new/enlarging T2 lesions), new T1 hypointense lesions, and BVL (derived by relative change in brain parenchymal fraction [BPF]).

Results: 299 patients (93%) completed TOPAZ Y1. After the initial 2 courses, 59% received neither alemtuzumab nor another DMT. At Y7, patients were free of MRI disease activity (68%), new Gd-enhancing lesions (91%), new/enlarging T2 lesions (68%), and new T1 hypointense lesions (85%). Median BPF change from baseline was –0.59%, –0.87%, –0.98%, –1.13%, –1.37%, –1.43%, and –1.62% in Y1–7, respectively. Median annual BPF change was reduced versus SC IFNB-1a over 2 y, remaining low in Y3–7 (Y3: –0.19%, Y4: –0.14%, Y5: –0.20%, Y6: –0.17%, Y7: –0.16%).

Conclusion: Alemtuzumab durably reduced MRI disease activity and slowed BVL over 7 y in treatment-naive patients. Alemtuzumab provides a unique treatment approach for RRMS patients, offering durable efficacy without continuous treatment.

Disclosure: Study supported by Sanofi and Bayer HealthCare Pharmaceuticals.

EPR3088

Cladribine tablets produce selective and discontinuous reduction of B and T lymphocytes and natural killer cells in patients with early and relapsing Multiple Sclerosis

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Background and aims: Efficacy of cladribine tablets 3.5 mg/kg (CT3.5) has been demonstrated in patients with early MS (ORACLE-MS) and in patients with relapsing MS in the CLARITY and CLARITY-Extension studies. Here, we evaluate B and T lymphocyte and natural killer (NK) cell profiles after the first administration CT3.5 in ORACLE-MS, CLARITY and CLARITY-Extension.

Methods: Longitudinal evaluation of peripheral blood lymphocyte subtypes was conducted for patients receiving the first course of CT either as part of the initial 3.5 mg/kg active treatment groups (ORACLE-MS and CLARITY) or the placebo switched to active treatment groups (CLARITY-Extension). Absolute lymphocyte counts (ALC) and lymphocyte subtype dispositions were evaluated at baseline, and Weeks 5, 13, 24 and 48.

Results: Baseline distributions of ALC were similar across studies. Temporal profiles of CD19+ B lymphocytes and CD4+ and CD8+ T lymphocytes were consistent across studies. Rapid reductions were observed for CD19+ B-cells (~75% reduction at Week 5 in each study), with nadir at ~Week 13 (Figure 1). Reconstitution of CD19+ B-cells towards baseline value occurred from Week 24 to 48. Lesser, discontinuous reductions also occurred for CD4+ and CD8+ T-cells that had not fully returned to baseline by Week 48. CD16+/CD56+ NK cells were also transiently reduced with CT, with recovery evident at Weeks 24 and 48.

Conclusion: CT3.5 achieved an early and discontinuous reduction of peripheral blood B-cells, with rapid reconstitution to baseline, and a moderate, discontinuous reduction of T-cells. Treatment with CT is associated with early, transient NK cell reductions.

Disclosure: This study was sponsored by EMD Serono Inc, a business of Merck KGaA, Darmstadt, Germany (in the USA), and Merck Serono SA, Geneva, an affiliate of Merck KGaA Darmstadt, Germany (ROW).

EPR3089

Innate immune cell counts in patients with Relapsing-Remitting Multiple Sclerosis (RRMS) treated with cladribine tablets 3.5mg/kg in CLARITY and CLARITY extension

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Background and aims: In CLARITY and CLARITY Extension, lymphopenia was the most common adverse event, consistent with the mechanism of action of cladribine tablets (CT). Absolute lymphocyte counts (ALC) were shown to recover towards the normal range over time in these studies. Here we evaluate the effect of CT on innate immune cell counts.

Methods: Data from patients randomised to CT 3.5mg/kg (CT3.5; cumulative dose over 2 years) in CLARITY or CLARITY Extension (N=685) were pooled to provide long-term follow-up data. Data from patients randomised to placebo in CLARITY and followed up in PREMIERE are also reported (N=435). Neutropenia was graded by Common Terminology Criteria for Adverse Events v3.0.

Results: Neutrophil counts remained within the normal range (>2.03x10^9/L) over the 2 treatment years and beyond, this included the small decrease observed shortly after (2 to 5 weeks) each dose of CT. Grade 3 or 4 neutropenia was reported in ≤6 (<2%) patients treated with CT3.5 at any single time point. Median monocyte counts at the end of each year ranged from 0.34×10^9/L to 0.36×10^9/L for CT3.5 and 0.40×10^9/L to 0.42×10^9/L for placebo.

Conclusion: These data, together with the previously-reported data on ALC, support the concept that CT selectivity reduces adaptive immune cell counts, and that the impact on the innate immune system is relatively minor.

Disclosure: This study was sponsored by EMD Serono Inc, a business of Merck KGaA, Darmstadt, Germany (in the USA), and Merck Serono SA, Geneva, an affiliate of Merck KGaA Darmstadt, Germany (ROW).

EPR3090

Incidence and outcomes of varicella zoster virus (VZV) reactivation in the ozanimod phase-3 clinical program (SUNBEAM and RADIANCE) in relapsing Multiple Sclerosis (RMS)

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Background and aims: VZV rates of 4.47 versus 11.5/1000 patient-years in immunocompetent (general medical population) versus immunocompromised patients have been reported (Johnson 2015; Schroder 2017). In an MS patient survey, VZV reactivation was reported in 17% of respondents, with mean age at onset of 37 years (Manouchehrinia 2017). We report VZV incidence in SUNBEAM (patients treated for at least 12 months) and RADIANCE (treatment duration 24 months).

Methods: Pooled safety data from 2 completed phase-3 trials were analyzed for VZV adverse events (AEs) of herpes zoster and varicella zoster virus infection. Positive VZV IgG antibody status or VZV vaccination 30+ days prior to randomisation was required to enroll.

Results: 2659 patients (ozanimod 1 mg, n=882; 0.5mg, n=892; interferon beta-1a [IFN], n=885) were treated. Five (0.6%) VZV cases were reported with ozanimod 1 mg, 3 (0.3%) with ozanimod 0.5mg, and 2 (0.2%; one with multiple reactivations) with IFN. All cases were single-dermatome distribution, non-serious, and treated with acyclovir. No patient discontinued treatment due to VZV. None of the VZV AEs were associated with Common Terminology Criteria Grade 4 lymphopenia (<0.2 x 10^9/L). Mean age at VZV AE onset was 45, 41, and 45 years (ozanimod 1 mg, 0.5 mg, IFN, respectively). Incidence rates of VZV were 3.73, 2.24, and 1.51 cases/1000 patient-years (ozanimod 1mg, 0.5mg, IFN, respectively).

Conclusion: With required immunity, VZV reactivation in SUNBEAM and RADIANCE was low, with no serious or complicated cases.

Disclosure: Nothing to disclose

EPR3091

Quantitative manual pupillometry as a valuable tool to assess visual pathway function in MS: first results on potential association with fatigue

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Background and aims: To evaluate the potential usefulness of pupillometry for assessing magnitude of relative afferent pupillary defects, EDSS, number of previous optic neuritis attacks (PONAs), fatigue severity in RRMS patients.

Methods: We analysed pupillometry data (NeurOptics®NPi-200TM) including neurological pupil index (NPi), pupil size (PS), minimum size of pupil (MinPS), percentage change of pupil size (CH), Constriction Velocity(CV), Maximum of Constriction Velocity (MCV), and Dilation Velocity (DV) from 182 RRMS and 90 healthy controls. To assess the changes across case and control subjects, multiple regression with age and group as independent variable was run. To address the effect of PONAs, an ANCOVA was run. The eye with no PONAs was considered as covariate. To address EDSS and fatigue, we categorized eyes with no PONAs into two category of high and low scores. age-adjusted control group were compared by ANCOVA.

Results: In multiple regressions, dichotomous variable of group statistically significantly predicted just PS and MinPS ($P<0.005$) with Adj. $R2=0.17$, Adj. $R2=0.19$, respectively. In ANCOVA analysis of PONAs, there was statistically significant differences in NPI, PS, MCV, DV and CH between groups. The notable effect size belongs to CH, ($p<0.0005$, partial η $2=0.105$). Statistical mean variations among control group and either groups of EDSS/MFIS was significant for PS and CH variable.

Conclusion: Our prospective study provides solid data that pupilometer is an easy to use, new technique to quantify the visual pathway function in MS. The results suggest that MS-related symptoms statistically affect pupillometry results, and thereby offers a new tool for measurements.

Disclosure: Nothing to disclose

EPR3092

withdrawn

EPR3093

Long-term, real-world effectiveness of natalizumab treatment in relapsing-remitting multiple sclerosis: data from ≥6 years in the TYSABRI® Observational Program (TOP) Portuguese, Spanish, and global cohorts

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Background and aims: TOP is an ongoing, global open-label study in relapsing-remitting multiple sclerosis patients treated with natalizumab in the real world. Country-specific data can provide information on natalizumab's effectiveness in local clinical practice.

Methods: Annualised relapse rates (ARRs) before and on natalizumab and the cumulative probability of 24-week confirmed Expanded Disability Status Scale (EDSS) worsening (score increase of ≥1.5 from 0.0, ≥1.0 from 1.0-5.5, or ≥0.5 from ≥6.0) or improvement (score decrease of ≥1.0 from ≥2.0) were analysed using data from study initiation to May 2016. Updated data (at November 2017) including pooled data from the Portuguese and Spanish cohorts will be presented.

Results: As of May 2016, Portuguese (n=67), Spanish (n=124), and global (N=5927) TOP patients had received a median (range) of 29 (1-77), 43 (2-84), and 34 (1-113) doses, respectively. ARR decreased from 1.51 pre-natalizumab to 0.14 on natalizumab (90.7% decrease; P<0.0001) in Portuguese patients, from 2.22 to 0.18 (91.9% decrease; P<0.0001) in Spanish patients, and from 1.99 to 0.22 (88.9% decrease; P<0.0001) in the global population. Through ≥6 years on natalizumab, ARR assessed annually remained ≤0.27 in all 3 cohorts. At year 6, cumulative probability of confirmed EDSS worsening was 30.6% (Portuguese patients), 26.7% (Spanish patients), and 24.2% (global), and cumulative probability of confirmed EDSS improvement was 39.9% (Portuguese patients), 37.4% (Spanish patients), and 32.4% (global).

Conclusion: Consistent with global TOP results, natalizumab ARRs and EDSS worsening rates remained low over ≥6 years in the Portuguese and Spanish cohorts. These results support natalizumab's long-term effectiveness in real-world settings.

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EPR3094

Teriflunomide use in european clinical practice in patients with relapsing forms of Multiple Sclerosis: an overview of regional real-world studies

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Background and aims: In Teri-PRO (NCT01895335), a global phase-4 study, patients reported high levels of treatment satisfaction and improvements in patient-reported outcomes (PROs) with teriflunomide treatment. Here, we present interim data from several European studies evaluating the effect of teriflunomide on PROs, including quality of life and treatment satisfaction.

Methods: TAURUS-MS I and II (Germany), TACO (Switzerland), Teri-LIFE (Nordics), AURELIO (Greece), and Teri-CARE (Spain) are multicentre, prospective, non-interventional, ≤2-year studies in patients with relapsing-remitting MS receiving teriflunomide 14mg, per local labelling. Target enrolment: TAURUS-MS I, n=1115; TAURUS-MS II, n=1080; TACO, n=70; Teri-LIFE, n=200; AURELIO, n=350; Teri-CARE, n=323.

Results: Most studies are ongoing; interim data are available for 733 patients who received teriflunomide for 1 year (≥9 months) in TAURUS-MS I (enrolment complete; n=1115), and for the first 57 and 200 patients enrolled in TACO and Teri-CARE, respectively. Interim baseline demographics were broadly similar across studies, with some differences (mean [SD] for TAURUS-MS I, TACO, and Teri-CARE, respectively): years since diagnosis, 8.6 (7.4), 11.7 (10.0), and 7.3 (7.5); EDSS scores, 2.4 (1.5), 2.4 (1.1), and 1.7 (1.6). In TAURUS-MS I, mean (SD) Treatment Satisfaction Questionnaire for Medication (TSQM; higher scores indicate greater treatment satisfaction)-9 scores at baseline/Month 12 were: Global Satisfaction, 64.7 (24.1)/74.6 (22.3); Convenience, 74.8 (24.2)/91.0 (11.2); Effectiveness, 62.1 (23.6)/69.0 (23.8); P<0.001 for all comparisons.

Conclusion: Interim results from TAURUS-MS I showed significantly improved treatment satisfaction with teriflunomide vs baseline. Data from these and other similar observational, regional studies will be pooled to further evaluate the real-world effectiveness of teriflunomide, and better inform treatment decisions.

Disclosure: Study supported by Sanofi.

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EPR3095

Efficacy of a fourth alemtuzumab course in RRMS patients with disease activity after three prior courses: analysis of CARE-MS I

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Background and aims: In treatment-naïve relapsing-remitting MS (RRMS) patients (CARE-MS I [NCT00530348]), alemtuzumab 12mg/day (baseline: 5 days; 12 months later: 3 days) improved clinical/MRI outcomes versus SC IFNB-1a over 2 years. In a 4-year extension (NCT00930553), patients could receive as-needed alemtuzumab retreatment (12mg/day, 3 days; ≥12 months apart) for relapse/MRI activity, or receive another disease-modifying therapy (DMT). Efficacy remained durable, despite 63% receiving neither alemtuzumab retreatment nor another DMT. Through Year 6, 325/349 (93%) remained on study; 42 (12%) received ≥4 alemtuzumab courses (13 [4%] received ≥5 courses). We evaluated efficacy of a fourth course (Course [C] 4) in CARE-MS I patients receiving ≥4 courses.

Methods: Assessments 12 months before and up to 3 years post-C4: annualised relapse rate (ARR); improved/stable Expanded Disability Status Scale (EDSS) score (versus core study baseline); 6-month confirmed disability improvement (CDI). Included patients (N=31 [9%]) received ≥4 courses by Month 60 (allowing for 1-year post-C4 follow-up), and received no other DMT. Data for patients receiving a fifth course (C5) were censored at C5 administration.

Results: ARR decreased post-C4 (12 months pre-C4: 0.65; 12 months post-C4: 0.42), remaining low (0.33) at Year 3 post-C4. EDSS scores versus core study baseline were stable/improved in 73.1% 12 months post-C4, compared with 58.1% at C4 administration. The percentage with CDI increased from 4.3% (12 months pre-C4) to 17.4% (12 months post-C4).

Conclusion: A fourth course reduced relapses and stabilised/improved disability in CARE-MS I patients receiving ≥4 courses due to disease activity after 3 prior alemtuzumab courses.

Disclosure: Study supported by Sanofi and Bayer HealthCare Pharmaceuticals.

EPR3096

Evolution of new lesions and its temporal patterns in patients with clinically isolated syndrome treated with subcutaneous interferon beta-1a

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Background and aims: Subcutaneous interferon beta-1a (scIFNbeta-1a) treatment improves standard imaging outcomes in clinically isolated syndrome (CIS) patients. We assessed whether scIFNbeta-1a reduced new lesion evolution and temporal patterns using MRI data from REFLEX.

Methods: In REFLEX, CIS patients were randomised to scIFNbeta-1a 44mcg three times weekly (tiw), once weekly (qw) or placebo for 24 months; upon clinically definite multiple sclerosis (MS) patients switched to open-label scIFNbeta-1a tiw. This analysis included patients with scans available at Month (M) 12 and ≥2 scans after M12 (tiw n=128; qw n=137; placebo n=128). New lesion intensity on T1-weighted images without contrast was assessed and classified with respect to the surrounding white matter at: first appearance (iso- or hypo-intense [black holes]); first appearance and M24 (iso-iso, iso-hypo, hypo-iso, hypo-hypo); and the majority of timepoints (mostly iso- or hypo-intensity). Data are median (IQR) lesion numbers, unless otherwise stated. Kruskal-Wallis tests were used to assess overall treatment effects and Mann-Whitney U tests for pairwise comparison treatments.

Results: Overall, numbers of new lesions at M24 were reduced vs placebo (Table 1). Numbers of iso-hypo and hypo-hypo lesions were reduced vs placebo (0.4 [mean] and 1 [0–3], respectively) with scIFNbeta-1a tiw (0.09 [mean], p=0.003; and 0 [0–4], p<0.001) but not with qw (0.13 [mean], p=0.052; and 1 [0–3], p=0.165). At the majority of timepoints, scIFNbeta-1a reduced the number of new lesions that were mostly iso- and hypo-intense (Table 2).

	Overall	New iso-intense lesions	New hypo-intense lesions
Placebo scIFNbeta-1a	5 [2–11]	4 [1–9]	1 [0–3.5]
tiw	2 [0–5] P<0.001	1 [0–3] P<0.001	0 [0–1] P<0.001
qw	3 [1–7] P<0.001	2 [0–4] P<0.001	1 [0–2] P=0.147

Table 1: The number of new iso- and hypo-intense lesions at M24

	New iso-intense lesions	New hypo-intense lesions
Placebo scIFNbeta-1a	2 [0–5]	4 [2–8.5]
tiw	1 [1–4] P=0.003	2 [1–4] P<0.001
qw	1 [0–3] P=0.273	2 [1–5] P<0.001

Table 2: The number of new iso- and hypo-lesions at the majority of timepoints

Conclusion: scIFNbeta-1a tiw treatment reduced evolution of new lesions into black holes in CIS patients.

Disclosure: Funded by Merck KGaA, Darmstadt, Germany

EPR3097

A systematic review of non-interventional studies reporting on humanistic and economic burden of cognitive decline in multiple sclerosis patients regardless of study design

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Background and aims: Prevalence of cognitive impairment (CI) varies across disease duration. A clinically meaningful change in CI may be of interest to clinicians. Our objective was to summarise humanistic and economic outcomes of cognitive decline (CD) in patients with multiple sclerosis (MS).

Methods: Medline, Embase and PUBMED databases were searched considering English language studies only. Paediatric studies were excluded. CD was expressed as either a change in CI over MS duration or comparing assessments between patients with MS and healthy controls.

Results: 55 studies from 11 countries (Canada, France, Germany, Hungary, Italy, Israel, Norway, Spain, Switzerland, The Netherlands, United States) were included. Assessment of MS diagnosis was not homogenous. Humanistic: Prevalence of CI increased between baseline and disease duration of >5 years. Frequently reported CI assessments: Selective reminding test (SRT), Spatial recall test (SPART), Symbol digit modalities test (SDMT), Paced Auditory Serial Addition test (PASAT) and Word List Generation (WLG). Weighted differences in test scores comparing MS patients to healthy controls: [mean (95% Confidence Interval)] SDMT: -8.1 (-2.3, -13.9); SRT. D: -2.3 (-0.5, -1.3); PASAT 2: -7.7(-6.0, -9.5) WLG:-4.2 (-2.2, -6.2). Economic: Studies reported employment status, caregiver burden, ability to drive car, resource use or burden of disease. SDMT, PASAT and poor episodic memory contributed to predicting employment status and work productivity. CI in MS patients negatively impacts caregiver quality of life.

Conclusion: Prevalence of CI increases with disease duration. Cognitive assessments in patients with MS show deteriorating scores when compared to matched controls. CI negatively impacts employment status and caregiver quality of life.

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EPR3098

Anti-CD20 antibodies ofatumumab and ocrelizumab have distinct effects on human B-cell survival

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Background and aims: Ofatumumab is a subcutaneous, fully human anti-CD20 monoclonal antibody (mAb), currently in Phase-3 clinical trials for Multiple Sclerosis (MS), whereas ocrelizumab is an intravenous humanised anti-CD20 mAb. This study investigated the mode of B-cell cytotoxicity of these antibodies as a potential basis for clinical efficacy.

Methods: The human B-cell lines RAJI and RAMOS were used as target cells. The cells were coated separately with both anti-CD20 mAbs before washing and incubation for various time points. Human complement was added to initiate complement-dependent cytotoxicity (CDC) and cell lysis was analysed by fluorescence-activated cell sorting (FACS). Rituximab, another anti-CD20 mAb, was used as a control.

Results: All the tested anti-CD20 mAbs induced CDC. The degree of human RAJI B-cell lysis was a function of the mAb tested and the time of incubation prior to the addition of complement: cell lysis was more pronounced with ofatumumab compared with ocrelizumab when the cells were exposed to mAb and complement together for 2 hours. Similar results were obtained with the RAMOS B-cell line. The strongest difference was observed when complement was added 8 hours after washing. Under this condition, the extent of cell lysis was highest with ofatumumab, followed by rituximab and ocrelizumab. Ongoing studies in other B-cell cytotoxicity assays will provide deeper insights into relevant modes of action.

Conclusion: The strong complement-dependent B-cell lysis by ofatumumab may contribute to its high potency in vivo that enables a low-dose subcutaneous dosing regimen.

Disclosure: This study was supported by Novartis Pharma AG, Basel, Switzerland. All authors are employees of Novartis.

EPR3099

Subgroup analyses of NEDA re-baselined at week 24 in ocrelizumab recipients with relapsing Multiple Sclerosis receiving ocrelizumab in OPERA I and II

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Background and aims: The Phase III OPERA I/II studies (NCT01247324/NCT01412333) demonstrated the efficacy of ocrelizumab versus interferon-beta-1a (IFNβ1a) on a broad range of clinical and imaging outcomes in patients with relapsing multiple sclerosis, including no evidence of disease activity (NEDA; 47.7% vs 27.1%; p<0.001; pooled analyses). Benefit on NEDA was maintained across patient subgroups; magnitude varied. Re-baselining at Week 24 might provide a different perspective of treatment efficacy.

Methods: Proportions of patients at Week 96 with NEDA (no 12-week confirmed disability progression, protocol-defined relapse, new/enlarging T2 lesions or T1 Gd-enhancing lesions) re-baselined to Week 24 were compared (Cochran-Mantel-Haenszel test) using the pooled OPERA I/II modified intent-to-treat (mITT) population (OCR [600mg IV/24 weeks], n=745; IFNβ1a [44μg SC three times weekly], n=706; excludes patients discontinuing treatment for reasons other than lack of efficacy/death with NEDA prior to discontinuation).

Results: Treatment benefit for NEDA seen in the mITT population with OCR vs IFNβ1a (72.2% vs 41.9%; relative improvement, 72%; p<0.001) was maintained across subgroups (OCR/IFNβ1a): age (<40 years: 73.9%/36.1%; ≥40 years: 69.8%/50.2%), gender (male: 72.7%/36.7%; female: 72.0%/44.6%), prior [last 2 years] disease-modifying therapy (yes: 72.1%/35.8%; no: 72.2%/44.0%), prior relapses [last 12 months] (≤1: 73.3%/43.0%; ≥2: 69.6%/39.5%), baseline T1 Gd-enhancing lesions (none: 71.2%/51.5%; ≥1: 72.9%/27.6%) and baseline EDSS score (EDSS <2.5/<4.0: OCR 77.8%/76.5%, IFNβ1a 45.6%/42.9%; EDSS ≥2.5/≥4.0: OCR 68.9%/58.4%, IFNβ1a 39.4%/38.9%). All p-values (OCR versus IFNβ1a) <0.001.

Conclusion: The results of these NEDA subgroup analyses with re-baselining were consistent with those of the overall pooled population on NEDA with re-baselining.

Disclosure: Sponsored by F. Hoffmann-La Roche Ltd.

EPR3100

Pregnancy outcomes in patients with MS treated with teriflunomide: clinical study data

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Background and aims: Teriflunomide is a once-daily oral immunomodulator approved for treatment of relapsing forms of MS. Results from the clinical programme showed no signal for human teratogenicity in teriflunomide-exposed pregnancies. Additionally, no teratogenic signal has been reported in post-marketing surveillance of the parent compound, leflunomide (approved to treat rheumatoid arthritis since 1998). However, teriflunomide is contraindicated in pregnancy based on embryo-foetal toxicity in rats and rabbits. Despite the requirement to use reliable contraception, pregnancies have occurred in teriflunomide-treated patients.

Methods: Pregnancy outcomes are summarised for females treated with teriflunomide monotherapy in the clinical programme. Data cut-off was May 17, 2016.

Results: Overall, 62 pregnancies were reported: live birth (n=22), elective abortion (n=30), spontaneous abortion (n=8), and ectopic pregnancy (n=2). Of 22 live births, 3 (14%) were pre-term (<37 weeks). No malformations/abnormalities were reported with elective abortions. Mean (SD) treatment duration prior to pregnancy was 19.6 (19.1) months; an accelerated elimination procedure for teriflunomide was used in 82% of the cases with live births. In all pregnancies, the last dose of teriflunomide was administered pre-conception or in the first trimester (>0 to <14 weeks). One structural abnormality, ureteropyeloectasia, was reported in a pre-term infant. Patient-level data from individual pregnancies in the clinical setting will also be presented.

Conclusion: Current data from pregnancies exposed to teriflunomide show no teratogenic signal, consistent with observations from post-marketing surveillance of leflunomide. These data from the clinical setting, together with those from the International Teriflunomide Pregnancy Exposure Registry, will provide valuable information to healthcare providers and female patients of child-bearing potential.

Disclosure: Study supported by Sanofi.

EPR3101

CSF biomarkers do not associate to early disability in Multiple Sclerosis

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Introduction: Neurodegeneration occurs early in Multiple Sclerosis (MS), and caused clinical deterioration and disability. Biomarkers reflecting this phenomena, such as neurofilament light chain (NF-L), tau and β-amyloid (Aβ), could be measured easily in the cerebrospinal fluid (CSF).
Aim: To evaluate if CSF biomarkers of neurodegeneration predict early MS disability.
Methods: CSF NF-L, Aβ and tau levels were determined with commercial enzyme-linked immunosorbent assay in 48 newly-diagnosed MS patients (33 females). Baseline disease-courses were: three radiological (RIS) and 18 clinical isolated syndrome (CIS), 24 relapsing-remitting (RR) and 3 primary of secondary progressive (PR)-MS. Our disability outcome was the MS severity score (MSSS) at the last follow up (minimum 1 year after disease onset). We estimated differences between CSF biomarkers in baseline MS courses and disability with ANOVA.
Results: First, only CSF NF-L differed significantly among MS courses (p=0.002). In fact RIS showed the lowest levels (CSF NF-L mean 206 ng/ml±standard deviation 220) if compared to CIS (1158±511), RR (1616±741), and PR-MS (1714±27). On contrast, none of the CSF biomarkers was related to MSSS at last follow up. Of note, we excluded a correlation among tau or Aβ levels with NF-L.
Conclusion: NF-L are the unique biomarker of neurodegeneration related to MS forms. Their levels increased progressively with MS-course severity reflecting the higher axonal damage in PR-MS.
CSF NF-L, Aβ and tau failed to predict early MS disability: short-term outcome could not reflect the natural disease history.
Disclosure: Dr. Domizia Vecchio has been supported by a research fellowship by Merck-Serono

EPR3102

Lack of apparent association between lymphocyte pharmacodynamics and clinical or MRI disease activity in alemtuzumab-treated relapsing-remitting Multiple Sclerosis patients through 6 years: CARE-MS extension

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Background and aims: In the CARE-MS studies (NCT00530348; NCT00548405), alemtuzumab (12mg/day, baseline: 5 days; 12 months later: 3 days) significantly improved clinical/MRI outcomes versus subcutaneous IFNB-1a over 2 years in patients with active relapsing-remitting MS. Durable efficacy was observed in a 4-year extension (NCT00930553) without continuous treatment; 53% of patients received no additional alemtuzumab or other disease-modifying therapy. The effects of alemtuzumab may be due to its selective depletion and distinctive repopulation of circulating CD52-expressing T and B lymphocytes. We examine the association between lymphocyte repopulation patterns and clinical/MRI disease activity through 6 years following alemtuzumab treatment.
Methods: Blood counts were performed monthly; lymphocytes were phenotyped by flow cytometry quarterly and at Months 1 and 13. Lymphocyte subset counts from the CARE-MS studies were pooled (CD4+/CD8+ T-cells: total/naïve/memory/regulatory [Treg]; CD19+ B-cells: total/immature/mature/memory). Further analyses examined ratios of CD19+ (total/immature/memory) to Treg (CD4+/CD8+) cell counts. Relationship between lymphocyte repopulation patterns and efficacy was assessed in patients with/without relapses, 6-month confirmed disability worsening (CDW; ≥1.0-point Expanded Disability Status Scale increase [≥1.5 points if baseline EDSS=0]), or MRI disease activity (new gadolinium-enhancing lesions or new/enlarging T2 lesions).
Results: Lymphocyte subset repopulation kinetics over 2 years did not differ in patients with or without relapses, CDW, or MRI disease activity through 6 years. No correlation was observed between any CD19+/Treg cell count ratio and relapse, CDW, or MRI disease activity.
Conclusion: Based on these analyses, lymphocyte repopulation kinetics were not associated with return of disease activity and likely cannot be used to predict need for further treatment.
Disclosure: Study supported by Sanofi and Bayer HealthCare Pharmaceuticals.

MS and related disorders 9

EPR3103

A double-blind placebo-controlled study of satralizumab (SA237), a recycling anti-IL-6 receptor monoclonal antibody, as add-on therapy for neuromyelitis optica (NMO) and NMO spectrum disorder (NMOSD)

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Background and aims: NMO/NMOSD is a severe neuroinflammatory disorder associated with auto-antibodies to aquaporin-4 (AQP4). Interleukin-6 stimulates antibody production by plasmablasts and increases blood-brain-barrier permeability, thus permitting the penetration of pathological auto-antibodies into the central nervous system. Satralizumab is a recycling anti-IL-6 receptor monoclonal antibody with a long plasma circulation. We present the design and baseline demographics of a randomised, multicenter, international, double-blind, placebo-controlled study of satralizumab, the SAkuraSky study (NCT02028884).

Methods: The study is a randomised, double-blind, phase 3 study of satralizumab compared to placebo as add-on to baseline treatment (immunosuppressants or corticosteroids). The primary endpoint is time to first relapse. Main inclusion criteria: Adult (aged 18 to 74 years) and adolescent (aged 12 to 17 years) patients with NMO by 2006 Wingerchuk criteria (any serostatus), or NMOSD by 2007 Wingerchuk criteria with anti-AQP4 antibody seropositive status. At least 2 relapses in the last 2 years prior to screening, at least one of which occurred in the last 12 months.

Results: Adult enrollment is complete (76 patients). The enrollment of adolescents is ongoing (6 patients as of Oct 2017). 93.9% of total patients are females (77 patients). Baseline annual relapse rate was 1.0 for 39 patients (47.6%) and greater than 1.0 for the remainder. The number of patients with anti-AQP4 antibody seropositive status at screening is 55 (67.1%).

Conclusion: The SAkuraSky study is designed to evaluate the safety and efficacy of satralizumab compared with placebo in patients with NMO/NMOSD.

Disclosure: This study was funded by Chugai Pharmaceutical Co., Ltd., Tokyo, Japan. Detailed disclosures of each author will be included in the poster/oral presentation.

EPR3104

Patients switching to fingolimod from other oral DMTs and different treatment frequencies in daily clinical routine: results from PANGAEA 2.0

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Background and aims: Fingolimod was approved as first oral drug for the treatment of relapsing MS. Since 2011, treatment options highly increased. We analyse the effectiveness of fingolimod in patients switching from different pre-treatment frequencies and other oral disease-modifying therapies (oDMTs, dimethylfumarate and teriflunomide) to fingolimod.

Methods: PANGAEA 2.0 is an ongoing non-interventional study conducted in Germany. As of January 2018 it included app. 1800 patients. 15% of these patients switched from oDMTs to fingolimod.

Results: Baseline characteristics of all patients were comparable to patients switching from oDMTs. Patients switching after 1, 2 or 3 pre-treatments had an increasing mean age, time since diagnosis and EDSS but similar ARR at baseline. Patients were pre-treated with interferons (4.1 ± 0.7; years$\pm$SD), glatiramer actetate (3.0 ± 0.8), oDMTs (1.3 ± 0.3); or other DMTs (3.2 ± 0.6). For 41.1% of the patients fingolimod was the second therapy since diagnosis. The ARR ($\pm95\%CI$) 12 months after switch to fingolimod was reduced by 88.0% from 1.58 ± 0.25 to 0.19 ± 0.07 for patients switching from oDMTs. Patients switching from 1 DMT to fingolimod had a significant lower relapse rate (0.07 ± 0.02). compared to patients switching from 2 ($p<0.001$) or 3 ($p=0.038$) DMTs to fingolimod.

Conclusion: Independently of the treatment sequence before switching to fingolimod all patients benefit from the switch within twelve months of treatment. Patients treated with one DMT before switching to fingolimod had a significant lower ARR twelve months after switch in comparison to patients treated with more than one DMT or oDMTs before switch.

Disclosure: This study was supported by the Novartis Pharma GmbH, Nuremberg, Germany.

EPR3105

PANGAEA: 5 years safety of fingolimod in daily clinical practice

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Background and aims: Fingolimod (Gilenya®) is a sphingosine-1-phosphate receptor modulator approved for the treatment of relapsing MS. By June 2017 total patient exposure exceeded 453.000 patient years. PANGAEA (Post-Authorisation Non-interventional German sAfety of GilEnyA in RRMS patients) is a non-interventional study conducted in Germany to investigate long-term safety, effectiveness and patient reported outcomes.

Methods: PANGAEA included 4229 patients. By Jan 2018 over 800 patients finished the 5 year documentation period. Here we present safety and adherence data from 5 years fingolimod treatment in daily clinical routine.

Results: The mean observation period in PANGAEA was 3.75 (±1.62SD) years. Over a period of 5 years, the annual mean study discontinuation rate was 10-12%. 65% of the patients are continuing treatment 79% of patients discontinuing the study also discontinued fingolimod treatment. Most frequent reasons for study discontinuation were patient's decision (33%), adverse events (28%), switch of physician (12%) and disease progression (11%).

85% of the patients had no therapy interruption so far. Over 5 years, the safety profile of fingolimod in real-life is comparable to that observed in phase III clinical trials. Common adverse events are lymphopenia (11.3%), increase in liver enzyme values (5.3%), upper respiratory tract infections (e.g. nasopharyngitis (9.9%); bronchitis (2.4%); cough (2.2%)), fatigue (3.4%) and depression (2.6%). 28% of the patients experienced no adverse events so far. 5.0% of all adverse events were rated as serious.

Conclusion: The results of the 5 year interim analysis of PANGAEA support the positive benefit-risk profile that fingolimod demonstrated in phase III clinical trials with real-world evidence data.

Disclosure: This study was supported by the Novartis Pharma GmbH, Nuremberg, Germany

EPR3106

PANGAEA: 5 years effectiveness of fingolimod in daily clinical practice

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Background and aims: Once-daily fingolimod (Gilenya®, Novartis Pharma AG) is a sphingosine 1-phosphate receptor modulator approved for the treatment of relapsing MS. As of June 2017 total patient exposure exceeds 453.000 patient-years. PANGAEA is a non-interventional study, conducted in Germany, to investigate long-term safety, effectiveness and patient reported outcomes in daily clinical practice.

Methods: PANGAEA included 4229 patients. By Jan 2018 over 800 patients finished the 5 year documentation period of fingolimod treatment. In this interim analysis we present effectiveness data of fingolimod in daily clinical practice.

Results: The proportion of female patients was 71.6% and the mean age was 39.9 (±10.1SD) years. The mean annual relapse rate of PANGAEA patients improved from 1.6±0.12 (95%CI) to 0.28±0.07 in the third year of treatment and remained stable over the following two years. The mean baseline EDSS in PANGAEA was 3.0 (±0.03; 95%CI) and remained stable over 5 years. In each year of treatment app. 90% of the patients had a stable or improved EDSS. In each year of treatment between 60.4% (year 1) and 71.1% (year 5) of the patients were free of relapses and 6 months confirmed disability progression (CDP). 42.8% of the patients neither had a relapse nor a 6 months CDP over 4 years. Patient reported outcomes evaluated in a substudy (n=830) also confirmed the good effectiveness and convenience profile of fingolimod.

Conclusion: The results of the 5 year interim analysis of PANGAEA support the positive effectiveness profile of fingolimod demonstrated in phase III clinical trials with real world evidence data.

Disclosure: This study was funded by the Novartis Pharma GmbH, Nuremberg, Germany.

EPR3107

The change of the fingolimod patient profile over time: a comparison of two non-interventional studies PANGAEA and PANGAEA 2.0.

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Background and aims: Therapeutic options for Multiple Sclerosis (MS) have increased over the years. Treatment guidelines have changed from baseline and escalation therapies to the treatment of mild to active forms of MS. How did this influence the demographic and clinical profile of fingolimod patients over time?

Methods: PANGAEA and PANGAEA 2.0 are two non-interventional studies conducted in Germany that recruited patients switching to fingolimod between 2011-13 and 2015-18 respectively. PANGAEA included 4229 patients. PANGAEA 2.0 included app. 1800 patients and recruitment is still ongoing.

Results: The mean age of PANGAEA 2.0 patients is comparable (38.7±10.6 vs 38.9±10.1 years) to PANGAEA. 84.4% of patients were treated with at least one other disease modifying therapy (DMT) before entering PANGAEA 2.0 (PANGAEA 92.3%). 15.6% of patients were not pre-treated with any DMT (41.1% one pre-treatment, 24.6% two pre-treatments, 18.6% three or more). Patients included in PANGAEA 2.0 have a shorter disease history (7.2±6.6 vs. 8.2±6.3 years), a similar relapse rate (1.3±1.0 vs. 1.6±1.2), lower EDSS (2.2±1.6 vs. 3.0±1.7) and MSSS (3.5±2.5 vs. 5.1±2.6). 40.5% of PANGAEA 2.0 patients had an EDSS ≤1.5 at baseline (PANGAEA: 23.3%). MSSS score of 49.5% of PANGAEA 2.0 patients ranged within the first 3 deciles (PANGAEA: 29.5%).

Conclusion: Treatment guidelines have influenced demographic and clinical profiles of fingolimod patients. Patients included into PANGEA 2.0 (2015/16) switched to fingolimod earlier from a demographic and clinical point of view in comparison to PANGAEA (2011-13). This might indicate a change to earlier optimization of sub-optimally treated patients with MS between 2011 and 2016 in Germany.

Disclosure: This study was funded by the Novartis Pharma GmbH, Nuremberg, Germany

EPR3108

Extended interval dosing (EID) of natalizumab is associated with significantly lower progressive multifocal leukoencephalopathy (PML) risk: sensitivity and post hoc analyses from the TOUCH registry

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Background and aims: Natalizumab, approved for intravenous 300mg every 4 weeks dosing, is associated with a risk of PML. Previous analyses of US TOUCH registry data found that, in anti-JC virus antibody positive (JCV Ab+) patients, natalizumab EID was associated with significantly lower PML risk compared with standard interval dosing (SID; Table). Those analyses were limited to patients with known JCV Ab seropositive status and excluded patients with infusions at >12-week intervals (ie, dosing gaps). Sensitivity and post-hoc analyses were conducted to explore the robustness of these results.

Methods: In the previous primary analysis, SID was based on average dosing intervals (ADIs) of ≥3 to <5 weeks; EID was based on ADIs of >5 to ≤12 weeks. In prespecified sensitivity analyses, alternative EID definitions and inclusion of PML cases occurring pre-2012, prior to JCV Ab testing, was evaluated. A post hoc analysis included patients with dosing gaps. EID and SID PML hazard ratios (HRs) were compared with covariate (age, sex, prior immunosuppressant use, initiation calendar year, and infusion number)–adjusted Cox regression models and Kaplan-Meier estimates.

Results: Across all sensitivity and post-hoc analyses, HRs and 95% CIs were similar to those in the primary analysis.

Conclusion: In the US, natalizumab EID is associated with a statistically significant, clinically meaningful lower PML risk in JCV Ab+ patients compared with SID; changes in EID definition and inclusion/exclusion criteria did not reveal differences from the primary analysis. As TOUCH does not collect effectiveness data, EID's benefit-risk could not be evaluated.

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EPR3109

Lack of apparent association between lymphocyte repopulation kinetics and autoimmune events in alemtuzumab-treated patients with relapsing-remitting Multiple Sclerosis through 6 years: CARE-MS extension

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Background and aims: Alemtuzumab 12mg significantly improved clinical and MRI outcomes versus subcutaneous IFNB-1a in patients with relapsing-remitting MS (RRMS) in the 2-year CARE-MS studies (NCT00530348; NCT00548405). Autoimmune adverse events (AEs), including thyroid events, immune thrombocytopenia (ITP), and nephropathies, were observed during the trials. Alemtuzumab selectively depletes CD52-expressing T and B lymphocytes; a distinct pattern of cellular repopulation then follows. This analysis tests the hypothesis that differential lymphocyte repopulation patterns following treatment with alemtuzumab create the environment for secondary autoimmunity.

Methods: Patients who completed the CARE-MS studies could enroll in a 4-year extension (NCT00930553). Autoimmune AE monitoring occurred at baseline and monthly (ITP; nephropathies) or quarterly (thyroid). Blood cell counts in the CARE-MS studies were performed monthly; lymphocytes were phenotyped by flow cytometry quarterly and at Months 1 and 13. Lymphocyte subset counts from the CARE-MS studies were pooled (CD4+/CD8+ T-cells: total/naïve/memory/regulatory [Treg]; CD19+ B-cells: total/immature/mature/memory). Further analyses examined ratios of CD19+ (total/immature/memory) to Treg (CD4+/CD8+) cell counts. The relationship between lymphocyte pharmacodynamics and autoimmune AEs over 6 years was assessed.

Results: There was no difference in either T or B lymphocyte depletion or repopulation patterns over 2 years in patients who did or did not experience autoimmune AEs through 6 years following alemtuzumab treatment. No correlation was observed between autoimmune AE occurrence and any CD19+/Treg cell count ratio.

Conclusion: The current analyses do not support the hypothesis that differences in lymphocyte subset count depletion or repopulation kinetics predict the occurrence of autoimmune AEs in alemtuzumab-treated RRMS patients.

Disclosure: Study supported by Sanofi and Bayer HealthCare Pharmaceuticals.

Muscle and neuromuscular junction disease 2

EPR3111

Ratio of creatine kinase to alanine aminotransferase as a biomarker of acute liver injury in dystrophinopathy

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Background and aims: To investigate the ratios of creatine kinase (CK) to aminotransferases as biomarkers of acute liver injury in dystrophinopathy.

Methods: We enrolled 658 male patients with dystrophinopathy and 378 male patients without muscle and liver injury as control. Patients were analySed for lower limb motor function, genotype, clinical phenotype, glucocorticoid management, and serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and CK. To examine whether CK-adjusted aminotransferase levels could indicate liver status in dystrophinopathy, the CK/ALT ratio was compared in mice treated or not with a hepatotoxic reagent D-galactosamine (D-GalN), as the number of patients with dystrophinopathy and acute liver injury were insufficient for analysis.

Results: In patients with dystrophinopathy, the correlations between CK and aminotransferases were significant (P<0.05). But only CK/ALT did not show association with factors related to muscle injury severity (P>0.05). Animal experiments indicated that D-GalN decreased the CK/ALT ratio both in C57 mice and mdx mice (P<0.001), suggesting that CK/ALT may also be decreased in patients with dystrophinopathy and acute liver injury. Lower reference limit of CK/ALT in patients with dystrophinopathy was determined as 22.16.

Conclusion: CK/ALT has potential clinical applicability for monitoring acute liver injury in dystrophinopathy.

EPR3112

Study on the origin of the electromyographic spontaneous electrical activity in an ex vivo muscle model

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Background and aims: Spontaneous electrical activity (SEA) is the electromyographic record obtained from relaxed healthy muscles. In non-pathological muscles SEA consists of end-plate noise (EPN) and end-plate spikes (EPS). Even though SEA has been studied since the 1950s, its origin in the spontaneous neurotransmission of the neuromuscular junction (NMJ) is not proven in a reliable way. The objective of this study is to assess the participation of NMJ in the generation of SEA.

Methods: Muscle areas were recorded by using electromyography at 1mm and at 10mm of the intramuscular nerves in ex vivo diaphragm. The presence of EPN and EPS in each area was recorded and their amplitude was calculated. The amplitude of EPN was also evaluated before and after a quick incubation with ClK (30 mM).

Results: The number of areas with EPN and EPS and their amplitude decrease progressively from near the nerve to 10mm away. Moreover, 10mm apart from the intramuscular nerve, no EPN was recorded. Finally, 3 seconds after CIK exposure the EPN amplitude increases by 300%.

Conclusion: The spontaneous electrical activity recorded with electromyography is related to the spontaneous release of acetylcholine by NMJ.

Disclosure: Nothing to disclose

EPR3113

Myopathy in trunk muscles in Myotonic Dystrophy type-1: a case control study with MRI

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Background and aims: Myotonic Dystrophy 1 (DM1) is an inherited multisystem disorder caused by a CTG nucleotide repeat expansion in the Myotonic dystrophy protein kinase (DMPK) gene on chromosome 19. The motor impairments in DM1 are assumed to progress from distal to proximal in the extremities. Resently, we documented early and severe impairments in trunk muscles when measured by manual muscle strength tests (MMT). Whether these impairments are caused by DM1 myopathy is not clear. We therefore investigate trunk muscles with MRI and relate the findings to different motor function in a case control design.

Methods: 20 patients and 20 age and geneder matched controls included in a case control design. MR imaging was performed using a 1.5-T MR unit of trunk muscles (abdominal flexors and trunk extensors). MRIs were analysed for% of muscle fat infiltration, and muscle size measured in mm and mm^2. Trunk muscle strength, general mobility, balance and forced vital capacity (FVC) are measured by clinical tools and related to MRI findings.

Results: We show a clear difference in fat infiltration and muscle size between patients and matched controls. We find strong relations between the different MRI measures and impairments for both motor-performance and respiratory function. Certain patterns of fat infiltration and atrophy are present.

Conclusion: MRI document pathological levels of fat infiltration and atrophy in DM1. The two forms of myopathy have different relations to function. The findings are important for managing DM1 and future interventions studies.

Disclosure: Nothing to disclose

EPR3114

Ultrasound for assessment of diaphragm function in late-onset Pompe disease

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Background and aims: To evaluate the correlation between diaphragm thickness and mobility assessed by ultrasound and classical pulmonary function tests (PFTs) in patients with late-onset Pompe disease (LOPD).

Methods: 17 LOPD patients (M/F ratio: 9/8) were studied comparing classical PFTs with diaphragm thickness and mobility measured by ultrasound.

Results: The mean age was 46.7±4.7 yrs and with a mean disease duration of 12.3±8.5 yrs. Ultrasound studies of diaphragm thickness in full inspiration correlated with maximal inspiratory pressure (MIP) (r=0.69; p=0.004) and maximal expiratory pressure (r=0.57; p=0.024), forced expiratory volume in one second (FEV1) (r=0.59; p=0.016), forced vital capacity (FVC) both in seated (r=0.70; p=0.002) and supine position (r=0.63; p=0.026). Diaphragm thickness at functional residual capacity correlated with maximal expiratory pressure (r=0.58; p=0.021) and seated FVC (r=0.57; p=0.021). Diaphragm thickening fraction correlated with MIP (r=0.80; p=0.0003), seated (r=0.68; p=0.003) and supine FEV1 (r=0.65; p=0.020), seated (r=0.66; p=0.005) and supine FVC (r=0.61; p=0.034).

Conclusion: Diaphragmatic function assessed by ultrasound is a simple, noninvasive tool that correlates significantly with classical PFTs in patients with LOPD.

Disclosure: Nothing to disclose

EPR3115

Antifibrotic efficacy of nintedanib in in vitro and in vivo models of Duchenne muscular dystrophy

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Background and aims: Several growth factors have been involved in the process of muscle fibrosis in Duchenne muscular dystrophy (DMD). Nintedanib, a tyrosine kinase inhibitor targeting FGFR, PDGFR and VEGFR, is approved for the treatment of idiopathic lung fibrosis. To study whether nintedanib is effective in reducing fibrosis in DMD.

Methods: Effect of nintedanib on proliferation, chemotaxis and gene expression of human muscle fibroblasts was explored in vitro. Effect of nintedanib on muscle function and structure was assessed in 10 months old mdx-mice treated with 60 mg/kg nintedanib for one month compared to age matched mdx mice and C57BL/6N control mice using digigait, electromyography (EMG) and histological studies.

Results: Nintedanib significantly decreased human fibroblast proliferation ($p<0.001$) and chemotaxis ($p<0.05$) and reduced collagen I and III and fibronectin expression in vitro. EMG detected motor unit action potentials of bigger amplitudes and shorter duration in nintedanib-treated mice compared to non-treated. Histological studies showed a significant reduction in the fibrotic tissue area in muscle sections of diaphragm ($p<0.001$) and quadriceps ($p=0.03$) of nintedanib-treated compared to non-treated animals. Real Time PCR and WB studies showed a reduction in the expression of collagen I and III and fibronectin in muscles obtained from nintedanib-treated mice compared to controls.

Conclusion: Nintedanib demonstated antifibrotic efficacy in a murine model of DMD by reducing the fibrotic area and markers of fibrosis in muscles. A reduction of the proliferation of fibroblasts is the assumed mode of action. This promising result suggests a potential value of nintedanib in the treatment of muscle dystrophies.

Disclosure: This study has been partially sponsored by Boehringer and buy Fondos FEDER-ISCIII PI15/01822 to JDM

EPR3117

Phenotype variability in a large Spanish family with Hyperkalemic Periodic Paralysis associated with mutations in SCN4A gene

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Background and aims: The Hiperkalemic Periodic Paralysis is a rare skeletal muscle channelopathy caused by mutations in the SCN4A gene, that encodes the a-subunit of the voltage-gated sodium channel. It's characterised by recurrent transient attacks of muscle weakness triggered by potassium-rich food, quick temperature changes, fasting and rest after heavy workload.

Methods: We report a case of a Spanish family with 16 affected members. They were all subjected to full anamnesis, physical examination and routine blood analysis, however, only 4 of them were studied genetically and were confirmed to have the mutation T704M.

Pseudohypertrophic calves on a patient that showed vacuolar myopathy on biopsy.
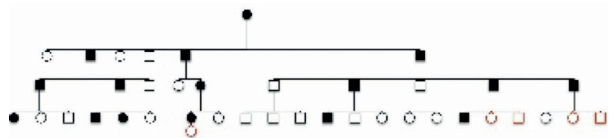
The family studied with 16 members affected. Healthy patients shown in red have been genetically selected.

Results: We observed two different clinical forms of presentation. A part of the family presents between 1-2 invalidating attacks per day of 30-180min; but the other part only presents 1-2 attacks every two weeks lasting for less than 120min, and with less severe weakness and better recovery with carbohydrates, despite that they all have the same mutation. Four of the patients that belong to the most severe clinical variant are over 40-50 years old and they all

have pseudohypertrophic calves and thighs, two of them with edema-like changes/fatty degeneration on MRI and vacuolar myophathy on biopsy. Prevention treatment with acetazolamide, hydrochlorthiazide and salbutamol has shown partial results, but the genetical selection of healthy embryos has proved to be the only way to avoid this disease in 5 members of the family.

Conclusion: Our findings are slightly different to cases reported previously as our patients have more attacks than described for this mutation and show a variable clinical presentation despite having the same mutation.

Disclosure: Nothing to disclose

Neuroepidemiology

EPR3118

Subacute neurological complications following living donor liver transplantation; Egyptian experience

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Background and aims: Liver transplantation (LT) is the only curative treatment in patients with end-stage liver disease. Of all the complications post-LT, the neurological complications (NC) are particularly relevant, since they affect up to a third of transplanted patients. The aim of this study is to assess the incidence, risk factors and clinical presentation of NC after liver transplantation in patients who underwent living donor liver transplantation (LDLT).
Methods: Between November 2011 and December 2013, 149 patients were admitted to ICU after LDLT and were evaluated by full general and neurological examination, full laboratory investigations including drug levels, brain CT and/or MRI, assessment of encephalopathy by West Haven classification, patients were observed after LT for one month.
Results: Of 149 transplanted patients 46 (30.9%) developed neurological complications. The most common neurological complications were Encephalopathy (14.1%) while the least were both Central pontine myelinolysis and Meningoencephalitis (0.7%). Out of the 149 patients, 146 (98%) patients were prescribed Tacrolimus (FK-506) 46 patients (30.9%) developed neurological complications, 30 of which (20.1%) developed side effects related to the drug administration. 29 patients (19.5%) prescribed cyclosporine, 2 patients (1.3%) developed side effects related to the drug administration.
Conclusion: There was a high incidence of neurological complications after LT, prolonging the patients stay in intensive care significantly and most common complications following LT were encephalopathy, delirium, hallucinations, delusions and seizures. Consequently, careful pre-operative and post-operative neurological evaluation and close observation and follow-up is important for early diagnosis of NCs and therefore their prompt treatment.
Disclosure: Nothing to disclose

EPR3119

Vitamin D supplementation in Multiple Sclerosis: time matters. A two-year observational study

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Background and aims: Consistent amounts of studies support the role of Vitamin D (vitD) in multiple sclerosis (MS) pathogenesis. This study investigates the relationship between time of beginning vitD supplementation and prognosis
Methods: We included consecutive MS patients who started vitD treatment, determining vitD blood levels before treatment initiation. We considered two groups according the time of treatment initiation: within the first three years from disease onset or later. We considered the following variables: age at MS onset, age at baseline, relapse rate, new MRI gadolinium enhancing lesions and T2/FLAIR lesions, EDSS at the end of follow-up (September 1st 2017). We used t test, Chi square analyses Kaplan-Meyer estimates to compare means or frequencies distribution between groups according to quartiles of vitD at baseline. We used Cox proportional analyses to calculate the effects of time to initiation of vitamin D on disease activity and progression.
Results: We included 231 MS patients. Patients starting vitD within the first three years from onset had a significantly lower mean EDSS score at the end of follow-up and a lower risk to reach an EDSS score of 3.5 (HR 0.86; CI 0.75-1.00; p=0.05). Trends were similar dividing patients according to quartiles of vitD distribution at baseline. Patients had a lower probability to develop new MRI lesions when they started vitD earlier (p=0.001).
Conclusion: Our study suggests that a time window opportunity could exists for vitD supplementation in MS patients. If confirmed, these results would add relevant information about the time and use of vitD among MS patients.
Disclosure: Nothing to disclose

EPR3120

Prevalence of Parkinson's disease – a repetitive epidemiological study in Estonia

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Background and aims: A previous epidemiological study on Parkinson's disease (PD) in the county of Tartu, Estonia found the adjusted prevalence rate to be 152/100,000. This study aimed at determining the PD prevalence almost twenty years later as well as evaluating the dynamic changes in the disease frequency compared to the first study.

Methods: This cross-sectional, community-based study was conducted in 2010-2016 in the county of Tartu, Estonia. Multiple case-finding sources including information from neurologists, family doctors, local PD Society, nursing institutions and the database of Estonian Health Insurance Fund were used to identify patients in all ages with PD.

Results: The total age-adjusted prevalence rate (standardized to the age structure of 2014 Estonian population) of PD was 314/100,000. After age-adjustment to the European 2011 standard population, the overall prevalence rate was 324/100,000. The adjusted prevalence rate was significantly higher for women compared to men (rate ratio [RR]=1.51; p=0.00003). No significant differences were found between PD prevalence in urban and rural areas (RR=1.09; p=0.40). After adjustment to the same standard population as used in the previous prevalence study, the overall age-adjusted prevalence rate was found to be 197/100,000. Patients in the current study were older, had more often a severe disease and a longer disease duration compared to those reported in the first epidemiological study.

Conclusion: The age-adjusted prevalence has moderately increased in past decades in Estonia. We believe that the substantial aging of the Estonian population and the improved diagnosis have the biggest contribution to the increase in the disease frequency.

Disclosure: The study has been supported by the Grants PUT1239, the IUT2-4 of the Estonian Research Council, and the Liisa Kolumbus Memorial Scholarship 2017 of the Tartu University Foundation.

EPR3121

Severity of impulsive compulsive behaviors in patients with Parkinson's disease

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Background and aims: Impulsive compulsive behaviors (ICBs) are clinically complications of Parkinson's disease. However, the clinical characteristics of ICBs in the Siberian population of patients with Parkinson's disease (PwPD) were rarely reported. We aimed to explore the prevalence and the clinical profile of ICBs in Siberian PwPD.

Methods: December, 2017, 819 patients were registered in movement disorders electronic database in Siberian region (women:men=346:473, mean age 66.3±8.4, PD mean duration 7.5±5.6, mean H&Y stage 2.89±2.63, mean UPDRS III 33.1±16.3). Each PwPD were examined by extended clinical and neuropsychological study with qualitative and quantitative analysis. Clinical assessments were carried out using UPDRS, H&Y Scale and Questionnaire for Impulsive-Compulsive Disorders in PD-Rating Scale. From all patients 293 of them were investigated using Montreal Cognitive Assessment (MoCA-test), Beck depression inventory-II, Hospital Anxiety and Depression Scale, Apathy Scale, PD Sleep Scale, Epworth Sleepiness Scale, PD Questionnaire-39 (PDQ-39), Bristol stool scale, Scale for Outcomes in PD for Autonomic Symptoms, Sniffing Stix Test.

Results: 19.8% PwPD were affected with ICBs. ICBs was negatively correlated with onset age (r=0.430; p<0.0001), illness duration (r=0.334; p<0.0001), quality of life (pain/discomfort, r=0.430; p<0.0001), UPDRS-III scores (r=0.025; p=0.025) and positively associated with anxiety score (r=0.436; p<0.0001), LEDD (L-Dopa) (r=0.177; p=0.011), apathy (r=0.201, p=0.004), sleepiness (r=0.203; p=0.003), ICBs score weren't associated with H&Y Stage, olfactory dysfunction and constipation.

Conclusion: This study demonstrates that ICBs are common in PwPD. Subsequent studies should consider syndromal and subsyndromal symptoms.

Disclosure: Nothing to disclose

EPR3122

eMSQOL-29: Prospective validation of the abbreviated, electronic version of the MSQOL-54

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Background: We recently devised a shortened version of the 54-item Multiple Sclerosis Quality of Life (MSQOL-54) in paper (MSQOL-29) and electronic format with integrated scoring routine (eMSQOL-29). MSQOL-29 consists of 25 items forming 7 subscales, and 4 single items; one filter question for 3 'sexual function' items.

Aims: To prospectively assess eMSQOL-29 psychometric properties, and its acceptability/equivalence vs. paper version.

Methods: MS patients (n=623; mean age 44 years; median Expanded Disability Status Scale, EDSS 2.5, range 0.0–9.0) from 5 Italian centres completed eMSQOL-29, Hospital Anxiety and Depression Scale, Functional Assessment of MS (FAMS), European Quality of life Five Dimensions-3L, and received EDSS and Symbol Digit Modality Test (SDMT). We assessed eMSQOL-29 reliability (Cronbach's alpha), factorial (confirmatory factor analysis, CFA) and concurrent validity (Pearson's r). Equivalence vs. paper MSQOL-29 was assessed in 242 patients (randomized cross-over design, two-week administration interval).

Results: 'Sexual function' items were filtered out by 273 patients (47%). No multi-item scale had floor effect, while 5 had ceiling effect. Cronbach's alpha range was 0.88–0.90. CFA (multi-item subscales) showed good overall fit, and the two-factor solution for composite scores was confirmed. Concurrent validity was sub-optimal for 'cognitive function' (vs. SDMT, r=0.25) and 'social function' (vs. FAMS social function, r=0.38). eMSQOL-29 equivalence was confirmed, and multivariate model found no version, order or sequence effect; its acceptability was good.

Conclusions: eMSQOL-29 showed good internal consistency, factor structure, no floor effect, while most subscales had some ceiling effect. Concurrent validity was sub-optimal for 2 subscales. Equivalence and acceptability were good.

EPR3123

Consumer involvement in formulation of the questions to be answered: findings from the EAN Guideline on Palliative Care of People with severe Multiple Sclerosis

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Background and aims: Consumer involvement in clinical practice guideline development is warranted through all stages to increase guideline trustworthiness and relevance. We aimed to engage Multiple Sclerosis (MS) patients and caregivers in definition of the key questions to be answered in the EAN Guideline on Palliative Care of People with severe MS.

Methods: We used a mixed approach: 1) International online survey launched by the national MS societies, after pilot testing/debriefing on 20 patients and 18 caregivers. 2) Focus group meetings (FGMs) of MS patients and caregivers.

Results: 1) Of 1199 participants, 951 (79%) completed the whole survey, and 934 from seven countries with above-threshold figures were analysed: 751 (80%) were MS patients (74% women, mean age 46.1) and 183 (20%) caregivers (36% spouses/partners, 72% women, mean age 47.4). Participants agreed/strongly agreed on inclusion of the nine pre-specified topics (from 89% for 'advance care

planning' to 98% or 'multidisciplinary rehabilitation'), and <5% answered 'I prefer not to answer' to any topic. Free comments were 569: 182 (32%) on pre-specified topics, 227 (40%) on additional topics (16 guideline-pertinent), and 160 (28%) on outcomes. 2) Five FGMs (three of MS patients, two of caregivers, overall 35 participants) corroborated survey findings, and helped to identify patient-important outcomes.

Conclusion: Consumer involvement was resource and time intensive, but rewarding. It was key for the formulation of the guideline questions, and for the identification of patient-important outcomes. Importantly, free comments from several participants concerned sensitive issues which were purposely excluded from the pre-specified topics.

Disclosure: This guideline is a joint initiative of the EAN, the European Association for Palliative Care (EAPC), the European network for best practice and research in MS Rehabilitation (RIMS), and has been endorsed by the European Committee for Treatment and Research in MS (ECTRIMS). This guideline has been granted by the EAN, and by the Foundation of the Italian MS Society (FISM grant 2017/S/2).

EPR3124

Correlation between vascular risk factors, arterial remodeling and systolic function in patients with leukemia

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Background and aims: The aim of this study was to assess if there is an impact of vascular risk factors in patients with leukemia on hemodynamics parameters before and after chemotherapy by determining the arterial remodeling Intima-Media-Thickness (IMT) using Extracranial-Doppler (ECD) and the systolic function by Left Ventricular Ejection Fraction (LVEF) calculation using echocardiography.

Methods: We enrolled 15 patients with leukemia aged between 33 and 79 scheduled for chemotherapy. The ECD and echocardiography were performed prior and 3 months after the treatment. Systolic blood pressure (SBP) and diastolic blood pressure (DBP), heart rate, IMT and LVEF were measured before and after chemotherapy and correlated with vascular risk factors.

Results: Out of the study patients, 3 (20%) had dyslipidemia, 2 (13,3%) had heart coronary disease, 6 (40%) had hypertension and 8 (53,3%) were smoking patients. IMT(mm) significantly increased from 0.64 ± 0.08 to 0.76 ± 0.09 (p<0.05) in left carotid artery. SBP(mmHg) significantly increased from 122 ± 10.98 to 132.6 ± 9.29 (p<0.05). LVEF(%) significantly decreased from 60.46 ± 9.67 to 56.53 ± 8.57 (p<0.05) post chemotherapy with slightly worse values in smoking and hypertensive patients (p<0.05). In smoking patients IMT(mm) significantly increased from 0.61 ± 0.08 to 0.73 ± 0.09 (p<0.05) and in hypertensive patients IMT(mm) significantly increased from 0.66 ± 0.05 to 0.78 ± 0.09 after chemotherapy.

Conclusion: Carotid and cardiac functions should be assessed at baseline with ECD and echocardiography before onset of chemotherapy. During and after treatment, repeated assessments should also be considered. Calculation of arterial remodeling- IMT and systolic function- LVEF and correlation with vascular risk factors are very useful in patients with leukemia in assessing the strategy for adherence to chemotherapy treatment.

Disclosure: Nothing to disclose

EPR3125

The prevalence of neuropsychiatric symptoms in Parkinson's disease on a nationwide level in Hungary

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Background and aims: Neuropsychiatric and cognitive symptoms are frequent in Parkinson's disease (PD) and may precede and exceed motor symptoms as major factors impacting disease course and quality of life. Neuropsychiatric symptoms (NPS) in PD are various and are attributed to pathologic changes within multiple brain regions, to psychological stress, and to adverse effects of dopamine replacement therapy. Our aim was to assess the prevalence of NPS in PD, analysing the whole Hungarian population.

Methods: In Hungary, a country with 10 million inhabitants and a single payer health insurance system we have set off the NEUROHUN 2004 – 2017 project. In the framework of the Hungarian Brain Research Program we created a database from medical and medication reports submitted for reimbursement purposes to the National Health Insurance Fund (NHIF) from all hospitals and outpatient services throughout the country in a ten-year period of time, between 2004–2013. For the current analysis, ICD-10 codes for PD and NPS were used from the database for patient selection.

Results: 96 874 patients were reported to the NHIF with PD between 2004 and 2013 out of which 56% had at least one NPS. Following the PD diagnosis, 60% of the NPS appeared within 2 years on average. The most common NPS were dementia, mood disorders and anxiety.

Conclusion: PD is a complex disease in which the prevalence of NPS is high. Therefore early and routine screening for a range of prevalent NPS is important and a multidisciplinary, personalised care is needed to initiate optimal treatment.

Disclosure: Nothing to disclose

EPR3126

Profile of Syrian Refugees from Neurological Outpatient Clinic in Turkey

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Background and aims: Turkey hosts the largest number of registered Syrian refugees – currently 3,424,237. Obstacles in the utilisations of medical services in this disadvantageous group may be viewed as financial, structural, and personal. We aimed to find out the sociodemographic and clinical profile of Syrian refugees who admitted to our clinic, changes in patient number across years, and the percentage of the patients on follow-ups.

Methods: Syrian patients who admitted to the our neurology outpatient clinics, neurology emergency department, and hospitalised in the neurology clinics were included in the study. Age, gender, number of admissions, year of admissions, chief complaints, diagnoses, and follow-up percentages of the patients were recorded retrospectively.

Results: Total number of patients who admitted to our hospital and consulted from other clinics were found to be 763. 547 (74%) of these patients did not come to the follow-ups even though their conditions required regular follow-ups. New admissions started in 2011 (0.3%), gained a momentum and peaked in 2014 (28.6%), continued to stay high in 2016 (27%), and decreased significantly in the year 2017 (9.2%). The most common diagnoses were primary headaches (22.9%), cerebrovascular diseases (20.6%), mental health problems (11.7%), and epilepsy (10.2%).

Conclusion: Most of the patients who admitted to our hospital did not come to the follow-ups and information regarding their treatments could not be obtained. Even though Turkish Republic provided the Syrian refugees with free medical care, utilization of these resources may be limited because of socioeconomic issues. Studies investigating why the people are not coming to the follow-ups are required.

Disclosure: Nothing to disclose

Neurogenetics 4

EPR3127

Spastic paraplegia 52 – a new AP4S1 variant?

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Background and aims: The identification of homozygous or heterozygous variants in highly preserved DNA regions by arrayCGH or whole exome sequencing is associated with interpretation difficulties.

Methods: We present a 2-year-old boy born of nonconsanguineous parents. He had a full term gestation with intrauterine growth restriction. In the first months of life he had poor weight gain, hyperammonemia, elevation of glutamine and ornithine, low citrulline and negative orotic acid. Weight recovery and normalisation of aminoacid profile occurred with hypoproteic diet and mantained with normal diet. Genetic study for NAGS, CPS and OTC were normal.

By nine months developmental delay, hypotonia and strabismus were evident. Brain MRI showed delayed myelination, polymycrogyria, corpus callosum dysgenesis and dysmorphic ventricules. Spectroscopy was normal. At fifteen months he had one episode of status epilepticus. Currently he has pyramidal signs in both legs.

Results: Exome revealed a splicing variant in homozygoty in AP4S1, c.294+1G>T. Additional genetic and metabolic studies were normal.

Conclusion: AP4S1 gene encodes a subunit of an adaptor-related protein that mediates vesicle formation and sorting of integral membrane proteins. Mutations in homozygoty in this gene were associated with spastic paraplegia 52. This is a very rare condition described in 11 children and consisting of dysmorphic features and neonatal hypotonia progressing to hypertonia, loss of ambulation, seizures and cognitive deficit without spoken language. Imaging abnormalities include aqueductal stenosis, hypomyelination, absent corpus callosum and lack of differentation of white/grey substance in basal nuclei ganglia. We present this case for discussion of the pathogenicity of the variant and genotype-phenotype correlation.

Disclosure: Nothing to disclose

EPR3128

Clinical whole-exome sequencing for the diagnosis of Mendelian neuromuscular disorders

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Background and aims: Whole-exome sequencing has recently become a widely used diagnostic test for individuals with rare Mendelian disorders. Its use for the diagnosis of neuromuscular disorders is promising, given the high genetic and clinical heterogeneity of this disease group. Previous data report a broad range of diagnostic yields between 25 and 50%, depending on the selected patient group and the used diagnostic approach.

Methods: We retrospectively selected all patients that were seen in the neuromuscular clinic of the Department of Neurology of the Medical University of Vienna (Austria) receiving whole-exome sequencing for a diagnostic purpose between 2014 and 2017. Whole-exome data were generated at the Institute of Human Genetics, Technical University Munich (Germany).

Results: Whole-exome data from 44 patients with various neuromuscular disorders including primary muscle diseases (n=20), motor neuron disorders (n=20) and peripheral neuropathies (n=4) were analysed. Likely or definite disease-causing variants were found in 20 of the 44 patients, leading to an overall diagnostic yield of 45.5%. This was similar for all analysed subgroups with 50% for primary muscle diseases (10/20) and peripheral neuropathies (2/4) and 40% for disorders affecting the motor neurons (8/20). Among the 20 patients with a genetic diagnosis, 10 had an autosomal recessive, 7 an autosomal dominant, 1 an X-linked and 2 a potential digenic inheritance pattern.

Conclusion: Diagnostic whole-exome sequencing is a useful and cost-effective tool in the clinical management of neuromuscular diseases with a suspected Mendelian aetiology.

Disclosure: Nothing to disclose

EPR3129

Distinct frontal lobe transcriptomes of FTLD and ALS phenotypes

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Background and aims: Fronto-Temporal Lobar Degenerations (FTLD), associated or not with amyotrophic lateral sclerosis (FTLD/ALS), have strong genetic component. Mutations in 3 genes are responsible for most genetic cases: MAPT, PGRN and C9orf72. Genetic or sporadic FTLDs share common neuropathological features such as neuronal TDP43 or TAU inclusions. Thus, independently of the genetic origin and because of the global and significant neurodegeneration, mostly frontal and temporal, it seems highly probable that the different subtypes share some similar molecular mechanisms. On the other hand, either due to the different genetic origin or to the nature of the protein aggregates we can also expect some specific molecular mechanisms to be involved in each disease subtype.
Methods: We analysed frontal cortices of FTLD patients by high-throughput RNA sequencing with a coverage sufficient to analyze transcriptome and splicing profiles. The samples were sorted according to the genetic mutation they carry, to their phenotype and to subtype.
Results: Hierarchical clustering revealed that the mutations in MAPT have a homogenous RNA metabolism response. Interestingly, some transcriptomic and splicing profiles are linked to the pathology (FTLD, FTLD/ALS) or to the subtype (TDP43 or TAU aggregates). Additionally, less than 10% of the changes in RNA maturation lead to modification of RNA expression. Therefore, the newly processed mRNAs could escape from surveillance mechanisms.
Conclusion: Misregulation of pre-mRNA processing could lead to the synthesis of many aberrant proteins in FTLD patients, so these proteinopathies can be due to an accumulation of RNA processing defects. As such, FTLD are not only proteinopathies but also general RNAopathies.
Disclosure: Nothing to disclose

EPR3130

A family-based approach to identify genetic modifiers of the age at onset in Frontotemporal Lobar Dementia

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Background and aims: Frontotemporal-lobar dementia (FTD) is a rare neurodegenerative disease associated with behavioral changes, language dysfunctions and may be associated with amyotrophic lateral sclerosis. The clinical variability, in particular the variability of Age at Onset (AAO) is largely unexplained.
Through family-based approaches, the objective of this work was to quantify the effect of genetic factors influencing the AAO and identify modifier genes in families with FTD due to C9ORF72 hexanucleotide repeat expansions and GRN mutations, two major genes responsible for FTD and/or ALS.
Methods: We studied 504 affected individuals from 133 families with C9ORF72 repeat expansion and 90 FTD families with mutations in GRN. Intra-familial correlations of AAO were analyzed and variance component methods were used for heritability estimates.
Forty-four pairs of relative with highly concordant (<2y) or discordant (>10y) AAO were selected for linkage and association analyses.
Results: The heritability of AAO was high in FTD caused by C9ORF72 repeat expansions, and to a lesser degree in GRN families. Intra-familial correlation analyses revealed significant level of correlations in C9ORF72 families according to the degree of kinship. Pattern of intra-familial correlations also suggested potential X-linked modifiers acting on AAO. Non-significant correlation values were observed in GRN families.
Linkage and association analyses identified 3 new candidate loci with suggestive scores. In particular, an X-linked locus has been highlighted.
Conclusion: Upcoming analyses with additional families will be held to confirm linkage/association signals. The most robust loci will be explored in depth to find causal variants and their functional effects will be tested as well.
Disclosure: Nothing to disclose

EPR3131

Genetic predisposition, modifiable riskfactor burden and the risk of dementia in the general population

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Background: Dementia prevention trials are increasingly recruiting high-risk individuals based on genetic or clinical information, but it remains unclear whether these targeted interventions can offset this increased risk.

Methods: Within the Rotterdam Study, we determined APOE-related risk in 6353 individuals aged ≥65 years for whom allele status and covariate data were available. We also determined adherence to a healthy lifestyle based on six modifiable riskfactors: smoking, depression, diabetes, physical activity, social isolation, and diet. We subsequently stratified individuals on both APOE-related risk and lifestyle categories. Instead of APOE, we also stratified individuals based on the presence of memory complaints.

Results: During a median follow-up of 13.2 years, 867 individuals developed dementia. Dementia risk was higher among individuals in high compared to low APOE-related risk (HR: 3.17, 95% CI: 2.45;4.09). An unfavorable lifestyle, defined as ≤2 protective factors, was associated with higher dementia risk (HR: 1.31, 95% CI: 1.05;1.63). These associations were also found among low and intermediate, but not in high APOE-related risk individuals. These findings correspond to a 15-year dementia risk reduction from 27.8% (95% CI: 5.7;50.0) for an unfavorable to 12.0% (7.9;16.2) for a favorable lifestyle in low, and from 23.8% (15.0;32.6) to 13.9% (12.3;15.6) in intermediate APOE-related risk categories. Riskreductions across lifestyle categories were similar for individuals with and without memory complaints. External validation of these findings in cohort studies is ongoing.

Conclusions: A favorable lifestyle during late-life offsets an increased risk based on memory complaints, but cannot offset high genetic risk based on APOE-carriership.

Disclosure: Nothing to disclose

EPR3132

High diversity of MJD haplotypes in Eastern China: result of an ancient lineage or signature of new mutational origin(s)?

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Background and aims: Machado-Joseph disease is a dominant spinocerebellar ataxia (SCA) caused by a (CAG)n expansion in ATXN3. De novo expansions from the polymorphic normal range seem rare, since only two ancestral MJD origins (Joseph and Machado) had been identified. MJD is spread worldwide, China showing its highest relative frequency (62.1% among SCAs). Our aim was to study MJD origins in families from Eastern China.

Methods: We analysed 69 individuals from 16 MJD families from Shanghai, Zhejiang and Fujian. The Sequenom MassARRAY® system was used to genotype 16 SNPs, within a region of 15 kb encompassing the (CAG)n. More distant flanking STRs were genotyped by capillary electrophoresis. Allelic phases were inferred by familial segregation and PHASEv2.2.

Results: At least two different SNP backgrounds segregated with the MJD expansion in these Chinese families, but none shared the full haplotype with the Joseph lineage, of Asian origin. All families differed in SNPs rs10146519 and rs10467858, when compared to Joseph families. Interestingly, 9 of them showed another variant in rs56268847, the SNP that differentiates the Joseph-derived lineage present in Australian aboriginal MJD families. STR flanking-haplotypes confirmed a closer phylogenetic distance among families of similar SNP lineages.

Conclusion: Two novel SNP backgrounds were identified in MJD families from Eastern China, differing from the Joseph lineage at two or three SNPs. Only one of these SNPs was shown to distinguish the Joseph-derived lineage in other Australasian MJD families, implying either a scenario of rare recurrent SNP mutations on a very ancient lineage, or new mutational origins for MJD.

Disclosure: Nothing to disclose

EPR3133

No evidence for host-pathogen genetic interaction in Neisseria meningitidis causing meningitis

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Background and aims: Neisseria meningitidis is a cause of severe sepsis and meningitis with a mortality of approximately 7%. While certain bacterial subgroups defined by a 7 gene locus typing scheme have been associated with poor disease outcome in patients, no specific genetic variants have emerged as virulence factors. Here we sequenced genetic data from 486 Neisseria meningitidis isolates causing meningitis, performed a genome wide association study on 103 patients with meningococcal meningitis and 4836 controls and analysed 82 paired patients and bacteria to discover new genetic risk factors and performed interaction analyses to search for evidence of epistasis.

Methods: Bacterial genomes were sequenced by whole genome sequencing on Illumina platforms. SNPs were called after mapping to a reference strain. In patients and controls, SNPs were determined with Illumina genotyping array after quality control and imputation.

Results: Bacterial whole genome SNP analyses in isolates reveal a region near phosphoglucosamine gene glmM and the transferrin binding protein gene tbpA/B to be suggestively associated with poor disease outcome, while not reaching statistical significance after correcting for multiple testing. A genome wide association study in patients reveals no genome wide hits for meningococcal meningitis. No evidence for host-pathogen genetic interaction emerges when probing SNPs near the human transferrin gene hTF with amino acid sequence variation in bacterial tbpA for overrepresentation.

Manhattan plot for SNPs in patients associated with meningococcal meningitis
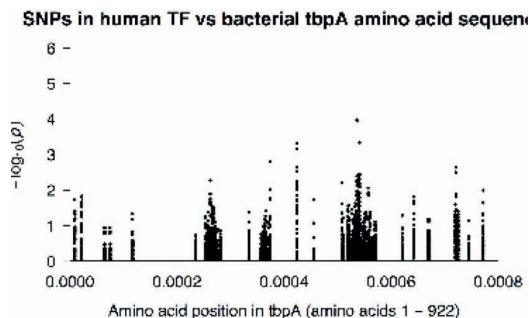
SNPs in human transferrin gene associated with bacterial tbpA

Conclusion: There is no evidence for host-pathogen genetic interaction in patients with meningococcal meningitis and causative Neisseria meningitidis isolates. A limitation of this study is the relatively small sample size; therefore this study might be underpowered to detect variants.

SNPs in meningococci associated with mortality in patients

Neuroimmunology 2

EPR3135

Autoantibodies to KCTD16 mark the presence of a tumor in patients with GABAb receptor encephalitis

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Background and aims: We report detailed clinical features of patients with anti-GABAB receptor (GABABR) encephalitis and optimise laboratory methods for the detection of GABABR antibodies. Also, we identify a novel auto-antibody that indicates the presence of an underlying small cell lung carcinoma (SCLC).
Methods: 2500 patients were tested for the presence of anti-GABABR antibodies using cell based assays (CBA), immunohistochemistry (IHC) and live hippocampal neurons (LN). Clinical data were obtained retrospectively. Antibodies to GABABR-accessory subunit potassium channel tetramerization domain 16 (KCTD16) were identified by immunoprecipitation, mass spectrometry analysis and CBA.
Results: Anti-KCTD16 antibodies were identified in 19/27 patients with anti-GABABR encephalitis and 1/26 patients with SCLC and anti-Hu antibodies. Of anti-GABABR encephalitis patients, 14/15 patients with KCTD16-antibodies had a tumor versus 2/8 anti-GABABR encephalitis patients without (p=0.0017). Patients presented with cognitive and/or behavioral changes (96%) and prominent seizures (93%). Twelve patients developed status epilepticus with ICU admittance (44%). Strikingly, 3/27 patients had rapidly progressive dementia (RPD). An underlying tumor was found in 16/23 patients, most commonly a SCLC (13 cases). IHC and LN were 100% sensitive for GABABR antibodies, while commercial CBA and in house fixed CBA had a lower sensitivity. The addition of KCTD16 to the GABABR-CBA improved sensitivity, without loss of specificity. Low and high titer anti-GABABR antibodies show functional effects on the GABABR in vitro.
Conclusion: GABABR encephalitis is a limbic encephalitis with prominent, severe seizures, but can also present with RPD. The co-occurrence of KCTD16 antibodies points towards a paraneoplastic origin. The addition of KCTD16 improves the sensitivity of the CBA.
Disclosure: Dr. Maarten Titulaer owns a patent for KCTD antibody CBA.

EPR3136

Retrospective study of patients with autoimmune encephalitis at a tertiary center

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Background and aims: Autoimmune encephalitis is an inflammatory disease with a complex differential diagnosis. Although the most frequently recognized causes are infectious, in the last years an increasing number of cases of autoimmune etiology have been identified. We aimed to characterize the patients diagnosed with probable and definitive autoimmune encephalitis in our center according the criteria proposed by Graus et al. (2016) and identify possible differences between the two groups.
Methods: Retrospective review of all cases diagnosed with probable and definitive autoimmune encephalitis at a tertiary center between January 2014 and August 2017. We review the clinical records and used descriptive statistical analysis, chi-square and t-student tests.
Results: We included 20 patients, 65% male, mean age 55 years. Six patients had positive autoantibody against extracellular neuronal antigens and definitive autoimmune encephalitis. The two groups did not differ in age or sex. The CSF study, was normal in 35% of the cases, but most frequently presented mild pleocytosis and increased protein levels. Brain MRI was positive in 27% of patients of the probable diagnosis group and in 83% with positive autoantibodies (p=0.026). All patients received intravenous methylprednisolone, while 4 patients in the negative autoantibodies study group and 5 in the positive autoantibody group received intravenous immunoglobulin (p=0.024).
Conclusion: The results suggest that patients with definitive autoimmune encephalitis had an history of more severe disease, requiring more intense immunotherapy. Brain MRI is more often positive in those patients.
Disclosure: Nothing to disclose

EPR3137

Autoimmune epilepsy in drug resistent and in new onset refractory epilepsy

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Background and aims: Autoimmune epilepsy (AE), is a rare condition, more responsive to immune treatments than to antiepileptic drugs (Graus et al 2016; Bien et al 2005), whose incidence and prevalence and frequency of anti-neuronal autoantibodies (AN-Abs) is unknown.

Methods: Adults with New Onset Refractory Epilepsy (NORE) of unknown etiology showing more than 4 seizures per month and Drug Resistant (DR) focal epilepsy with known (controls) and unknown etiology (DRUE) were recruited between 2014- and 2016. In these patients the diagnostic workup included search for AN-Abs in sera and CSF analysis with AN-Abs when indicated. Follow up was at least one year.

Results: Patients recruited, n=31. 29 gave consensus to the study: 13 DRUE, 9 NOE and 7 controls. 11 patients (6 NORE, 5 DRUE) received diagnosis of AE (6 autoimmune, 2 paraneoplastic, 3 Rasmussen encephalitis), resulting in an incidence of 75% and prevalence of 55%. Sensitivity of AN-Abs was 36,36%, while specifity 94,11%.

Inflammatory MRI abnormalitis1 (p=0.036) and neuropsychiatric symptoms at onset (p=0.00034) and at follow up (p=0.017) were associated with AE, but not infectious prodromes, autoimmune diseases, new onset refractory status epilepticus. DR was similar between groups. Positive AN-Abs or an early immunosoppressive treatment did not result in different long-term outcome.

Conclusion: High incidence and prevalence of AE was observed in this cohort with respect to other studies (Dubey et al, 2017). AN-Abs presence was not mandatory for the diagnosis of NORE or of DRUE, did not exclude other possible diagnosis and was not associate with longterm outcome.

Disclosure: Nothing to disclose

EPR3138

Olfactory and gustatory dysfunction in patients with Autoimmune Encephalitis

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Background and aims: We tested the hypothesis that olfactory (OF) and gustatory function (GF) is disturbed in patients with Autoimmune Encephalitis (AE).

Methods: In 32 AE patients and 32 age and sex matching healthy controls (HC), the orthonasal OF was tested with the standardized Threshold Discrimination Identification test (TDI). The GF was assessed with the Taste Strip Test (TST). Patients with olfactory dysfunction due to an alternative primary etiology were excluded.

Results: 75% of the AE patients were hyposmic and none of the HC (p<0.001). The results of the Threshold subtest, the Discrimination subtest and the Identification subtest were significantly reduced in AE patients compared to HC (all p<0.001). The GF was significantly limited in 26.3% of AE patients and in none of HC (p<0.001). Neither age, sex, disease duration or disability (assessed with the modified ranking scale) were associated with the olfactory or gustatory capacity.

Conclusion: This is the first study investigating olfactory and gustatory function in AE patients. AE patients showed a significantly reduced olfactory and gustatory capacity compared to HC. Further studies that perform imaging of the olfactory pathway are needed to investigate the reasons for olfactory and gustatory dysfunction in these patients.

Disclosure: Nothing to disclose

EPR3139

Serum and CSF neurofilament light chain as possible biomarker in anti-neuropil antibody-associated encephalitis

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Background and aims: A correlation between disease activity and neurofilament light chain (NfL) levels has been recently described in several inflammatory conditions reflecting ongoing axonal damage. High cerebrospinal fluid (CSF) levels of NfL have been observed in the acute stage of autoimmune encephalitis, while significantly lower values were noted after clinical improvement. However, a comparison between serum vs CSF NfL concentrations and the evaluation of these results vs clinical data has never been performed in anti-neuropil antibody-associated encephalitis.

Methods: We enrolled well-characterised subjects with anti-neuropil antibody-mediated encephalitis referred to the Neuropathology Laboratory, University of Verona in the last 5 years. Clinical, radiological, CSF, and follow-up data were collected. Serum and CSF samples obtained at onset were analysed for NfL levels using a high sensitive technology (Simoa, Quanterix) and compared with a group of healthy controls.

Results: 12 patients with anti-neuropil antibody-mediated encephalitis were studied (NMDAR-IgG, n=7, LGI1-IgG, n=3, CASPR2-IgG, n=1, and GABAbR-IgG, n=1). NfL concentration was higher in the CSF (median 509.85pg/ml, range 337.25-4274.04), than in serum. Serum NfL levels were higher in subjects with autoimmune encephalitis (median 9.87 pg/ml, range 4.48-61.41) than in healthy controls (median 6.62pg/ml, range 3.76-11.54) and in patients with LGI1/CASPR2-antibodies (median 1112.185 pg/ml in the CSF, and 23.64pg/ml in serum) compared to those with NMDAR-antibodies (median 400.67pg/ml in the CSF, and 8.92pg/ml in serum).

Conclusion: NfL levels are increased in subjects with anti-neuropil antibody-associated encephalitis, and in particular in cases with LG1/CASPR2-antibodies. Future studies will be useful to determine their prognostic value.

Disclosure: Nothing to disclose

EPR3140

IVIg long-term treatment in CIDP: a non-interventional, prospective study to assess safety, tolerability, fatigue and depression (GAMEDIS-2)

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Background and aims: Chronic inflammatory demyelinating polyneuropathy (CIDP) is a rare progressively disabling, relapsing immune-mediated disorder of the PNS. Though there is broad clinical experience in long-term treatments, real world evidence from systematic prospective studies is sparse. Therefore, an observational study to collect real world data on CIDP patients treated with IVIg (Gamunex® 10%, Grifols) has been designed.

Methods: GAMEDIS-2 is a multicentric, prospective, open-label, non-interventional study conducted on a large cohort of adult CIDP patients treated with Gamunex® 10% in Germany. Functional impairment (Inflammatory Neuropathy Cause and Treatment INCAT disability scale), fatigue (Fatigue Severity Scale, FSS) and depression (Beck Depression Inventory II, BDI) have been systematically documented at baseline and quarterly during an observational period of 96 weeks (8 visits). Safety and tolerability have been assessed. Descriptive statistics of baseline data have been performed. Analyses of efficacy and safety data are in progress.

Results: A total of 158 patients have been recruited in 46 centers throughout Germany (147 evaluable; 66.7% male). The mean age is 64.6±12.4 years (median: 66; range 24-89); 68% older than 60); At enrollment, the mean time since CIDP diagnosis was 5.2±4.7 years; 15% of the patients had no pre-treatment with IVIg, 85.0% received IVIg, 46.3% corticosteroids and 21.8% immunosuppressants. The mean baseline INCAT, FSS and BDI scores were 2.4±1.8, 4.0±1.7 and 8.7±7.7, respectively.

Conclusion: GAMEDIS 2 describes the real world, long-term treatment of a large cohort of CIDP patients with Gamunex 10%. Safety and tolerability findings and longitudinal changes in functioning measured in this real world setting will be reported.

Disclosure: This study was funded by Grifols.

EPR3141

A first phase of seizures characterizes paraneoplastic encephalitis with GABA B receptor autoantibodies.

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Background and aims: To report the clinical features and long term outcome of 22 newly diagnosed paraneoplastic patients with GABAB receptor antibodies (GABABR-Abs).

Methods: Retrospective clinical study of CSF-confirmed cases of GABABR-Abs encephalitis.

Results: We identified 22 patients (4 female) with GABABR-Abs, with a median age of 64 years (range: 55-85). All were paraneoplastic: 20 small-cell lung cancer, one malignant thymoma and one uncharacterised lung mass. The most frequent first symptom was isolated recurrent seizures without cognitive or affective inter-ictal impairment in 17 patients (77%). In the other, 3 presented first behavioral disorders and 2 de novo status epilepticus. After a median delay of 10 days (range: 1-30), the recurrent seizures phase was followed by an encephalitic phase characterized by confusion in 100% of cases and status epilepticus (SE) in 81% (n=17) with 53% (n=9) non-convulsive SE. During the encephalitic phase, dysautonomic episodes were frequent and killed 3 patients. First-line immunotherapy was initiated after a median delay of 26 days (range: 6-65) after disease onset and a partial response was observed in 10 out of 20 patients (50%). No complete response was observed. Two years after onset, a massive anterograde amnesia affected all still alive patients but all of them were able to live autonomously at home. 9 patients died from cancer progression (median survival: 1.2 years).

Conclusion: Paraneoplastic GABABR Abs encephalitis is characterised by a stereotype presentation with an epilepsy phase of a few days in duration without inter-ictal impairment before an encephalitic phase with dysautonomia. The functional prognosis is poor.

Disclosure: Nothing to disclose

Neuro-ophthalmology/ neuro-otology

EPR3143

Ocular motor palsies in the emergency room

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Background and aims: Double vision due to isolated ocular motor nerve palsy represents a common presenting symptom in the emergency room. However, no clear consensus regarding urgency and scope of required diagnostic work-up has emerged. In a majority of cases, no specific etiology is identified and a presumptive diagnosis of diabetic/microvascular ischemic or idiopathic etiology is finally made. Consequently, a recent case series suggested that under certain conditions, imaging may be dispensable in patients older than the age of 50.

Methods: We retrospectively analyzed records of patients presenting in the emergency room of a large tertiary care center with ocular motor nerve palsies as main presenting complaint.

Results: In approximately half of patients, a benign diagnosis of diabetic, idiopathic or microvascular ischemic etiology was made. In the other half of patients, a specific underlying etiology of ocular palsy was identified (e.g., autoimmune etiology, brainstem ischemia, neoplasm). MR imaging displayed pathological results directly related to underlying etiology in approximately 40% of patients with VI and III palsies. In IV palsies, this number was significantly smaller. In VI cranial nerve palsy, a central brainstem pathology represents a relevant differential diagnosis. Frequency of aneurysms was between 3 and 6% and thus less frequent than reported previously.

Conclusion: Cerebral MR imaging in ocular motor palsies seems warranted obligatorily, independent of patient's age. On the other hand, CT scans in the emergency room are probably dispensable in most patients without clinical red flags.

Disclosure: Nothing to disclose

EPR3144

Vertical one-and-a-half syndrome accompanying contralateral abduction and incomplete depression palsy due to thalamo-mesencephalic infarction

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Background and aims: Vertical gaze palsy is usually associated with lesions of the rostral midbrain and thalamo-mesencephalic junction. We describe a case of vertical one-and-a-half syndrome accompanying contralateral abduction and incomplete depression palsy due to thalamo-mesencephalic infarction.

Methods: A 79-year-old man visited to neurology department with sudden onset of dizziness, dysarthria, and diplopia. He was on treatment for hypertension and diabetes for 15 years and was taking aspirin for five years with right cerebellar infarction.

Fig.1.
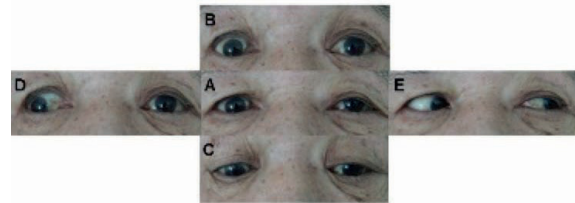
Fig.2.
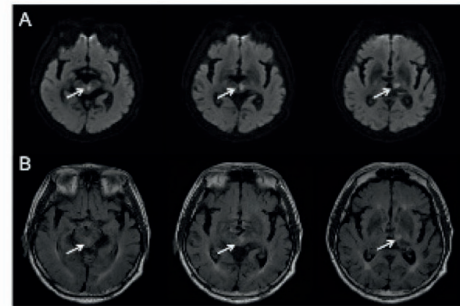
Results: On neurological examination the size of the pupil was 2.5 mm on the right side and 3.5 mm on the left side. There was no strabismus or spontaneous nystagmus at the primary position. Vertical eye movements showed bilateral upward gaze paralysis, left paralysis of the left eye, and incomplete right paralysis of the right eye. The left eye was normal in the horizontal eye movement, but there was an adduction paresis of the left eye and an incomplete abduction of the right eye in the right eye. Horizontal vestibuloocular reflex was normal. Oculocephalic movements in vertical plane were absent. Convergence was absent. Electrocardiogram showed atrial fibrillation. On admission, the diffusion-weighted MRI revealed an infarct in the left thalamomesencephalic junction and the left paramedian midbrain. He was treated with anticoagulant. Three months later, bilateral upper gaze paralysis did not improve but downgaze paralysis partially recovered.

Conclusion: These vertical eye movement abnormalities are presumed to be caused by damage to the ipsilateral riMLF, interstitial nucleus of Cajal, and oculomotor fascicles.

Disclosure: Nothing to disclose

EPR3145

Vestibulo-ocular deficits without otolithic dysfunction in Machado-Joseph disease: a neurophysiologic biomarker of the disease?

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Background and aims: Although ocular motor abnormalities are frequent in all forms of Spinocerebellar ataxias (SCAs), vestibulo-ocular reflex (VOR) deficit seems to be a characteristic of SCA-3 (Machado-Joseph disease - MJD). However, all previous studies were focused on lateral semicircular canals function without information regarding the anterior and posterior canal responses and the otolithic function. We evaluated all canals VOR and otholithic functions in Jew Yemenite patients with SCA-3 in a search for a better neurophysiologic biomarker of the disease.

Methods: 16 MJD patients underwent a detailed clinical and laboratory neuro-otological evaluation including VOR recordings with the video head impulse test (vHIT) system and eight of them cervical vestibular evoked myogenic potentials (cVEMP) by bilateral tone burst stimulation measuring saccular function.

Results: All MJD patients had significant angular VOR gain decrease (about 50% of normal values) in both horizontal and vertical planes. cVEMP responses (latency of P13 and N23) were normal in all eight examined patients. Ataxia severity evaluated by the Scale for the Assessment and Rating of Ataxia (SARA) was mildly correlated with the degree of VOR impairment.

Conclusion: Angular VOR impairment in all semicircular canals seems to be a characteristic of MJD and could be explained by rostral vestibular nuclei degeneration. We suggest that quantitative VOR measures could probably be a neurophysiologic biomarker for detecting the appearance and progression of neurodegeneration in MJD.

Disclosure: Nothing to disclose

EPR3146

VPA induced sensorineural hearing loss; a case report of partial reversible hearing loss in a patient treated with valproic acid (VPA)

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Background and aims: Valproic acid (VPA) is a frequently used anti-epileptic drug (AED) with several common neurological side effects. Ototoxicty is a less frequent but serious side effect

Methods: Case report

Results: A 34-year-old woman with mental retardation and congenital microcephaly of unknown etiology was treated with VPA since several years because of epileptic seizures. Hearing loss was reported after she started using VPA. The audiogram showed mild to moderate sensorineural hearing loss (SNHL). Fletcher index: right ear 45 (H), air 40 bone 35 dB. Left ear 42 (H) air 50 bone 45 dB. After replacing VPA by levetiracetam the hearing loss resolved partially. Fletcher index: right 35 (H) air 35, left: 42 (H) air 43 bone 40. VPA induced reversible sensorineural hearing has been described in 5 patients previously. All these patients had prior hearing loss and therefor this is suggested to be a risk factor for VPA induced SNHL. In our patient hearing was never examined before. The neurotransmitter GABA and sodium channels are suspected to be involved because SNHL is also described in carbamazepine, gabapentin and vigabatrin. VPA is one of the most commonly used AED's but only 5 cases have been described. We assume the actual incidence of VPA induced sensorineural hearing loss may be underreported.
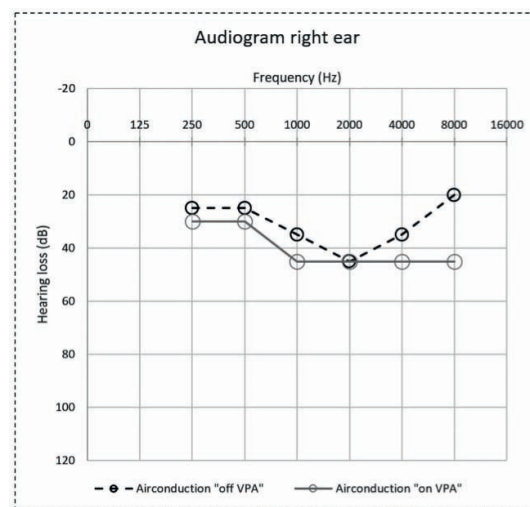
Figure 1: "Audiogram right ear"

Figure 1
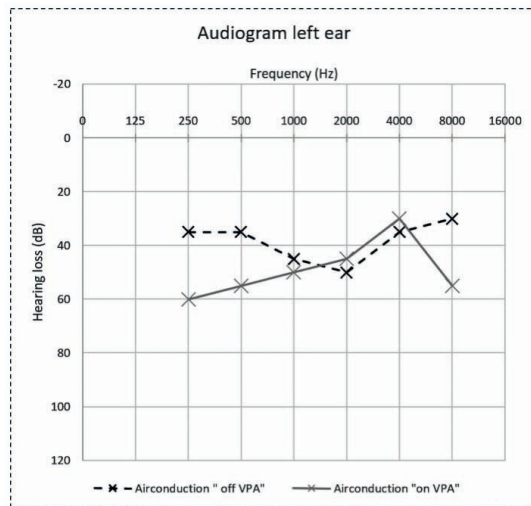
Figure 2: "Audiogram left ear"

Figure 2

Conclusion: It is recommended to ask for the existence of hearing loss before VPA is prescribed as pre-existent hearing loss seems to be an important risk factor. Further research is needed for better understanding of VPA related ototoxicity and to determine the actual incidence.

Disclosure: Nothing to disclose

EPR3147

Suppression of downbeat nystagmus during active motion

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Background and aims: Patients with downbeat nystagmus (DBN) – the most common form of acquired fixation nystagmus – typically suffer from oscillopsia and postural instability. Postural imbalance is reduced during active locomotion; hence, also ocular motor symptoms are likely to improve. We thus investigated the frequency and timing of downbeats nystagmus events during quiet standing compared to walking at different velocities.

Methods: Eye movements of DBN patients were recorded using video-oculography during standing and treadmill walking at slow, preferred and fast speeds. Angular and linear components of the vestibulo-ocular reflex (VOR) were analysed to assess general gaze stabilization performance. The occurrence of DBN events was determined and related to the phase of gait cycles.

Results: Walking significantly lowered the frequency of DBN occurrence in all patients compared to rest, indicating a re-weighting of the involved vestibulo-cerebellar pathways during active motion. This reduction became larger with increasing locomotor speeds and in some subjects the nystagmus was fully suppressed during fast walking. Furthermore, DBN events were phase-coupled to distinct periods of the gait cycle, predominantly occurring at the start of the swing phase. Whereas angular VOR gains of patients were comparable to those of healthy subjects, linear VOR gains were significantly decreased.

Conclusion: These findings suggest that a phase-coupled locomotor feedback (e.g. spinal motor efference copies) influences the brain networks linked to downbeat nystagmus. Deficits in compensating linear head motion during locomotion further point to a specific impairment in pathways processing otolithic inputs.

Disclosure: Nothing to disclose

EPR3148

An Algorithm as a diagnostic tool for ocular motor disorders

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Background and aims: To create an algorithm which can assist physicians as a "digital expert" with the diagnosis, particularly of rare diseases associated with central ocular motor disorders.

Methods: The algorithm's input consists of a maximum of 60 symptoms. The output is a list of the most probable diagnoses out of 14 alternatives and the most likely topographical anatomical localisations out of 8 alternatives. Positive points are given for disease-associated symptoms and negative points for symptoms unlikely to be found in a specific disease. The algorithm was evaluated using the two diagnoses and two brain zones with the highest scores. A dataset of 102 patients (56 males, age 48.0±22yrs) was used for developing the algorithm. After this the algorithm was validated with a dataset of 104 patients (59 males, age 46.0±23yrs).

Results: For 12/14 diseases the algorithm showed a sensitivity between 80 and 100% and the specificity of 9/14 diseases was between 82 and 95%. For instance, it showed 100% sensitivity and 75.5% specificity for Niemann Pick type C and 80% specificity and 91.5% sensitivity for Gaucher's disease, both of which are rare diseases. In terms of a topographic anatomical diagnosis, the sensitivity was between 77 and 100% for 4/8 brain zones, and the specificity of 5/8 zones ranged between 79 and 99%.

Conclusion: This algorithm using our knowledge on the functional anatomy of the central ocular system and possible underlying diseases is a useful tool, in particular for the diagnosis of rare diseases which are otherwise often overlooked.

EPR3149

Slow vertical saccades as a hallmark of hereditary spastic paraplegia type-7

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Background and aims: Hereditary spastic paraplegia (HSP) is a rare autosomal recessive disorder, resulting from homozygous or compound heterozygous mutations in the HSP7 gene (16q24.3), coding the paraplegin protein. Clinically it can present as pure HSP or as complicated phenotype including supranuclear palsy with ophthalmoparesis. However, there is still a paucity of data on the spectrum of oculomotor disorders in HSP7. Thus, this study aimed to investigate oculomotor and vestibular dysfunction in patients with verified mutation of HSP7 gene.

Methods: 4 patients with HSP type-7 were included in this study and investigated using video-oculography and rotational chair testing. 2 patients were siblings harbouring c.1552+1G>T homozygote splice variant. The third patient harboured c.233T>A homozygote mutation and the fourth patient harboured two heterozygous mutations (c.1450_1458del9 and c.1529C>T). We analysed saccadic eye movements, smooth pursuit, the vestibulo-ocular reflex (VOR) and VOR suppression during fixation.

Results: All four patients exhibited slow velocities of vertical saccades. Three patients additionally exhibited slow velocities of horizontal saccades. The fourth patient with compound heterozygote mutation showed borderline slowed horizontal saccades. Both siblings (c.1552+1G>T) exhibited prolonged latencies of horizontal and vertical saccades. Furthermore, the two siblings showed saccadic smooth pursuit movements and impaired VOR-suppression during fixation. In these two patients, the VOR was elicited with regular gain at 0.32Hz, contrasting patients three and four.

Conclusion: Slowing of vertical saccades might be a hallmark of the HSP7. The range of horizontal saccade velocities and cerebellar oculomotor disturbance might be dependent on the mutation type.

Disclosure: Nothing to disclose

EPR3150

Imaging neuroinflammation along the vestibular nerve and nucleus in acute unilateral vestibulopathy by [18F]GE180-PET

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Background and aims: The aetiology of acute unilateral vestibulopathy (AUV) is unknown. Some histological findings suggest that it may originate from inflammation of the peripheral vestibular afferents, e.g. vestibular neuritis. In the present study a novel PET-based approach was used to show neuroinflammation along the vestibular nerve and brainstem entry zone in patients with AUV in vivo.

Methods: 5 patients with an AUV were included in the study. All patients underwent detailed neuro-ophthalmological and vestibular testing to confirm the clinical diagnosis. MRI was done to exclude a central aetiology. Glial activation as a marker of neuroinflammation was visualised by [18F]GE180-PET within the first 8 days after symptom onset.

Results: All patients showed signs of an AUV including spontaneous nystagmus, pathological video-head impulse test and caloric asymmetry towards the affected side, ipsilesional SVV deviation and falling tendency; no ear symptoms. Central ocular motor and vestibular signs were absent. Cranial MRI was unremarkable in all patients. [18F]GE180-PET depicted glial activation in the ipsilesional vestibular nerve and /or vestibular nucleus in 4 patients with typical AUV. During follow-up the one patient without [18F]GE180 uptake developed additional clinical signs indicative for Meniére's disease (i.e. transient tinnitus, acute and recurrent hearing loss), challenging the initial diagnosis of an acute unilateral vestibulopathy.

Conclusion: In the majority of patients with AUV it was possible to visualize in vivo tracer uptake in the ipsilesional vestibular nerve and nucleus during the acute and subacute stage of symptoms by [18F]GE180-PET. This points towards primary or secondary neuroinflammatory processes involved in the pathophysiology of AUV.

Neurorehabilitation 3

EPR3151

32-contacts spinal cord stimulator

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Background and aims: Spinal cord stimulation (SCS) is one of the most advanced interventional treatments available and many thousands of devices are universally implanted each year. We report a SCS case of successful treatment of chronic neuropathic pain following an old spine injury with a new 32-contacts surgical lead neurostimulator.

Methods: A 46-year-old wheel chaired male presented with five years history of neuropathic pain following a car accident with a burst T12 fracture eight years ago. Patient was in a Frankel's grade C and underwent a T9 – L2 stabilization procedure. During last years he developed a severe neuropathic pain not relieving by standard methods. After a detailed discussion, he underwent a successful placement of one 32-electrode (4x8) paddle lead that was caudally positioned at T9 – T11 connected to a Precision Spectra™ generator.
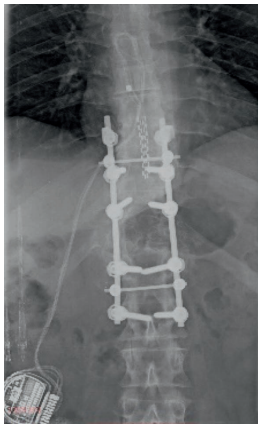
32-contacts paddle lead at T9 - T11 connected to a Precision Spectra generator

Results: After implantation, the neurostimulator was programmed according to desirable programming parameters. During early postoperative period, patient reported greater than 70% improvement of the pain syndrome and was gradually able to decrease oral pain medications. Later, he reported other positive outcomes including the ability to return to some social activities with improved family relationships.

Conclusion: SCS may be a therapeutic alternative for patients with an intractable neuropathic pain that exhausts conservative treatments. New paddles of 8 + 8 + 8 + 8 – poles provide better an complex coverage and are less prone to migration in comparison to percutaneous leads. Surgical experience and proper preoperative planning are useful when technical difficulties and singularities are present.

Disclosure: Nothing to disclose

EPR3152

Stimulation of the frontoparietal network using tDCS in patients with disorders of consciousness: a double blind sham controlled randomised clinical trial

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Background and aims: Patients in disorders of consciousness (DoC) lack of effective treatment options. In the present study we aimed to assess the behavioral effect of bilateral frontoparietal transcranial direct current stimulation (tDCS), targeting the external consciousness network, in severely brain-injured patient with DoC.

Methods: In this double-blind sham controlled randomised cross-over study we included 23 adult patients in vegetative state (VS; n=8) and in minimal conscious state (MCS; n=15), from traumatic and non-traumatic etiologies. Two sessions of tDCS were delivered, using either anodal or sham stimulation in a randomised order. Frontoparietal areas (F3-F4 & CP5-CP6) were stimulated. Level of consciousness was assessed with the Coma Recovery Scale-Revised (CRS-R) before and after each stimulation session.

Results: At the group level, no treatment effect was identified between the active and sham tDCS sessions. When looking at the subgroup of MCS patients from traumatic etiology, we did observe a treatment effect along with a significant increase in CRS-R total scores after the active tDCS session as compared to baseline, while no changes were found for the sham session. Finally, we did not identify any tDCS related side effect.

Conclusion: Our results showed that bilateral frontoparietal tDCS seems to be a safe technique to improve the level of consciousness of MCS patients from traumatic etiology. This non-invasive brain stimulation technique represents a promising tool to improve the recovery of severely brain-injured patients with disorders of consciousness.

Disclosure: Nothing to disclose

EPR3153

Efficacy and feasibility of home-based cooperative hand movement training in chronic stroke patients

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Background and aims: Cooperative hand movements (e.g. opening a bottle) are controlled by a task specific neural coupling mechanism which is partly preserved in chronic stroke subjects. Thus, cooperative hand movement training could be a promising tool for upper limb recovery in stroke rehabilitation. We developed a novel therapeutic device (ARCO) for cooperative hand movements which is supposed to be used not only in a clinical setting but also at the patients' home to increase training accessibility and dose. The study addresses (i) if cooperative hand movement training improves upper limb recovery in chronic stroke patients and (ii) if training with the ARCO is feasible for an unsupervised use at the patients' home.

Methods: Four chronic stroke patients trained with the ARCO for 2 weeks in our facilities followed by 6 week of unsupervised training at their home. Clinical and electrophysiological assessments of the upper limbs were performed before and after the training period. The feasibility of the device as well as the home training was assessed with questionnaires.

Results: After the training period, patients showed functional improvements and an enhancement of the neural coupling. The evaluation of the questionnaires indicated that our device was rated as easy to use, highly motivating and beneficial for health. Furthermore, all patients declared that they would continue the home training.

Conclusion: Due to its benefit in recovery, easy handling, transportability, and motivating design we suggest cooperative hand movement training with the ARCO to be a promising tool for the use at the patients' home.

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EPR3154

Computerised cognitive rehabilitation improves executive functions in benign Multiple Sclerosis patients

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Background and aims: Although benign Multiple Sclerosis (B-MS) patients display preserved somatic neurological functions, they may nevertheless develop cognitive dysfunction. Our aim was to explore the impact of computerized cognitive rehabilitation (CCR) on cognitive functions of B-MS patients.

Methods: Age-gender matched 21 B-MS (EDSS£3.0 at 10 years of disease duration), 22 conventional MS (C-MS, EDSS>3.0 at 10 years) and 38 healthy individuals were recruited. CCR was administered to 10 B-MS patients and a panel of neuropsychological tests were employed to B-MS patients with (n=10) and without (n=11) CCR at baseline and at 6 months. CCR was based on a mental exercise software containing attention, memory, reasoning, visual and verbal task modules. Patients supervised with program's institutional interface every week and were assessed by a psychologist every month.

Results: Both B-MS and C-MS patients showed significantly impaired selective reminding, spatial recall, symbol digit modalities (SDM), controlled oral word association (COWAT) and paced auditory serial addition (PASAT) tests. Stroop, 9-hole peg and timed 25-foot walk test results of B-MS patients were comparable to healthy controls. B-MS patients with CCR showed significantly improved SDM, COWAT and Stroop test results than those without CCR. CCR also had a moderate positive effect on selective reminding and spatial recall tests, albeit without attaining statistical significance.

Conclusion: Several cognitive domains including memory and executive functions are impaired in B-MS patients. CCR has an ameliorating impact particularly on executive functions of B-MS patients.

Disclosure: Nothing to disclose

EPR3155

Mobile accelerometry for assessment of changes in body position in early neurorehabilitation

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Background: Verticalisation and mobilisation in early neurorehabilitation are most important to improve function in severely affected immobile patients, e.g. after stroke, traumatic brain injuries or peripheral neuropathy. However, optimal mobilisation frequencies, both during in-patient and out-patient treatment, are not sufficiently known. Therefore, the aim of the current study was to investigate whether accelerometers on upper trunk can reliably detect changes in body position in immobile patients during early neurorehabilitation.

Methods: 30 patients in early neurorehabilitation (Barthel Index ≤ 30) were enrolled. Two ActivPAL micro™ tri-axial accelerometers were placed on upper trunk and on thigh. Accelerometer data on position changes were compared to care documentation over 24 hours. Frequencies and duration of different body positions (supine, side lying, sitting) were measured. Data are presented as mean±SEM. Groups were compared using one-way ANOVA followed by Kruskal-Wallis-test. Differences were considered significant if $p<0.05$.

Results: Trunk recording (99.5±0.4%) was significantly better able to detect changes in body positions compared to thigh sensors (92±4.7%) or care documentation (81.8±4.4%) ($p<0.0001$). Trunk sensors detected 100% and thigh sensors 66% of position changes.

Conclusions: Mobile accelerometric trunk sensors are suitable to record position changes during neurorehabilitation. Our findings are the prerequisite for the use of mobile accelerometry in severely affected patients after discharge from hospital. Follow-up studies are needed to gain insights into mobilisation frequencies after discharge. This again helps to understand if and how effects of early neurorehabilitation carry over to care after hospital discharge.

Disclosure: Nothing to disclose

EPR3156

Cerebrolysin after stroke leads to spontaneous motor recovery in the absence of reduced stroke volume in a mouse model of stroke

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Background and aims: Most functional upper extremity motor recovery occurs in the first 4 weeks after ischemic stroke both in humans and in rodent models. The majority of recovery in humans is spontaneous (i.e. occurs as a result of endogenous repair processes rather than rehabilitative interventions). However, in rodents models, spontaneous recovery is rare. In a mouse model of stroke, we tested the hypothesis that Cerebrolysin, a polypeptide preparation shown to enhance neuronal plasticity, can act early after stroke to enhance motor recovery, either spontaneous or training-associated recovery.

Methods: Adult mice were trained to perform a skilled prehension task to an asymptotic level of performance after which they underwent photocoagulation-induced stroke in the caudal forelimb area. The mice were then retrained after a 7-day delay in the presence or absence of Cerebrolysin injected IP daily.

Results: We have previously shown that training-associated recovery of prehension is complete if training is initiated after a 1-day delay but incomplete if training is initiated after a 7-day delay, even with additional training days. However, daily Cerebrolysin administration beginning 24 hours after stroke was associated with complete recovery of prehension by day 8 even in the absence of training. Stroke volumes were similar across all groups.

Conclusion: We conclude that Cerebrolysion administration beginning during an early time window can lead to spontaneous recovery of motor function (independent of rehabilitative interventions) and that this recovery is independent of a protective effect on stroke volume. This is the first demonstration of spontaneous motor recovery in a mouse model of stroke.

Disclosure: This research was paid for by a grant from EVER Pharma pharmaceuticals.

EPR3157

Transcranial direct current stimulation in post-stroke aphasia rehabilitation: bilateral vs unilateral online stimulation

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Background and aims: Aphasia is the most common post-stroke cognitive disorder and it severely impacts activities of daily living and social interactions. Transcranial Direct Current Stimulation (tDCS) recently showed good results in post-stroke aphasia rehabilitiation, even if no agreement at now exists about the stimulation parameters to employ to achieve the best rehabilitative outcome. Our aim is to evaluate the efficacy of repeated sessions of tDCS as additional treatment to standard behavioural rehabilitation in post-stroke aphasic patients, comparing bilateral with unilateral left-sided and sham-tDCS.

Methods: We enrolled 22 patients with single left-brain lesion. Aphasia was investigated through selected subitems of Aachener Aphasie Test (AAT), used as outcome measures. Patients were randomly assigned to 3 groups: bilateral-tDCS(7); unilateral-tDCS(8); sham-tDCS(7). Anode was placed on the left inferior frontal gyrus (IFG), while cathode was positioned over contralateral supraorbital area (unilateral-tDCS) or over the right-IFG (bilateral-tDCS). The direct current (1.5mA for 20 min) was delivered online in daily sessions during two consecutive weeks for a total of 10 stimulations.

Results: A repeated measures ANOVA showed as both dual and single-tDCS lead to significant improvements in outcome measures as compared to baseline evaluation and sham-tDCS. A Post Hoc Duncan's test highlighted how the most significant AAT score improvement concerned naming subitem, followed by the others.
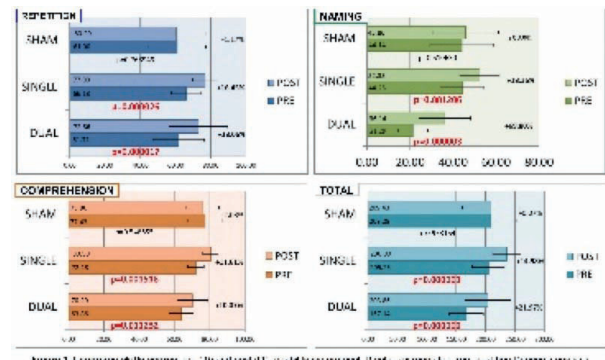
Figure 1. Language skills scores, pre (t0) and post (t1) rehabilitative protocol. P value extrapolated from post hoc Duncan's analysis.

Conclusion: tDCS over IFG showed to be an effective and safe tool to improve aphasia symptoms with no difference between the two montages, so it is worth to be further explored as additional rehabilitative tool for post stroke aphasic patients.

Disclosure: Nothing to disclose

Peripheral nerve disorders 5

EPR3158

Morvan's syndrome: A case report and literature review

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Background and aims: Morvan's syndrome is a rare autoimmune disorder characterised by peripheral nerve hyperexcitability (neuromyotonia), encephalopathy and dysautonomia. We present the case of a 75-year-old male patient who was diagnosed with this condition and made a dramatic improvement following treatment. The clinical presentation, investigation and management of our case alongside a literature review of this rare neurological disorder are discussed.

Methods: A previously well 75-year-old male presented with a six-month history of progressive weakness, unintentional weight loss and muscle twitching. Further questioning demonstrated a disturbed sleep cycle alongside periods of confusion. Neurological examination demonstrated a fluctuating level of consciousness associated with cognitive impairment. Physical examination demonstrated widespread muscle wasting and visible twitching of muscles. Tendon reflexes were preserved and there was no sensory impairment.

Results: Investigations included NCS/EMG which demonstrated evidence of peripheral nerve hyper-excitability. Serum voltage gated potassium channel antibody was positive for both LGI-1 and CASPR2 subtypes. MRI brain demonstrated subtle increased signal intensity and swelling within both limbic systems. A malignancy was excluded following investigation.

The patient was managed with high dose intravenous methylprednisolone over 3 days and made a dramatic improvement with improvement.

Conclusion: Morvan's syndrome is characterised by neuromyotonia, weight loss, hyperhidrosis and sleep disturbance. This rare autoimmune disorder is associated with antibodies to voltage-gated potassium channels which are implicated in the pathophysiology of this condition. There are a limited number of publications in the English literature regarding this disorder. Our case, supplemented by patient video provides a valuable reminder of this rare disorder.

Disclosure: Nothing to disclose

EPR3159

The diagnosis of carpal tunnel syndrome using sonography, sensitivity of this method

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Background and aims: Sonography of carpal tunnel syndrom (CTS) has recently been presented as a diagnostic method comparable with electromyography. The study's aim was to determine normative data and sensitivity of sonography in the diagnosis of CTS.

Methods: We included 40 limbs with CTS confirmed by EMG. Patients were divided into subgroup with mild lesion (MCTS) and severe lesion (SCTS). The threshold between MCTS and SCTS was sensory velocity of 38m/s and distal motor latency of 5.3ms in EMG. Control group included 61 limbs. Sonography of median nerve was conducted at the wrist and elbow and area, circumference, vertical and horizontal diameter were measured. The data of patients were statistically compared with control group and correlated with EMG.

Results: Normative data in sonography: area 12.84mm^2, circumference 16.42mm, vertical diameter 2.95mm, horizontal diameter 7.03mm. At the wrist for all parameters there was statistically significant difference between patients and controls (p<0.002). But no difference between MCTS and SCTS.

However sensitivity of parameters was different in MCTS and SCTS. The most sensitive was area – patients had abnormalities in 50% of MCTS and 73% of SCTS. The dependence of parameters at the wrist with EMG was very strong, the strongest correlation being to sensitive amplitude.

Conclusion: The sensitivity of area is 73% for severe carpal tunnel syndrome, but is much lower for mild carpal tunnel syndrome and result can often be false negative according to our data. The border of normal value for area at wrist is 12.84mm².

Disclosure: Nothing to disclose

EPR3160

A novel LITAF mutation (Charcot-Marie-Tooth type 1C) in a patient with chronic sensory-motor demyelinating neuropathy

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Background and aims: Charcot-Marie-Tooth (CMT) diseases are a heterogeneous group of inherited peripheral neuropathies. Mutations in LITAF gene are causative for CMT type 1C disease, a rare demyelinating CMT form characterized by weakness of distal limbs and panmodal sensory loss, sometimes with upper limbs tremor.

Methods: In this study we present the case of a patient affected by a sensory-motor demyelinating neuropathy resembling a chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) who carried a novel variant in LITAF gene.

Results: A 43-year-old man presented with a 12-year history of paresthesias and weakness of limbs, followed by involuntary tremor both upper limbs. Family history was unremarkable. Previously he had received CIDP diagnosis and treatment with corticosteroids, intravenous Immunoglobulins and plasma-exchange were ineffective. On our admission, neurological examination revealed gait imbalance, upper limbs muscle weakness, postural and kinetic tremor, areflexia, hypopallesthesia, distal pin-prick hypoesthesia in the four limbs. Antibodies against gangliosides, human neurofascin-155 and contactin-1 were absent. Electrophysiological study revealed a sensory-motor demyelinating neuropathy with conduction blocks. Genetic testing for CMT revealed a new mutation in LITAF gene (c.44C>T, p.S15L), located in the exon 2.

Conclusion: Herein we report on a patient with a chronic demyelinating neuropathy, with a clinical picture similar to a neurofascin antibodies-related CIDP, that carried a novel LITAF mutation. The pathogenic role of the LITAF c.44C>T, p.S15L variant is uncertain. Genetic tests to other five asymptomatic family members are ongoing to confirm the pathogenic role of this mutation.

Disclosure: Nothing to disclose

EPR3161

Glyphosate-based herbicide, but not pure glyphosate, affects peripheral nervous system myelination

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Background and aims: Glyphosate-based formulations comprise the world's most commonly used herbicides. While glyphosate is the active ingredient, it is often provided as isopropylamine salt and in combination with undisclosed auxiliary agents. Although glyphosate has long been considered safe for use in humans and animals, several studies have implicated glyphosate and/or auxiliary agents and surfactants in cytotoxicity, carcinogenicity and endocrine disruption. However, it remains unclear whether pure glyphosate or glyphosate-based formulations may have detrimental effects on myelin integrity in the peripheral nervous system.

Methods: We assessed the impact of pure glyphosate and a glyphosate-based herbicide (Roundup LB Plus, Monsanto) on myelination and demyelination in an ex vivo model of the peripheral nervous system. Dorsal root ganglia (DRG) cultures were treated with pure glyphosate or Roundup corresponding to 0.005 or 0.0005% glyphosate content in the culture medium. The glyphosate concentration in the Roundup formulation was 36% as isopropylamine salt. Controls were treated with equal volumes of vehicle adjusted for pH.

Results: Whereas pure glyphosate did neither affect myelination nor cause demyelination, Roundup exerted a concentration-dependent demyelinating effect. While there were no specific effects of Roundup on markers for oxidative and nitrosative stress or cell death, we recognized Roundup to cause the induction of TNF-alpha expression in Schwann cells. In line with its demyelinating effect, TNF-alpha expression appeared to depend on the concentration of Roundup.

Conclusion: These findings raise the possibility that not glyphosate itself, but isopropylamine or undisclosed additives in herbicide formulations may impact myelin integrity via a mechanism involving inflammatory Schwann cell activation.

Disclosure: Nothing to disclose

EPR3162

Post-occlusive Reactive Hyperemia in Diabetic Polyneuropathy

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Background and aims: Diabetes mellitus (DM) is hugely increasing worldwide, type 2 diabetes (T2DM) is prevalent among diabetics, and the most common complication is diabetic polyneuropathy (DPN) associated with microcirculatory disorders. The aim of the study was to investigate microcirculatory alterations and post-occlusive reactive hyperemia responses in patients with T2DM and polyneuropathy.

Methods: 79 patients with T2DM fulfilled the criteria for DPN and were included in the study with 44 sex and age matched healthy controls. The nutritious skin vessels were investigated by nailfold videocapillaroscopy. The skin perfusions of the big tiptoe were monitored by laser Doppler flowmetry (LDF) in arbitrary perfusion units (PU) as initial values (PUi) in supine position, during and after toe arterial occlusion by inflation of a blood pressure cuff. Vasodilator indices were calculated and assessed by SPSS software package.

Results: Reduced capillary density and spastic capillaries were found in most of the patients (89.87%) while the initial LDF perfusions (67.23±50.37 PU vs 39.29±25.31 PU) were higher compared with the controls (p<0.001). The postocclusive reactive hyperemic peak (102.54±62.7 PU vs 170.1±153.8 PU) was lower in T2DM patients (p<0.05). The post-occlusive hyperemic perfusion responses and vasodilator indices differed significantly between DM patients and healthy controls.

Conclusion: Decreased number and spasm of dermal capillaries but increased global skin blood flow at rest were established. The microvascular post-occlusive vasodilator capacity and reactive hyperemic indices were significantly reduced. Laser-Doppler flowmetry is an easy non-invasive method for investigation of skin microcirculation and vasomotor reactivity.

Disclosure: Nothing to disclose

EPR3163

Inotersen improved Norfolk quality of life–diabetic neuropathy (Norfolk QOL-DN) measures in patients with hereditary transthyretin (hATTR) amyloidosis treated in the phase-3 study NEURO-TTR

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Background and aims: hATTR is a rare, progressive, fatal disease caused by systemic build-up of transthyretin (TTR) protein, which causes significant morbidity and progressive decline in quality of life (QOL). The effects of inotersen, an antisense oligonucleotide inhibitor of TTR protein production, on QOL in patients with hATTR are described.

Methods: NEURO-TTR (NCT01737398) is a global, randomised, double-blind, placebo-controlled phase-3 study. Adults (n=172) with hATTR (stage 1 or 2) were randomized (2:1) and received 300-mg weekly subcutaneous inotersen or placebo for 15 months. QOL was evaluated using the Norfolk QOL-DN questionnaire and the SF-36v2 Health Survey (SF-36v2). Norfolk QOL-DN includes 136 points (higher score indicates worse QOL) derived from 5 domains (physical functioning/large-fibre neuropathy, symptoms, activities of daily living [ADL], small-fibre neuropathy and autonomic neuropathy).

Results: Statistically significant improvement in least-squares mean change from baseline [95% CI] in Norfolk

QOL-DN total score favouring inotersen-treated subjects compared with placebo was observed at week 35 (–6.14 [–11.77 to –0.52]; P=0.032). At week 66, significant improvement in favour of inotersen compared with placebo was observed in Norfolk QOL-DN total score (–11.68 [–18.29 to –5.06]; P=0.0006), physical functioning/large-fibre neuropathy (–6.33 [–10.03 to –2.62]; P=0.001), ADLs (–2.10 [–3.34 to –0.85]; P=0.001), and symptoms (–2.80 [–4.47 to –1.13]; P=0.001), as well as SF-36v2 Physical Component Summary score. Key safety findings of thrombocytopenia and renal events were monitorable and manageable.

Conclusion: Inotersen-treated patients demonstrated rapid, significant and sustained improvement in QOL measures compared with placebo-treated patients.

Disclosure: This study was sponsored by Ionis Pharmaceuticals (Carlsbad, CA, USA).

EPR3164

Chemotherapy-induced polyneuropathy in patients treated with vinca-alcaloids

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Background and aims: Chemotherapy-induced peripheral neuropathy (CIPN) represents one of the most worrisome and common long-term adverse effects of chemotherapy treatment of cancer. In patients treated with vinca-alcaloids (V-A), the clinical manifestation is mainly sensory and may affect predominantly small sensory fibers. The aim was to assess the incidence of CIPN in patients treated with V-A and compare diagnostic validity of quantitative sensory testing (QST) reflecting the function of both small and large sensory nerve fibers with routinely used electromyography/ nerve conduction studies (EMG/NCS).

Methods: A group of 20 patients (12 men, 8 women, median age 39; range 23-72 years) with malignant lymphoma underwent detailed clinical examination, evaluation of medical history, pain status, EMG/NCS and comprehensive QST before and 6 months after the end of administration of anti-cancer V-A chemotherapy.

Results: At the follow-up examination, twelve patients (60%) reported some sensory symptoms and/or neuropathic pain in lower (11 cases) and/or upper (7 cases) extremities. The symptoms were usually of mild to moderate intensity. In upper extremities, the symptoms mostly corresponded with clinically symptomatic carpal tunnel syndrome. The EMG/NCS examination confirmed polyneuropathy in 10 patients (50%) (7 symptomatic, 3 asymptomatic). Eighteen patients (90%) displayed at least one new QST abnormity in feet (and 8 in hands), most frequently in thermal sensation and thermal pain modalities.

Conclusion: Symptoms of CIPN persist at least 6 month after the end of V-A chemotherapy in about 60% of treated patients, and relevant QST abnormities (mainly suggesting small nerve fiber dysfunction) can be found even in 90% of the treated patients.

Disclosure: Nothing to disclose

Sleep disorders

EPR3165

Timing and patterns of nocturnal melatonin secretion in Alzheimer patients at an early stage of the disease.

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Background and aims: Circadian dysfunction plays a crucial role in the intricate, biunivocal relationship between Alzheimer's disease (AD) and disordered sleep. Our study focused on melatonin secretion timing with calculation of dim light melatonin onset (DLMO) as a biological marker of the circadian phase in patients with mild to moderate forms of AD.

Methods: 21 patients with a diagnosis of AD according to McKhann criteria (2011) were consecutively enrolled. 22 healthy subjects comparable for age and sex served as controls. Nocturnal sleep parameters, subjective measures of chronotype and the social jet lag (SJL) were determined. DLMO and quantitative aspects of the initial nocturnal melatonin secretion were calculated by means of a five-point melatonin salivary test.

Results: Subjective sleep quality did not differ between groups. Sleep onset on workdays and freedays ad midsleep on freedays used to occur earlier in patients. The subjective chronotype distribution by global MEQ score did not differ between groups. The mean DLMO time in AD patients occurred significantly later respect to controls (p=0.028). The post-DLMO melatonin measures were significantly lower in AD patients. This result was confirmed by evaluating the single and global melatonine AUC semicurve between groups (p=0.003).

Conclusion: AD patients present a delay and impairment of melatonin secretion, despite sleep parameters and subjective chronotype similar to those of healthy controls. This data indicate that, subclinical, peculiar patterns of melatonin secretion exist in subjects with AD at an early stage of the disease.

Disclosure: Nothing to disclose

EPR3166

REM-Sleep Behavior Disorder (RBD) in Anti-IgLON-5 disease

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Background and aims: To evaluate the presence of RBD and its characteristics in 5 cases with IgLON5 disease. Anti-IgLON-5 disease is associated with IgG4 antibodies to IgLON5, a neuronal surface cell adhesion molecule, and deposits of tau in the brainstem and hypothalamus. It is characterised by a parasomnia involving NREM and REM-sleep. Obstructive sleep apnea syndrome (OSA) with stridor is often observed. Other symptoms involve gait- instability, bulbar, oculomotor and autonomic symptoms, and cognitive impairment.

Methods: 5 patients (4 male, age 62.6±11.65) underwent video-polysomnography. REM sleep without atonia (RWA) was defined according to SINBAR criteria. RBD was diagnosed when RWA combined with abnormal movements during REM sleep occured. To rate the severity of RBD the RBD Severity Scale was used.

Results: 2 were diagnosed with bulbar syndrome, 2 with PSP-like-syndrome and 1 with sleep-disorder. Anti-IgLON5 antibodies were positive in 5/5. Sleep related breathing disorders were present in all patients (2/5 OSA), OSA+hypoventilation 2/5, 1/5 tracheostomy). REM sleep without atonia was present 5/5. REM sleep behavior severity range was 1.0 to 2.1. Complex behaviors during NREM sleep were observed in 2/5.

Conclusion: All patients showed RBD. RBD seems to be "mild" in Anti- IgLON5 disease. In these case series, Non REM behaviors were not present in patients with the PSP like syndrome. If this is a characteristic of a typical subtype of IgLON5 disease has to be determined in the future. The combination sleep disorder with REM and NREM abnormalities accompanied by of multifocal neurological symptoms Anti-IgLON5 disease should be considered.

Disclosure: Nothing to disclose

EPR3167

Movement disorders during sleep in children with Narcolepsy type-1 after treatment with sodium oxybate

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Background and aims: Recently, the occurrence of a severe and peculiar motor disorder occurring mainly during REM sleep in pediatric NT1 has been pointed out (Antelmi et al, 2017). Here, we aimed at assessing the effect of stable treatment with Sodium Oxybate (SO) on motor events occurring during nighttime in children with NT1.

Methods: 15 children with NT1 (40% females; mean age 12.8±2.86) were followed up after the at least three months of stable treatment with SO. All patients repeated video-PSG and the recordings were then reviewed by two independent experts in the field in order to analyse motor events. These latter were classified as previously reported (Antelmi et al, 2017) in elementary movements and complex behaviors. Baseline and follow-up data were confronted (within-subjects).

Results: When compared to baseline evaluation, NT1 patients taking SO showed a significant decrease of the pentad of NT1 symptoms, but for sleep paralyses. When analyzing motor patter during nighttime, it emerged that elementary movements emerging from NREM sleep were significantly increased after the start of treatment. Conversely, complex behaviors could be detected in a decreased number of patients and showed also a decrease in frequency. There was a concomitant increase of atonia index.

Conclusion: Motor events/behaviors emerging during REM sleep decreased after treatment with SO. The concordant increase in REM atonia index leads to infer on a direct role of the drug in modulating motor control during REM sleep.

Disclosure: Nothing to disclose

EPR3168

Different response to CPAP in man and women with chronic insomnia disorder and OSAS

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Background and aims: Obstructive Sleep Apnea Syndrome (OSAS) and insomnia are pathologies that frequently co-occur. Few studies have documented that CPAP (continuous positive airway pressure) may improve insomnia symptoms.
The objective of this study was to evaluate the response to CPAP in patients with chronic insomnia disorder (CID) with OSAS.

Methods: Retrospective study of patients with OSAS and CID, from an outpatient sleep clinic. OSAS and CID were diagnosed according ICSD-3. OSAS was considered mild/moderate if Respiratory Disturb Index (RDI) was 5-30 and severe if RDI ≥30. The main outcome was insomnia clinical improvement following CPAP. Other variables were gender, sex, PSG variables, CPAP compliance, insomnia subtypes, OSAS type, anxiety/depressive disorder and use of sedative pharmacological. Differences between responder and non-responders were evaluated with T test, Qui2 or Fischer test, p<0.05.

Results: From a database of 827 patient, 90 were identified with OSAS and CID (53.3% women). Middle/moderate OSAS was diagnosed in 68.9% and severe in 31.1%. Most patients (61.1%) improved insomnia after CPAP. Responders to CPAP were more frequently women (women 61.8%, men 38.2%, p=0.035), and there was no other difference between responders and non-responders. On subgroup analysis, this difference was significant only in severe OSAS (p=0.013).

Conclusion: Our study re-inforces that CPAP therapy improves CID, irrespective of insomnia type, across all OSA categories and in patients with psychiatric symptoms. This response is more frequent in women. Our results suggest that in men with severe OSA, the insomnia phenotype is less dependent on the respiratory symptoms and further studies are needed to understand this.

Disclosure: Nothing to disclose

EPR3169

Orexin and beta-amyloid pathologies in Obstructive Sleep Apnea Syndrome

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Background and aims: Obstructive Sleep Apnea Syndrome (OSAS) is an increasingly frequent sleep disorder. OSAS pathologically changes cerebral beta-amyloid dynamics and orexin may interfere with beta-amyloid metabolism.
On these bases, the aim of this study was to investigate beta-amyloid and orexin CSF levels in OSAS patients.
Methods: We evaluated OSAS patients compared to patients affected by Alzheimer's Disease (AD) and controls. All patients and controls underwent: lumbar puncture for CSF levels of beta-amyloid 40 (AB40) and 42 (AB42) and orexin; polysomnography (PG) to evaluate nocturnal sleep architecture.
Results: We include 20 OSAS patients, 10 AD patients, and 10 controls. We documented higher orexin levels in OSAS patients compared to AD and controls; moreover, AD patients showed higher orexin levels than controls. Considering beta-amyloid, OSAS showed lower AB40 levels compared to AD and controls, whereas AD patients showed lower AB42 levels than OSAS, who showed lower AB42 levels than controls.
Sleep macrostructure was similarly altered in OSAS and AD patients compared to controls. Finally, CSF beta-amyloid proteins levels correlated with PSG parameters in the OSAS group, while CSF orexin levels correlated with CSF beta-amyloid levels in the AD group.
Conclusion: This study documented the alteration of orexinergic system and beta-amyloid metabolism in OSAS patients. Sleep fragmentation and apneas correlated with CSF orexin and beta-amyloid levels in OSAS patients. Conversely, orexin CSF levels correlated with beta-amyloid CSF levels in AD patients. Hence, we suppose that orexinergic system impairment, sleep impairment, and beta-amyloid pathology may be present in OSAS patients as a possible preclinical stage of AD neurodegeneration.
Disclosure: Nothing to disclose

EPR3170

Diagnostic accuracy and validity of the swiss Narcolepsy Scale and a short-form version for the diagnosis of type-1 and type-2 narcolepsy against other central disorders of hypersomnolence

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Background and aims: The Swiss Narcolepsy Scale (SNS) was previously reported in two independent studies to have a sensitivity-specificity of about 80-90% for the diagnosis of narcolepsy with cataplexy. We aim 1) to assess the validity of the SNS and the Epworth sleepiness scale (ESS) in detecting type 1 (NT-1) and type 2 (NT-2) narcolepsy against other central disorders of hypersomnolence (CDH), 2) to develop a simplified form of the SNS.
Methods: Data from the Bern Sleep-Wake Registry were used. A two-item simplified form (sf-SNS) was created from the SNS based on the discriminative capability of the models.
Results: There were 299 individuals with CDH who completed the SNS scale, including 69 with NT-1, 16 with NT-2 and 214 with other CDH. For the diagnosis of NT-1 the sensitivity and the specificity of the SNS was 86% and 88%. The Hosmer-Lemeshow goodness of fit test indicates sufficient calibration (p=0.700) but the Brier score was relatively high (0.87), indicating relatively high disagreement. Therefore, we recalculated the model coefficients for scoring SNS and improved sensitivity (93%), but reduced specificity to 82%.
The sensitivity and specificity of the sf-SNS in identifying NT-1 were 80% and 92% respectively. For the diagnosis of NT-2 the following sensitivities and specificities were found: SNS 63% and 70%, sf-SNS 44% and 83%. For the diagnosis of narcolepsy the sensitivity and specificity of ESS was 53% and 70% respectively.
Conclusion: The updated SNS and its simplified form sf-SNS are useful and valid screening tools for NT-1 and superior to the ESS.
Disclosure: This work was financially supported by Jazz Pharmaceuticals

EPR3172

Sleep pattern and day time sleepiness in patients with mild cognitive impairment and mild Alzheimer's dementia

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Background and aims: Previous studies suggest that patients with advanced Alzheimer's dementia (AD) suffer from sleep disorders more frequently, however results are less conclusive for patients with mild cognitive impairment (MCI) and mild AD. Aim of our study was to evaluate sleep pattern and excessive daytime sleepiness in patients with mild AD dementia.

Methods: 61 healthy controls, 41 MCI and 44 mild AD patients were included. Cognitive status of patients was evaluated with Mini-Mental State Examination (MMSE). Excessive daytime sleepiness and sleep pattern were evaluated with Epworth scale and Insomnia Severity Index (ISI). Means between groups were compared with 1-way ANOVA. At the end, we correlated Epworth, ISI and MMSE scores.

Results: All three groups were age matched. MCI patients had significant higher MMSE score than AD patients (27 ± 3 vs. 22 ± 3; $p<0.001$). Mean Epworth Scale score did not differ between groups (healthy controls 5.9 ± 4.6; MCI 5.9 ± 4.3; mild AD 6.1 ± 4.9). Insomnia Severity Index was the highest in healthy controls (8.1 ± 6.0), followed by MCI (7.1 ± 5.4) and mild AD (6.2 ± 6.3), however differences were not statistically significant. There were no correlation between MMSE and Epworth or ISI score.

Conclusion: Our results indicate that patients with MCI and mild AD had similar excessive daytime sleepiness and sleep pattern as age-matched controls. No group have reached threshold for excessive daytime sleepiness and clinical significant insomnia. Disturbed sleep pattern may be a clinical sign of progression of AD as part of complex behavioral changes in addition to memory impairment.

Disclosure: Nothing to disclose

EPR3173

Narcolepsy-cataplexy and Sydenham's chorea

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Background and aims: Sydenham's chorea (SC) results from a post-streptococcal autoimmune process targeting basal ganglia neurons. In narcolepsy type-1 (NT1) streptococcal infection as potential trigger of the disorder was reported and clinical features in children include SC-like features (hypotonia, dyskinesias). The association SC-NT1 was reported only once in the literature (Natarjan, JCSM 2013).

Aim: To analyse the association between NT1 and SC in 3 tertiary sleep centers.

Methods: Retrospective international study in 3 large tertiary sleep centers.

Results: We report 3 patients with NT1 and SC.

Patient 1 (female, 22y, HLA DQB1*0602+) had an acute hemichorea followed within weeks by excessive daytime sleepiness (EDS), low CSF hypocretin (125pg/mL), and no SOREM with a mean sleep latency (MSL) of 2.8min on MSLT. EDS severely increased within 3 month accompanied by a further decrease of hypocretin (24pg/ml), MSL of 1.4min and 3 SOREM at subsequent MSLT.

Patient 2 (female, 10y, HLA DR15+) had acute hypotonia and dyskinetic movements followed within few weeks by EDS, typical cataplexy, disturbed nocturnal sleep, and 3 SOREM with a MSL of 3.5min on MSLT.

Patient 3 (female, 11y) had acute chorea followed within months by EDS, typical, cataplexy, undetectable CSF hypocretin and a mean latency of 1min on MSLT (without SOREM).

Conclusion: Further studies are needed to clarify the clinical and etio-pathophysiological implications of the reported rare association.

Disclosure: Nothing to disclose

Poster on Display

POD001

Adult-onset neuronal intranuclear inclusion disease – Clinical analysis of 14 patients

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POD002

Follow-me: a system designed for patients with neurocognitive impairment

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POD003

Sporadic Creutzfeldt-Jakob disease in the region of Cartagena: a case series

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POD006

Eating behavior changed in the severity of dementia, and eating disturbance may contribute to the early admission into the facility through the observational study for two years

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POD007

Frontotemporal lobar degeneration with argyrophilic grains: a clinicopathological report

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POD009

The Nonverbal CogScreen as a screening tool for limited language dementia patients

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POD010

Early onset degenerative dementias: etiological classification and demographic characteristics in Serbian tertiary referral center

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POD011

Changes in antipsychotic treatment at time of dementia diagnosis

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POD012

Computer-based personal training effects on mild cognitive impairment. Does APOE genotype influence outcome? A two-year follow-up study

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POD013

Case report: familial prion disease as an underdiagnosed cause of rapidly progressive dementia

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POD014

Depression is not associated with amyloid positivity but contributes to cognitive decline in amyloid negative individuals

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POD015

Does social activity and continuing education decelerate cognitive decline with normal ageing

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POD016

Caregiver burden for informal caregivers of patients referring to the Memory Clinic of Bozen

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POD017

Initiation of a culturally oriented screening test for major neuro-cognitive disorder (MNCD)

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POD018

Employees in homecare services' professional conduct related to persons with dementia who use dietary supplements: results from a Norwegian survey

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POD019

Specific cognitive complaints can differentiate between patients with mild cognitive impairment and subjective cognitive decline: data from the Czech Brain Aging Study

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POD020

Polysomnography, brain volumetry and mismatch negativity as early biomarkers of amnestic mild cognitive impairment progression

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POD021

Visuospatial ability and visual memory - differences between multi-infarct dementia and small vessel disease dementia

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POD022

The effects of moderate level aerobic exercise on caregivers of patients with Alzhiermer's disease: a randomized controlled study

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POD024

Neuropsychiatric symptoms in variants of Primary Progressive Aphasia (PPA)

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POD026

Two brothers with dementia with fronto-temporal phenotype

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POD027

Globular glial tauopathy, frontotemporal and limbic TDP-43 proteinopathy - a rare comorbidity clinically presenting as primary progressive aphasia with parkinsonism

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POD028

Effects of post-training transcranial alternating current stimulation on motor consolidation

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POD029

SQSTM1 mutations associated with Lewy body dementia

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POD031

The biopsychosocial assessment method: a novel instrument for comprehensive geriatric assessment

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POD033

TMS evaluation in cognitive impaired patients according to new criteria for AD: a 36-month follow-up study

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POD034

MRI can predict development of POTS and OH in multiple sclerosis

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POD035

Retrospective review of patients with multiple admissions to the comprehensive stroke centre

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POD036

Adult moyamoya disease associated with abundant phosphorylated tau accumulation in the brainstem

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POD037

Prehospital acute stroke treatment by critical care physicians in a mobile stroke unit

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POD038

The clinical features of ischemic stroke patients for whom smoking was considered the sole risk factor for ischemic stroke

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POD039

A systematic review and meta-analysis of randomised controlled trials of electro-acupuncture in the treatment of stroke patients

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POD040

Venous thromboembolism following acute ischemic stroke: a prospective study in Korea

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POD043

withdrawn

POD044

Global world, local epidemics: the case of intra-cerebral haemorrhagic strokes

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POD045

Life events as potential triggers of stroke

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POD046

A case of watershed infarction with hypereosinophilia in ANCA-associated vasculitis

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POD047

PCSK9 gene polymorphism is associated with LDL-C level in young Chinese patients with ischemic stroke

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POD048

Rare presentation of spontaneous carotid artery dissection

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POD049

Pre-hospital CT angiography in acute stroke management

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POD050

Comparison of thrombophilic mutations (factor V Leiden, PAI- 4G/5G) among young patients experiencing stroke

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POD051

Comparison of the number of circulating CD34 + stem cells in patients on the first day of ischemic stroke and in the control group of patients without vascular disease

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POD052

Posterior Reversible Encephalopathy Syndrome (PRES) associated with acute pancreatitis. Case report and literature review.

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POD053

Capsular warning syndrome: do fluctuations go with the flow?

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POD054

Safety and efficacy of mechanical thrombectomy with stent-retrievers in anticoagulated patients with anterior circulation stroke

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POD055

SUSAC Syndrome- not always recognizabale, diagnognostic difficulties

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POD059

Spontaneous recurrent chronic subdural hematoma secondary to arachnoid cyst

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POD060

Risk factors for potential warfarin drug-drug interactions in stroke patients

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POD061

Diagnostic challenges, risk factors and outcomes in the patients with cerebral venous sinus thrombosis in Moldovan tertiary neurological center

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POD063

Fulminant giant cell arteritis with multiple cerebral and myocardial infarction

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POD064

Mortality and predictors of death in-hospital and 1-year post stroke: data from a multicenter cohort of Lebanese stroke patients

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POD065

Contralateral stent assisted thrombectomy via fenestrated anterior communicating artery in tandem middle cerebral artery occlusion: a case report

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POD066

Carotid artery dissection after road cycling

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POD067

Genetic predisposition to thrombosis in patients with hypertension

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POD068

Malnutrition rate in stroke patients on admission

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POD069

Cervical artery dissection: a case series study

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POD070

Assessment of relationship between serum NT-proBNP levels with clinical features and prognosis in acute ischemic stroke patients

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POD071

Could Trigliceride/HDL ratio be a good predictor of ischemic cerebrovascular accident risk in young people?

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POD072

Cerebral air embolism after cardiac ablation procedure

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POD073

An assessment of pneumonia frequency and risk factors in acute stroke

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POD074

Use of cerebrolysin after rt-PA: a single-center cohort analysis of 3-month results

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POD075

Occult malignancy to cause embolic stroke in a young patient – How often can it be?

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POD076

Prospective investigation of etiological and clinical features of patients with posterior circulation infarction

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POD078

Negative impact diabetes mellitus on the outcome of stroke

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POD079

Neurological peculiarities of the course of cerebrovascular disorders in patients after cardiac surgery

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POD080

withdrawn

POD081

Safety of intra-arterial tirofiban during endovascular treatment after intravenous tissue plasminogen activator in patients with acute ischemic stroke

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POD082

Case report: association of internal carotid agenesis and polydactyly

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POD083

Posterior reversible encephalopathy syndrome and familial amyloid polyneuropathy: where do they meet?

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POD084

Outcomes and blood rheology in acute ischemic stroke

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POD085

Understanding subarachnoid haemorrhage - atypical modes of onset and imaging features

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POD086

The efficiency of intravenous tissue type plasminogen activator administration in acute ischemic stroke patients without visualised arterial occlusion

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POD088

The impact of intracerebral haemorrhage specific intensity of care on the 30-day mortality associated with spontaneous intracerebral haemorrhage in Algarve region, Portugal

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POD089

Recombinant tissue plasminogen activator therapy for acute ischemic stroke of older patients

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POD090

Mechanical thrombectomy in the neoplastic patients with acute ischemic stroke – case series

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POD091

To stent or not to stent? - Experiences in endovascular treatment of acute tandem occlusions of internal carotid artery and middle cerebral artery

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POD092

Takotsubo cardiomyopathy in the context of spontaneous vertebral artery dissection stroke - case report

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POD093

Serious falls after spontaneous intracerebral haemorrhage in Algarve region, Portugal

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POD096

Long-term external ECG monitorisation applicability in cerebrovascular disease

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POD098

The clinical characteristics of acute cerebrovascular accidents resulting from ovarian hyperstimulation syndrome

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POD099

Lambl's excrescences associated with cerebral infarction and Transient ischemic attack

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POD100

Code stroke and acute treatment in our hospital. Does the previous stop at an external center influence the outcomes of patients?

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POD101

withdrawn

POD102

Differences in serum uric acid concentration between deep cerebral haemorrhages and amyloid angiopathy related cerebral haemorrhages

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POD103

withdrawn

POD104

withdrawn

POD106

Prevalence of risk factors in stroke patients: a two-year hospital-based study

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POD108

Carotid "Web-like" stenosis as a complication of endarterectomy

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POD113

The neurocognitive development of premature infants at 14 months of age

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POD114

Deficit in attention and abilities for programming in children with hypoxic-ischaemic encephalopathy

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Chronic pancerebellar syndrome presenting as Tuberous Sclerosis

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Clinical and electrophysiological investigation of spasticity in patients with disorders of consciousness

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Brainstem Evoked Potentials (BEP) z-score is a predictor of disability progression in people with clinically isolated syndrome

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Prognostic value of phrenic nerve conduction study in amyotrophic lateral sclerosis: a systematic review and meta-analysis

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Concussion: changes of Brainstem Auditory Evoked Potentials (BAEP) as diagnostic and prognostic neurophysiological markers of the pathological process

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Median nerve somatosensory evoked potentials predict hand function in people with clinically isolated syndrome

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Serum vitamin D levels do not affect neurophysiological results of people with relapsing-remitting multiple sclerosis

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Impact of individualised I-Wave periodicity TMS on cortical excitability

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EEG features accompanying Intermittent Rhythmic Delta Activity (IRDA)

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The sudomotor skin response in the acute phase after stroke

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Posterior reversible encephalopathy syndrome as the initial manifestation of acute axonal Guillain-Barré syndrome

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Neurophysiological criteria of disadaptive neuroplasticity in patients with recurrent low back pain acording to the somatosensory evoked potentials data

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The role of cutaneous silent period assessing the small nerve fibres at patients with uremic neuropathy

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Say No to NO in mood disorders: 4 decades of discovery

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The deficit of brain holistic mechanism in Russian-speaking children with specific language impairment

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Atypical Alzheimer's disease dementia following moderate Traumatic Brain Injury

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Clinical spectrum of Hashimoto encephalitis: 5-year experience at Siriraj Hospital, Thailand

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Cognitive and emotional disorders of injured soldiers, who are fighting on Donbass

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Nomia and repetition in testing language skills

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Vitamin D: influence in the development of mild cognitive impairment

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CREC: a new creativity/cognitive training for patients with acquired brain injury

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Wernicke's encephalopathy in a patient treated with Fluorouracil-based chemotherapy

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Olive, olive oil and cognitive functions: results from Turkish Cypriot community

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Facial and body emotion recognition in Parkinson's disease: preliminary results

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Effect of dispositional mindfulness on perceived sleep-quality, daytime sleepiness and depression in patients with narcolepsy

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Cognitive dysfunction as one of the symptoms of manifestations of complicated forms of migraine

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Depression and Alzheimer's disease

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Effect of 3 months ACE-I therapy on asymptomatic hypertensive patients: vessel wall properties and cognition

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Dependence of acoustic working memory on knowledge of language

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Cognitive Deficits in a Randomly-selected sample of Multiple Sclerosis patients

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Lewy Body Dementia and SIADH: a challenging diagnosis

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Motor symptoms associated with neuroleptics in psychotic-spectrum disorders

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Clinoco-radiological profile of Posterior Reversible Encephalopathy Syndrome (PRES) in a tertiary care centre in India

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Risk factors for intrahospital mortality of severe Guillain-Barré syndrome forms treated in a neurological intensive care unit

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Oto-acoustic emissions for outcome prediction in postanoxic brain injury

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Mirror, mirror in my hand, who's the fairest in the land? First quality assessment of stroke care quality in 10 tertiary stroke centers in Romania inside RES-Q Registry and ESO- EAST project

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Improving the educational gaps about epilepsy in healthcare providers from Cameroon: impact of an educational program

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Evaluation of the education in basic neurology and neuro-anatomy in healthcare providers from Cameroon before a National Neurology course

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Risk predictors of weight gain in chronic treatment with valproate in epileptic patients

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Seizure related injuries in Guinea

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A case of extensive and long-lasting peri-ictal changes in focal status epilepticus

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Epilepsy with myoclonic–atonic seizures (Doose syndrome) with good results of treatment

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Hospitalisations for epilepsy and epileptic seizures: population based study in Bahia, northeast Brazil

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Four women with similar uncommon traits: refractory focal and generalised seizures, photosensitivity and catamenial precipitation - case series

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Neurophysiological aspects of epilepsy according to the spectral and coherent analysis of bioelectric activity of the EEG

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Long-term outcome in patients with ictal asystole implanted with a cardiac pacemaker

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Stigmatisation and social impact in two epilepsy syndromes: mesial temporal lobe epilepsy and genetic generalised epilepsy

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Anti-LGI1 limbic encephalitis: beyond faciobrachial dystonic seizures

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Demystifying epilepsy

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Multiple cavernomas of the brain

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Post-ictal psychiatric manifestations in epilepsy

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Usefulness of partial sleep-deprived EEG in epilepsy diagnosis after a first possible seizure

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Effect of Eslicarbazepine on cognition in patients with focal epilepsy

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Paroxysmal pain as the only presentation of epileptic seizures

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Epilepsy and chromosomal abnormalities: more than meets the eye

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Cognition in genetic generalised epilepsy: a clinical and video-EEG study

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Filming and photographing patients and health care workers: legal and ethical aspects

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New daily persistent headache in adults: a clinic-based study in a specialist headache service

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Factors associated to episodic migraine and to chronic migraine with medication overuse: a cross-sectional study

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Visual Snow syndrome: comparison between an Italian and English population

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Chronic lower back pain and metabolic disorders

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Stroke-like Migraine Attacks after Radiation Therapy (SMART) Syndrome – two different illustrative cases

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Multiple craniocervical dissections imitating complications of migraine: a case report

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Correlation between the model of family relationships in childhood and perception of pain in adulthood

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Permanent monocular visual loss in migraine patients

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Treatment strategies in chronic migraine on a Portuguese cohort

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Bilateral carotid dissection presenting as episodic cluster headache

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The effect of cervical epidural steroid injections on the cerebral blood flow velocities in patients with chronic neck pain

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Chronification of migraine is not always chronic migraine: hypnic headache overlap

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Headache associated with sexual activity in conjunction with false positive basilar artery fenestration

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Migraine prophylaxis in a sample of migraine patients referred to the headache consultation

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Cerebral venous thrombosis in a patient with spontaneous intracranial hypotension: cause and consequence

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Influence adrenergic stimulus on excitability of cultured trigeminal ganglion neurons

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When the mouth is on fire – characterisation of a cohort of patients with burning mouth syndrome

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Persistent idiopathic facial pain – think again!

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Idiopathic intracranial hypertension during pregnancy: management and outcome

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Classification of cases with a diagnosis of acute headache, to emergency division in Regional Hospital Durres, Albania.

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Low beta EEG peak amplitude is a GABAergic biomarker of chronic neuropathic pain: a pilot study

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Headache in old age: characteristics in a series of 331 patients

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Comparative assessment of botulinumtoxinA efficiency for use in migraine status and chronic migraine

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Diagnostic and therapeutic errors in classical trigeminal neuralgia

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POD229

Clinical heterogeneity of Red Ear Syndrome

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Restless legs syndrome as a clinical manifestation of migraine attacks

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Occipital neuralgia: characteristics and therapeutic results in a serie of 68 patients

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POD232

What do Cameroonian health providers understand as secondary headaches and how are they managed?

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High frequency repetitive transcranial magnetic stimulation for chronic migraine treatment – comparison of two cortical target areas

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POD235

Diagnosing retinal migraine – characterisation of a hospital population

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Gallbladder disease as a migraine trigger?

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Efficacy of erenumab in women with and without a history of menstrually-related migraine

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Efficacy of erenumab for the treatment of patients with episodic migraine with depression and/or anxiety

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The GABAergic high beta EEG peak amplitude could underlie interaction between chronic pain and sleep loss: preliminary results

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POD240

Chronic migraine: epidemiological analysis of a Portuguese cohort

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POD241

Protracted and repeated cessation of headache after greater occipital nerve infiltration in a patient with short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms and chronic migraine with aura

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Clinical presentation of neuropathic pain in patients with chronic low back pain: a multi-centre trial

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Neuropathic pain significantly influences quality of life in patients with chronic low back pain: a multi-centre trial

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Tolosa Hunting – a series of nine Portuguese patients

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Jane Avril: Toulouse-Lautrec's favourite courtisan and Moulin Rouge's choreic dancer

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Geste antagoniste in Catalan art - Santiago Rusiñol's laughing girl

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Tsutsugamushi disease presenting with nonconvulsive status epilepticus

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Case report of visceral Leishmaniasis with neurological manifestations: a diagnostic approach by molecular methods

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Co-existing pneumococcal meningitis and arthritis revealing IgM monoclonal gammopathy of undetermined significance (MGUS)

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POD250

Nocardia paucivorans recurrent brain abscesses in a patient with Waldenström's disease

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Meningomyeloradiculitis following yellow fever 17D vaccination: a case report

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Evaluation of WNV and TBEV as potential causative agents of acute meningitis and encephalitis in Georgia

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POD253

Brainstem Encephalitis (BE) associated to Anti-GQ1b antibody or Listeria rhombencephalitis: a diagnostic and therapeutic challenge

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Neurocysticercosis: something to think about in daily routine

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POD256

Cerebrospinal fluid polymorphonuclear leukocytes in diagnosis of inflammatory CNS disease

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Herpes simplex Encephalitis: an unusual presentation

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POD258

First human case of tick-borne encephalitis virus in Spain

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A case of conglomerate ring enhancing cerebral lesion treated in an unconventional way

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Deep brain stimulation: a case of a 33-year-old man with a recurrent HSV encephalitis

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Virus Varicella-Zoster (VVZ) meningitis retrospective review

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Pontocerebellar atrophy in a HIV-infected patient

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Late-onset progressive multifocal leukoencephalopathy in a renal transplant patient on mycophenolate mofetil immunosuppressive therapy

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POD264

Human immunodeficiency virus infection and Burkitt Lymphoma's Wasting syndrome: an unusual cause of Wernicke encephalopathy

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A rare case of bilateral abducens nerve palsy in a patient with West Nile meningoencephalitis

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Peculiarities of the nervous system disorder in Neuro-AIDS

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Characteristic features of the content of natural augutantitiels of the class IgG to nervous tissue proteins with Neuro-AIDS

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Progressive multifocal leuko-encephalopathy in patients with undiagnosed congenital immunodeficiency: report of two cases

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Neurosyphilis with mesiotemporal involvement mimicking herpes encephalitis

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Meningoencephalitis query cause: dealing with Red Herrings

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Acute motor pure lumbosacral polyradiculopathy in association with HIV infection

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Pasteurella multocida meningitis in a healthy adult

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Difference in the care of patients with amyotrophic lateral sclerosis with or without intervention from the palliative team in Japan.

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Association of CSF NFh and FA-DTI parameters with types and severity of motor neuron disease in Tamil population from South India

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Creatine kinase levels in motor neuron disease

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Diseases that simulate Amyotrophic Lateral sclerosis: clinical differences

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Voluntary posture control apraxia in patients with motor neuron disease

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Polio-like syndrome

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Screening for the C9orf72 hexanucleotid repeat expansion in a Hungarian motoneuron disease cohort

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The spectrum of involuntary movements in patients with motor neuron disease – a prospective study

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withdrawn

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Facial-onset sensory and motor neuronopathy-a new phenotype?

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Albanian adaptation of the Edinburgh Cognitive and Behavioural Amyotrophic Lateral Sclerosis Screen (ECAS)

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Dopamine transporter scan: the plymouth hospital experience from 2013-15

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Auditory and vestibular dysfunction in patients with Parkinson's disease

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Safinamide can improve depression symptoms in Parkinson's disease patients

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Depression in patients with Parkinson's disease (PwPD) in the Siberian region, Russia

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Acute cerebral posthypoxic dystonia and chorea: a case report

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COPPADIS-2015 (COhort of Patient's with Parkinson's disease in Spain, 2015): an ongoing global Parkinson's disease Project about disease progression with more than 700 patients included. Preliminary results of baseline evaluations

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Assessment of cognitive functions in drug naive patients with isolated adult-onset cervical dystonia: a single-center case-controle study

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Hyperhomocysteinemia influenced malnutrition in Parkinson's disease patients

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Cognitive function measurement comparing Vascular Parkinsonism (VP) and Parkinson's disease (PD) patients in a Portuguese Hospital-based sample

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Neurological examination differences between early stages of Vascular Parkinsonism (VP) and Parkinson´s Disease (PD) patients

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Interferences of cognition on upper extremity motor function and posture control in patients with schizophrenia with high and low risk of falls

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Miid cognitive impairment subtypes in Parkinson's disease

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POD300

McLeod syndrome: go for genes, not thorns

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POD301

Evaluation of pain in Parkinson's disease patients

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POD302

Co-occurrence of spinocerebellar ataxia type-2 and Huntington disease in three patients

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POD303

Volumetric measurements of subcortical structures in the adult patients with primary dystonia

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POD304

Voluntary control of posture in patients with Parkinson's disease in the course of DBS

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POD305

Risk of falls in advanced Parkinson's disease patients treated with continuous intestinal infusion of Levodopa gel versus oral therapy

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POD306

Diagnostic tests for Multiple system atrophy: a systematic review by the Movement Disorders Society Multiple system atrophy (MoDiMSA) study group

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POD307

Huntington's disease in Albania: epidemiological data from patients during the last 10 years at a national reference centre

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POD308

Balance evaluation in Parkinson's disease using simple, diagnostic tests versus posturography – pilot study

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POD310

Low and combination frequency deep brain stimulation in Parkinson's disease patients with gait & speech problems

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POD312

Beta-propellerprotein associated neurodegeneration (BPAN) – from phenotype to genotype

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POD314

Adult-onset post-pump chorea: acute presentation following major cardiac surgery

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POD315

Effect of ageing on speech characteristics in de novo Parkinson's disease compared to healthy controls

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POD316

Sudden onset of Parkinson's disease after a major life event: report of three cases and literature review

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POD318

Phantom Chorea

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POD319

Status dystonicus in a patient with ADCY5-related dyskinesia

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POD320

Neuromodulatory role of subthalamic nucleus deep brain stimulation (STN-DBS) in Parkinson's disease (PD) patients

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POD322

Brain MRI findings in SCA 17: the "hot cross bun" sign is associated with low expanded alleles

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POD323

EIF4G1 p.P992P mutation in a family with parkinson´s disease

G. Valero López, J. López Sánchez, A.E. Báidez Guerrero, J. Jimenez Veiga, E. García Molina, J. Diaz Perez, J.M. Cabrera Maqueda, L. Fuentes Rumí, M.T. Alba Isasi, J. Vazquez Lorenzo, F.A. Martinez Garcia, O. Morsi Hassan
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POD325

A case of Familial Fahr's disease with normal DaTSCAN imaging and a moderate response to Levodopa

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POD326

A remarkable case of primary progressive freezing gait with impressive response to the use of a laserlight visual cueing device

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POD327

withdrawn

POD328

Validation of the MDS-UPDRS

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POD329

Hypertrophic olivary degeneration and progresive cerebellar ataxia secondary to bleeding of cavernous malformation in the midbrain

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POD330

Clinical effect of Safinamide in patients with Parkinson's disease with motor fluctuations and freezing of gait

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POD331

Non-motor symptoms of Parkinson's disease and their impact on quality of life in 117 Moroccan patients

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POD332

Using pick and place virtual reality task to investigate the precise movement in patients with Parkinson's disease

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POD333

Deep brain stimulation for treatment of structure lesions tremor: report of two cases

L. Fuentes Rumí, O. Morsi Hassan, J. López Sánchez, J.M. Cabrera Maqueda, G. Valero López, A.E. Báidez Guerrero, M.T. Alba Isasi, J. Vazquez Lorenzo, E. García Molina, J. Diaz Perez, J. Jimenez Veiga, F.A. Martinez Garcia
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POD334

A study to evaluate the efficacy of PRX002/RG7935 in participants with early Parkinson's disease (PASADENA) – study design

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POD336

Cortical atrophy in Parkinson's disease with mild cognitive impairment: a VBM study

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POD337

3D visual cueing improves gait in Parkinson's disease treated with subthalamic deep brain stimulation

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POD338

Temperament traits and executive functions in Parkinson's disease

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POD339

Beneficial effects of deep brain stimulation on urinary and sexual problems in Parkinson's disease

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POD340

Impact of change in antiparkinsonian medication of hospitalized Parkinson's disease patients in clinical outcome

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POD341

A single center retrospective analysis of Opicapone treatment in 90 Parkinson patients

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POD342

"Normally appearing grey matter in Multiple Sclerosis - Is it really functionally normal?" - An Egyptian clinical and imaging study

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POD343

Vitamin D and quality of life in multiple sclerosis sufferers

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POD344

Spanish validation of a specific measure to assess work-related problems in people with multiple sclerosis: the Multiple Sclerosis Work Difficulties Questionnaire (MSWDQ-23)

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POD345

Relationship between perceived social support, anxiety and depression in French vs Italian MS samples

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POD346

Aggressive presentation of a case of Tumefactive Multiple Sclerosis

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POD347

Satisfaction, safety and it cost of the treatment for multiple sclerosis relapses with Intravenous versus oral methylprednisolone

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POD348

Adherence to fingolimod treatment. Our center's experience.

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POD349

Real life efficacy and safety of Teriflunomide: a prospective, observational, hospital-based study with 94 Relapsing Remiting Multiple Sclerosis (RRMS) patients

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POD351

The effect of natalizumab in disability and cognitive function of multiple sclerosis patients: the experience of a tertiary MS center

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POD352

Cerebrospinal fluid Feutin-A levels in Multiple Sclerosis compared to controls: can it be a marker of disease activity

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POD353

Ocrelizumab pre-approval access for primary progressive multiple sclerosis in Austria

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POD355

Disease activity after Fingolimod - three cases of rebound syndrome

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POD356

Usefulness of the Beck depression inventory during treatment of relapses in patients with Multiple Sclerosis

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POD357

withdrawn

POD358

Vesicosphincteric disorders in multiples sclerosis: a descriptive study

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POD359

CNS Demyelination in relation with Golimumab

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POD360

Screening of cognitive impairment in patients with multiple sclerosis

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POD361

Causes of hospitalisation in patients with multiple sclerosis. Single-center study

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POD362

Immune-cell BDNF expression in treatment-naïve relapsing-remitting multiple sclerosis patients and after one year of immunomodulation

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POD363

Aphasia and hemiparesis on the high seas

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POD364

Application of autologous transplantation of mesenchymal stem cells for relapsing-remitting multiple sclerosis

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POD365

Autologous mesenchymal stem-cell transplantation effects on disease progression of relapsing-remitting multiple sclerosis patients

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POD366

Does the information about the diagnosis of multiple sclerosis should be disclosed to the employer at the disease onset?

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POD367

White spots on the MRI

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POD368

Gastrontestinal dysautonomia measured with COMPASS 31 can predict disease progression in patients with clinically isolated syndrome

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Quality of life changes in early-onset Multiple Sclerosis: 2-year follow-up

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POD370

Cognitive abilities in pediatric and juvenile multiple sclerosis: 2-year follow-up.

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POD371

Changes in ophthalmic circulation and retinal oxygen saturation in Multiple Sclerosis patients with optic neuritis

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POD372

Patient involvement in treatment decision-making: a sub-analysis of the 'MS in the 21st Century international unmet needs survey' comparing patient and healthcare professional perspectives

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POD373

Clinical, immunological, radiological correlation in Multiple sclerosis

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POD374

Observational study of the effect of Fingolimod (Gilenya) on cerebral atrophy and cognitive impairment in patients with Relapsing-Remitting Multiple Sclerosis in Argentina (FINDER Study): study design and Interim analysis

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POD376

Chronic intestinal pseudo-obstruction and Progressive Multiple Sclerosis: beware of an uncommon gastrointestinal presentation

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POD377

Optical coherence tomography in optic neuritis in demyelinating disorders

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POD378

Rebound syndrome in Multiple Sclerosis after withdrawal of Fingolimod treatment

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POD379

No effect of smoking on disability progression in patients with Multiple Sclerosis

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POD381

Leptin and not adiponectin determines activity and progression in multiple sclerosis patients

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POD383

Management of an early-onset Alemtuzumab-induced symptomatic Immune Thrombocytopenia in a Multiple Sclerosis treatment context

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POD385

Fingolimod treatment in children with RRMS

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POD386

The influence of glatiramer acetate on Th17-immune response in Multiple Sclerosis

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POD387

Autoimmune hepatitis after high-dose methylprednisolone for multiple sclerosis relapse in a patient with autoimmune thyroiditis: a coincidental association?

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POD388

Estimation of cerebral atrophy in multiple sclerosis patients by two-dimensional linear measurements

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POD389

Does the diagnosis of Multiple Sclerosis change the relationship with the life partner?

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POD390

Comorbid diseases in patients with Multiple Sclerosis

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POD391

Combined cycling and rTMS to enhance the effects of Sativex in Progressive Multiple Sclerosis: a pilot randomised, sham-controlled study

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POD392

Patient-reported fatigue in progressive Multiple Sclerosis

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POD393

Slower articulation rate reflects greater brain atrophy in Multiple Sclerosis

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POD394

Headache in Multiple Sclerosis

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POD395

A method to compare prospective and historical cohorts to evaluate drug effects – application to the analysis of early treatment efficacy of intramuscular interferon-β1a in Multiple Sclerosis patients

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POD396

Neuroimmunology in children: a multicentric study of pediatric onset demyelinating diseases

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POD398

Routine laboratory measures in the controlled-treatment period of Phase III Ocrelizumab trials in relapsing and progressive Multiple Sclerosis

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POD399

Effect of Ocrelizumab on vaccine responses in patients with Multiple Sclerosis

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POD400

Unusual serious adverse effect in a lymphopenic dimethylfumarate treated Multiple Sclerosis patient

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POD401

Family planning in Multiple Sclerosis patients: an observational study

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POD402

Parameters of oxidative stress in Relapsing-Remitting Multiple Sclerosis (RRMS) patients on different Disease Modifying Treatments (DMT)

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POD403

Real-world effectiveness and safety of pegylated interferon beta-1a in patients with Multiple Sclerosis: a multicentre retrospective study in Central Italy

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POD404

REALMS Study: a non-interventional retrospective, multicenter study to evaluate the effectiveness and safety of fingolimod therapy in real-life clinical practice in patients with Relapsing-Remitting Multiple Sclerosis (RRMS) in Portugal

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POD405

An electroglottography derived, discriminant function model differentiating Multiple Sclerosis patients from healthy controls

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POD406

Early prediction of relapses in Multiple Sclerosis at onset

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POD407

Interferon beta-1A biosimilar in patients with relapsing remitting Multiple Sclerosis

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POD408

Relation of EDSS bladder functional system score to clinical features in Multiple Sclerosis

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POD409

Area postrema syndrome with NMO spectrum disorders in russian population

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POD413

The predictive value of the first symptoms for time to secondary progression in Multiple Sclerosis

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POD414

The associations between commonly used walking measures and physical and psychosocial outcomes in persons with Multiple Sclerosis

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POD416

Usefulness of CSF oligoclonal bands detection and anti-Aquaporin-4 antibodies screening in Tunisian patients with central nervous system inflammatory disorders

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POD418

Anti-PM-Scl-50-postitive inclusion body myositis: a case report and literature review

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POD420

Distal myopathy due to MATR3 mutation in a Portuguese family

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POD421

Acute concomitant presentation of polymyositis and myasthenia gravis: a diagnostic challenge

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POD422

Poor sleep quality in patients with myasthenia gravis and related factors

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POD423

Launching a multicenter study of tranilast for cardiomyopathy of muscular dystrophy

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POD424

Functional exercise capacity in generalized myastenia gravis patients: a reliability and construct validity study of six minute walk test and two-minute walk test

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POD425

Ocular Pharyngeal Muscular Dystrophy (OPMD) - a greek kindred of a rare disease in the Greek population

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POD426

Reliability and construct validity analyses of the 6-minute walk test in Brazilian patients with duchenne muscular dystrophy

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POD429

The course of pregnancy and delivery in patients with myasthenia gravis

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POD430

Serum creatinine and genotype phenotype correlation in dystrophinopathy

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POD431

Clinical spectrum and genetic variability in a Chinese cohort of limb-girdle muscular dystrophy patients

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POD432

Hypokalemic periodic paralysis induced by glucocorticoids

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POD433

Facioscapulohumeral dystrophy with dilated cardiomyopathy a diagnostic overlap

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POD434

Kinesiotaping with myofascial pain syndrome in the craniomandibular region

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POD435

Clinical, morphological and immunological findings in myasthenia – myositis association

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withdrawn

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Autoantibodies in Idiopathic inflammatory myopathy: about 2 clinical cases and review of the literature

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POD438

MERRF Classification: implications for diagnosis and clinical trials

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POD439

Muscle biopsy and electromyography correlation in a cohort of 125 patient with neuromuscular disorders

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POD441

Prevalence and disability of MND in Republic of Belarus

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POD442

Amyotrophic Lateral Sclerosis incidence in Albania: data from the Neurodegenerative Diseases Albania (NDAL) study group

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POD443

Rare mitochondrial homoplasmic mutation m.3733G>A in a patient with Leber's hereditary optic neuropathy (LHON) and axonal neuropathy

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POD444

Late-onset recessive ataxia, ophthalmoplegia and dementia due to homozygous c.5825T>C p.Ile1942Thr mutation in the Senataxin (SETX) gene - the utility of next generation sequencing panels

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POD445

COL4A1 variant – a rare cause of fetal haemorrhagic stroke

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POD446

Limb-girdle muscular dystrophies (LGMD) in Bulgaria

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POD447

Aphasic status epilepticus as the initial presentation of Mitochondrial Encephalopathy, Lactic Acidosis and Stroke-like episodes (MELAS)

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POD448

The Italian national registry for spinal and bulbar muscular atrophy

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POD450

Muscle hypotonia in children and its possible causes

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POD451

A new SLC20A2 mutation identified in a Portuguese family with Fahr's disease

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POD454

Prevalence of Apolipoprotein E polymorphisms in Alzheimer's disease, mild cognitive impairment, and healthy elderly. A Greek population study

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POD455

A novel NOTCH3 frameshift variant - no evidence for a link with CADASIL

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POD456

Transthyretin-related amyloidosis in Crete, Greece

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POD457

Microduplication within the SEPT9 gene is associated with hereditary neuralgic amyotrophy in one Czech family

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POD458

Diagnostics of the neuronal ceroidlipofuscinosis in children

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POD460

Broadening the spectrum of adulthood x-linked adrenoleukodystrophy: two inusual clinical phenotypes

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POD461

POLG1 mutations in an adult case of the ataxia neuropathy spectrum without progressive external ophthalmoplegia

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POD462

Transthyretin familial amyloid polyneuropathy in Macedonia - could this be a new endemic cluster?

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POD463

Encephalopathy in Maple Syrup Urine disease decompensation: the importance of early recognition and treatment

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POD464

Niemann-Pick Type-C disease: a case report

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POD465

The clinical-genetic manifestation in tuberous sclerosis: a case report

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POD466

MR confirmed Wernicke encephalopathy misleading the diagnosis of MELAS

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POD467

Common and rarer demyelinating forms of Charcot-Marie-Tooth disease (CMT1 and CMT4) in the Greek population: a 20-year experience from a reference center

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POD468

Spastic paraplegia type-4 due to a novel SPAST gene mutation, misdiagnosed as cerebral palsy

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POD469

Caveolin-3 mutation presenting with severe exercise induced myalgia and muscle weakness

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POD470

Mitochondrial cytochrome c oxidase deficiency presenting as primary progressive Multiple Sclerosis

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POD471

A "candidate-interactome" approach in gene-environment interactions in Multiple Sclerosis

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POD472

Immunological features of recessive autosomal LGMD in the Tunisian population

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POD473

Myotonic dystrophy type-2: what is the situation in the Maltese islands?

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POD475

Validation of clinical criteria for referral to head CT in the emergency setting

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POD476

Contrast enhanced ultrasound carotid sonography and multimodal imaging in a case of TIPIC syndrome

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POD477

The effect of aging on the cerebral blood flow measured using IMP SPECT in normal subjects and patients with Alzheimer's disease

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POD478

A complex case of multiple neurological adverse drug reactions for the liaison neurology service

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POD479

An anatomical analysis of the lesions in patients with somatoparaphrenia using 123I-IMP SPECT

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POD480

Brain atrophy in Multiple Sclerosis: influence of racial and environmental factors on disease related volumetric measurements

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POD481

Semiology as search tools to help locate the injury. Looking to petrous apex

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POD483

Sudden coma from acute bilateral internal carotid artery occlusion

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POD484

Prolonged loss of consciousness revealing a lumbosacral dermoid cyst rupture

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POD485

Heterogeneous brain FDG-PET patterns in patients with C9orf72 mutation

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POD486

Implication of hyperintensity acute reperfusion markers in patient with transient neurologic manifestation

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POD487

Cerebrotendınous Xanthomatosis: a rare but potentially treatable cause of cerebellar ataxia

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POD488

Interest of multimodal imaging in carotidynia

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POD489

Multifocal evanescent lesions as manifestation of possible isolated neurosarcoidosis

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POD490

CT perfusion in reversible cerebral vasoconstriction syndrome

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POD492

Accuracy of Schelten's score in cerebro-spinal fluid confirmed Alzheimer's disease patients

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POD493

Quantitative muscle ultrasound analysis in FSHD patients

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POD494

Diffuse cortical calcifications associated with Mitochondrial Encepalopathy with Lactic Acidosis and Stroke-like episodes (MELAS)

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POD495

The correlation between the localisation of stroke and the risk of post-stroke depression

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POD497

Serial magnetic resonance spectroscopy findings in acute disseminated encephalomyelitis

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POD499

Features of paraneoplastic sensory polyneuropathy "anti-Hu syndrome" in patients with Small Cell Lung Cancer (SCLC)

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POD500

Circulating B-cell subsets in chronic inflammatory demyelinating polyneuropathy

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POD501

Dysgeusia as the initial symptom of acute-onset inflammatory demyelinating polyneuropathy: a case report and review of the literature

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POD502

Pioglitazone neuroprotective effect through the link between Nrf2/HO-1 signaling pathway and miR-155 in a Mouse model of systematic inflammation

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POD503

AKBA, a terpenoid from Boswellia serrata modulates Nrf2/HO-1 signaling pathway in a mouse model of neurodegeneration

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POD504

A case of glycine receptor antibody positive stiff-person spectrum disorder presenting with nocturnal attacks of rhythmic abdominal movements

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POD506

A case of Miller Fisher syndrome followed by ocular myasthenia gravis

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POD507

Fulminant multifocal ADEM-like relapse in a fingolimod-treated Multiple Sclerosis patient

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POD508

Conus medullaris syndrome after influenza vaccine

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POD509

Cerebellar syndrome as isolated manifestation of Hashimoto's encephalitis: case report and literature review

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POD511

Monocyte CD16 expression in Portuguese Multiple Sclerosis patients

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POD512

Changes in neurological status in patients on chronic hemodyalisis

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POD513

Takayasu Arteritis with rare association of Moyamoya phenomenon

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POD514

Motor Complications of herpes varicella-zoster virus (VZV) infections

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POD516

Is status epilepticus a clinical manifestation of transthyretin familial amyloid polyneuropathy?

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POD517

Optic neuritis and Erdheim Chester: a case report

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POD520

Hashimoto's Encephalopathy: a heterogeneous and reversible syndrome

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POD521

Leptomeningeal enhancement with subacute parkinsonism presentation: when the asymmetry is the key for diagnosis

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POD523

A case of systemic lupus erythematosus presenting as acute motor axonal neuropathy

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POD524

withdrawn

POD525

Subacute combined degeneration of spinal cord: a case report from Skopje, Macedonia

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POD526

A case report of Hashimoto encephalopathy

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POD527

Internal carotid artery dissection associated with antiphospholipid antibody syndrome

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POD528

Wegener's Granulomatosis with otoneurological local onset

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POD530

Neurology in the pictures of Dutch painters of XVI-XVII century

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POD531

Surgical treatment of aggressive vertebral hemangiomas

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POD532

Factors affecting the duration of emergence of brain metastases in patients at Notre Dame des Secours University Hospital Lebanon between the years of 2010 and 2015

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POD533

A case report: Anti-Hu associated paraneoplastic encephalomyelitis treated as myasthenia gravis

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POD534

Late-onset of a cerebellar syndrome in a patient treated with 5-fluorouracil and Oxaliplatin

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POD535

Sensory neuronopathy, thinking about paraneoplastic

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POD536

Neurofibromatosis type-2 associated with medulloblastoma in a paediatric patient

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POD537

Garcin syndrome as a rare presentation of metastatic colorectal cancer

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POD538

withdrawn

POD539

Recurrent subarachnoid haemorrhage caused by leptomeningeal infiltration secondary to lung carcinoma: clinical case study

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POD540

Vanishing mass lesion

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POD541

Intramedullary tumors - essential work-up to provide an accurate diagnosis

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POD542

Is vision loss always due to optic neuritis? Differential diagnosis challenges

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POD543

Chronic Relapsing Inflammatory Optic Neuropathy (CRION): report of a clinical case of rare disease and atypical presentation

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POD545

Cervical Vestibular Evoked Myogenic Potentials (cVEMPs): optimum recording position does not change in the elderly

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POD546

Recurrent painful ophthalmoplegic neuropathy – the novel ophthalmoplegic migraine

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POD547

Amaurosis Fugax: multiple etiologies

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POD550

Auditory Charles-Bonnet syndrome: an underrecognized condition

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POD551

Ocular neuromyotonia responsive to lacosamide

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POD552

Reversible peripheral facial nerve palsy during airplane travel

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POD553

Bilateral optic nerve atrophy and spastic paraparesis caused by a new OPA1 gene mutation

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POD554

Acute onset bilateral myopia in a patient receiving topiramate for migraine prophylaxis

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POD555

Recurrent benign episodic unilateral mydriasis and hyperthyroidism

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POD556

Gabapentin suppresses nystagmus due to Arnold-Chiari malformation

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POD557

Visual snow: clinical characterization, quality of life and treatment responses in a case series from a Spanish tertiary hospital

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POD559

A multimodal approach in upper extremity recovery after stroke: the combination of non invasive brain stimulation with cerebrolysin and task specific training

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POD560

Kinesiological correction of the muscle imbalance after surgical treatment of lumbar herniated disk

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POD562

withdrawn

POD563

Comparative efficacy of various dual-task interventions on standing balance and cognitive performance after stroke

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POD565

Pontine myelinolysis secondary to acute lithium toxicity

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POD566

Accelerometric recording of changes in voice production in teachers after their daily task

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POD567

Trephined syndrome following decompressive craniectomy

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POD568

Head trauma and seizure: 7-day follow-up of patients in Notre Dame University Hospital Byblos, Lebanon

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POD570

Cliniconeurophysiological features of combined injuries in the acute period

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POD571

Predictors of worse quality of life in chronic inflammatory demyelinating polyneuropathy

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POD572

Chronic idiopathic axonal polyneuropathy: prevalence of pain and impact on quality of life

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POD574

The correlations between functional and laboratory tests in atypical forms of chronic inflammatory demyelinating polyneuropathies

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POD575

withdrawn

POD576

Peripheral nerve disorders related to gastrointestinal infections: two case reports

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POD579

Association between obesity and inflammation among diabetic polyneuropathy

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POD580

Charcot-Marie-Tooth 1A and demyelinating brain white matter lesions

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POD581

GBS demographic, clinical, electrophysiological and prognostic features; a Turkey study

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POD582

Rapidly progressive neuropathy in pancreatitis

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POD583

Is late intravenous immunoglobulin treatment in multifocal motor neuropathy effective? A case report

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POD587

Recurrent spinal cord infarction secondary to fibrocartilaginous embolism

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POD588

Idiopathic ventral cord herniation: a photodocumented case report

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POD589

Spinal cord infarction due to patent foramen ovale (PFO)

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POD590

Ischemic medulopathy as result of spinal arteriovenous fistula

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POD591

Varicella zoster virus meningoradiculitis presenting with cauda equina syndrome

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POD592

Hirayama disease – a disorder to be recognised also in the West

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POD593

Subacute combined degeneration due to vitamin B12 deficiency in the absence of macrocytic anemia

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POD594

Asymmetrical lower extremity weakness and fever - considerations regarding diagnosis and management

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POD595

Spastic paraparesis and neurogenic pelvic organ dysfunction due to masked vitamin B12 deficiency (increased methylmalonic acid levels) in patient with microcytosis and thalassemia minor

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POD596

A retrospective two-year analysis of the diagnosis of paraplegia made in the emergency room

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POD597

Acute transverse myelitis: a case report after influenza vaccination

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POD598

Acute myeloradiculopathy secondary to spinal anesthesia

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POD599

Nitrous oxide induced subacute combined degeneration with longitudinally extensive myelopathy with inverted V-sign on spinal MRI: a case report and literature review

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POD600

Cervical spondylotic myelopathy mimicking amyotrophic lateral sclerosis: difficulties in differential diagnosis

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POD601

Secondary spinal cord compression due to heterotopic ossification: follow-ups in a patient with implant in the cervical spine

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POD602

Superficial siderosis secundary to myxopapillary ependymoma

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POD603

Syringomyelia associated with a spinal arachnoid cyst

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POD604

Impact of chronic nonspecific low back pain in quality of life of patients

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Yerevan, Armenia

POD605

The importance of prenatal genetic diagnosis in prophylaxis of Duchenne progressive muscular dystrophy: clinical case

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Focused Workshop

Saturday, June 16 2018

Brain health in Multiple Sclerosis: a catalyst for a new approach to management

FW01_1

Treating-2-target: the case for maximising brain health in MS

G. Giovannoni
London, United Kingdom

Abstract: The principle of treating to target is a widely accepted goal for the clinical management of a growing number of diseases, including cardiovascular disease and rheumatoid arthritis, and should be extended to include Multiple Sclerosis (MS). Currently, however, significant delays are common at all stages in the referral–diagnosis–treatment pathway in MS. A therapeutic strategy that offers the best chance of preserving brain and spinal cord tissue, by intervening early and effectively in the disease course, needs to be widely adopted.

An initiative to drive major changes in public policy management is underway that aims to minimize delays in diagnosis and treatment, involve patients in decision-making and manage MS holistically in order to improve outcomes for people with MS. MS Brain Health, which emerged from the publication of an evidence-based international consensus report, promotes a strategy to maximize lifelong brain health by early identification and treatment of MS, to minimize disease activity. The long-term aim of MS Brain Health is the global implementation of the recommendations from that consensus report. In this workshop, we will invite participants to discuss how their current clinical practice aligns with these recommendations.
Disclosure: G. Giovannoni has received consulting fees from AbbVie, Atara Biotherapeutics, Almirall, Biogen, Celgene, GlaxoSmithKline, MedDay Pharmaceuticals, Merck and Company (US), Merck Group (Europe), Novartis, Oxford PharmaGenesis, Roche, Sanofi Genzyme, Synthon, Takeda, Teva Pharmaceutical Industries Ltd. and UCB; and has received grant/research support from Biogen, Sanofi Genzyme and Takeda.

FW01_2

The economic cost of MS in Europe

G. Kobelt
Stockholm, Sweden

Abstract: The introduction of disease-modifying therapies has changed the management of Multiple Sclerosis (MS) and the financing of patient care. The expectation that the treatments will slow disability progression, in addition to reducing relapses, has led to a focus on early diagnosis and intervention. A number of studies in European countries have shown that health-related quality of life (HRQoL) deteriorates as disability progresses, while costs increase four-to-five fold. However, different healthcare systems adopt different strategies.

New data on HRQoL and costs of MS from a European study with 16,800 participants from 16 countries have recently been published. Although disability remains the main driver of overall costs, the results from this study suggest that the use of direct healthcare resources is influenced as much by the organisation of healthcare systems as by disease severity. Further research into the differences in healthcare systems, incentives and payment-driven resource utilization in different countries is required to assess the economic impact of changes in MS care.

In this workshop, the results from the European burden-of-illness study will be presented, and participants will be invited to discuss how the economics of MS are changing in their countries.
Disclosure: G. Kobelt has received consulting fees from Almirall, Bayer, Biogen, Merck Serono, Novartis, Oxford PharmaGenesis, Roche, Sanofi Genzyme and Teva.

FW01_3

Translating recommendations for improving MS care into improved outcomes

J. Hobart

Plymouth, United Kingdom

Abstract: This workshop concerns the logical next step following the report Brain health: time matters in multiple sclerosis,1 which is to turn the published evidence into practical realizations. Specifically, our aim is to generate an audit tool that Multiple Sclerosis (MS) clinicians can use to their advantage.

International standards defining what constitutes 'early' diagnosis and treatment are needed to act as a benchmark for MS clinics striving to deliver high-quality care. We conducted a modified Delphi process to gain consensus among an international group of MS neurologists for the timing of key steps in the MS care pathway. Through a series of online surveys, neurologists agreed standards related to brain health in MS, covering symptom onset, referral, diagnosis, treatment decisions, lifestyle, monitoring and managing new symptoms. Using these new standards, we hope to develop (1) a quality improvement tool for use in clinical practice; and (2) a resource to inform people with MS about what to expect from MS care services. In the future, a web-based application could be developed to allow patients to give feedback to their clinics on the various metrics. The proposed tools should help clinics that are striving to improve services, and thereby contribute to improving clinical outcomes. Participants in the workshop will be invited to discuss the new consensus standards and consider how they could be used in their local clinics.

Reference

1. Giovannoni G et al. Mult Scler Relat Disord 2016;9 Suppl 1:S5–S48.

Biomarkers of neuromuscular disorders

FW02_1

Micro-RNA in muscular dystrophies

C. Angelini

Venice, Italy

Abstract: MicroRNAs (miRNAs) are small non-coding RNAs that have been shown to modulate a wide range of biological functions under various pathophysiological conditions. MiRNAs are 17-27 nucleotides long molecules that regulate post-transcriptional mRNA expression, typically by binding to the 3'-untranslated region of the complementary mRNA sequence, and resulting in translational repression and gene silencing.The circulating microRNAs (miRNA) are stable and resist to RNAse activities. They can be actively released by muscle, carried by exosomes, microparticles and apoptotic bodies or can be passively released after sarcolemmal damage or injury. We have particulary studied "Canonical myomiRs" (miR-1; miR-206; miR-133a and miR-133b), they are considered as markers of muscle regeneration, myogenesis, fiber type differentiation, degeneration, injury and might represent indicators of residual muscle mass consequent to a chronic atrophy of muscle.

Alteration of circulating miRNA has been associated with several muscular dystrophes and myopathies such as Duchenne and Becker muscular dystrophy, FSHD.

Circulating miRNAs have recently gained attention for their potential as cost effective biomarkers in DM1 and their down regulation due to modulatory action after physical rehabilitation.

In neuromuscular disorders they act as negative regulators we have found a significantly higher expression of miR-206 in muscle of genetic ALS respect to control and different serum expression of myomiR in bulbar versus spinal ALS. A similar behaviour we observed in LGMD (transportinopathies, sarcoglycanopathies) and in a series of metabolic myopathies (i.e. NLSD-M), carnitine deficiency, ETF dehydrogenase defects). These data highlights the importance of non coding RNA as biomarkers of NMD.

Disclosure: Nothing to disclose

FW02_2

Inflammatory neuropathies and antibodies

L. Querol

Barcelona, Spain

Abstract: Autoantibodies have traditionally been proposed as the key effector molecules driving pathogenesis in inflammatory neuropathies. Antiganglioside antibodies in Guillain-barre syndrome and multifocal motor neuropathy or anti-MAG antibodies in paraproteinemic neuropathies are examples of their importance. In the recent years diverse antibodies targeting structures of the node of Ranvier have been described in patients with inflammatory neuropathies, particularly in chronic inflammatory demyelinating polyradiculoneuropathy. These antibodies, associating with specific clinical phenotypes, have helped understanding pathogenesis of CIDP and provided novel approaches to the study of CIDP and GBS pathogenesis, placing the focus at the node of Ranvier. Moreover, the description of these antibodies, most of them of the IgG4 isotype, have helped tayloring the type of therapy used ind these patients depending on their autoantibody status. This presentation will review the pathophysiological, diagnostic and therapeutic implications of the detectin of autoantibodies in inflammatory neuropathies, with special focus in the recent findings on paranodal autoantibodies

Disclosure: Expert testimony for Grifols and CSL Behring and received research funds from Novartis Spain and Grifols

FW02_3

Mitochondrial disorders and biomarkers

R. Horváth

Newcastle, United Kingdom

Abstract: Diagnosing primary mitochondrial diseases is challenging in clinical practice. Although, defective oxidative phosphorylation is the common final pathway, it is unknown why different mtDNA or nuclear mutations result in largely heterogeneous and often tissue specific clinical presentations. Mitochondrial tRNA mutations are frequent causes of mitochondrial disease both in children and adults. However numerous nuclear mutations involved in mitochondrial protein synthesis affecting ubiquitously expressed genes have been reported in association with very tissue specific clinical manifestations suggesting that there are so far unknown factors determining the tissue specificity in mitochondrial translation. Most of these gene defects result in histological abnormalities and multiple respiratory chain defects in the affected organs. The clinical phenotypes are usually early-onset, severe, and often fatal, implying the importance of mitochondrial translation from birth. However, some rare, reversible infantile mitochondrial diseases are caused by very specific defects of mitochondrial translation (m.14674T>C, TRMU). An unbiased genetic approach (whole exome sequencing, RNA sequencing) combined with proteomics and functional studies revealed novel factors involved in mitochondrial translation which contribute to the clinical manifestation and recovery in these rare reversible mitochondrial conditions. Recently FGF21 and GDF15 were identified as potential biomarkers in mitochondrial myopathy and recent studies are ongoing to validate their role in the diagnosis and in monitoring progression of mitochondrial disease. The identification of specific and sensitive biomarkers should be validated in natural history studies and clinical trials in mitochondrial disease.

Disclosure: Nothing to disclose.

The importance of brain network reorganisation in old age and for successful rehabilitation after stroke

FW03_1

Methods of directly interacting with brain function

W. Paulus
Göttingen, Germany

Abstract: Repetitive transcranial magnetic stimulation (rTMS) allows increasing or decreasing the excitability of corticospinal or cortico-cortical pathways depending on the intensity and frequency of short stimulation pulses in the range of 100μs. Here magnetic stimulation is the vehicle which allows transferring transcranially short-pulsed electric energy without inducing skin pain. Decreasing or increasing cortical excitability can be achieved by varying intensity, stimulation frequency, intervals, number of pulses, number of sessions, location of stimulation, directions of induced current flow and pharmacological manipulation. Alternatively transcranial electric stimulation techniques have been developed as cheap and efficient tools for modifying cortical plasticity. Direct transcranial electric stimulation of the human brain can be used painlessly if less steep voltage gradients are involved. Weak transcranial direct current stimulation (tDCS) with a homogenous DC field fulfils this requirement ideally (Nitsche and Paulus, 2000). TDCS induces plastic aftereffects via membrane polarization: cathodal stimulation hyperpolarises, while anodal stimulation depolarises the resting membrane potential, whereby the induced after-effects depend on polarity, duration and intensity of the stimulation. Transcranial alternating current (tACS) (Antal et al, 2008) and random noise stimulation (tRNS) intend to interfere with ongoing cortical oscillations (Terney et al., 2008). Using these techniques, we can induce and modify differently neuroplastic changes with different advantages and disadvantages of tDCS, tACS and tRNS. Plastic aftereffects need a minimal stimulation duration time and may reverse with too long stimulation. They are also less current flow direction sensitive as compared to rTMS or tDCS.
Disclosure: member scientic advisory board Precisis AG

FW03_2

The importance of shifting our models of the effects of NIBS from producing pure excitation or inhibition of target structures to considering the wider network effects

J.C. Rothwell
London, United Kingdom

Abstract: It is often claimed that non-invasive brain stimulation (NIBS) methods such as anodal transcranial direct current stimulation (aTDCS), or high frequency repetitive transcranial magnetic stimulation (rTMS) increase the excitability of the stimulated area whereas cathodal TDCS or low frequency rTMS do the opposite. Although they may be correct descriptors of the effects of these methods on the excitability of the corticospinal output of the hand area of primary motor cortex, they may not be true of other brain areas, or of their effects on behaviours. More importantly this idea masks the important fact that NIBS methods always produce effects at connected sites distant from the point of stimulation. This is clearly recognised many therapeutic examples, where for example, 1 Hz rTMS or cathodal TDCS is applied to the hemisphere contralateral to a stroke. The assumption is that suppression of local excitability will enhance the excitability of the affected hemisphere and thereby improve functional recovery. A good example of the remote effects of NIBS in healthy individuals is the influence of TDCS or rTMS over cerebellum on the plasticity of the contralateral primary motor cortex. I will discuss possible mechanisms of these remote effects and show that they depend on the excitability of the functional connections between the areas at the time of study. Breakdown of these network wide effects in the elderly could potentially limit the usefulness of these methods.
Disclosure: Nothing to disclose.

FW03_3

Connectivity disturbances in stroke as revealed by integrated multimodal neuroimaging by fMRI, EEG and TMS-EEG

P.M. Rossini
Rome, Italy

Abstract: Post-stroke brain plasticity has been repeatedly investigated via functional neuroimaging techniques mainly based on blood flow/metabolism. However, little is known concerning how topological properties of widely distributed neural networks could be modulated by location and size of focal ischemic brain lesions in the acute stages. In this direction, recent studies have provided insight into functional organisation after stroke from the viewpoint of network topology, suggesting that brain lesions can provoke changes in the spontaneous functional architecture of the brain connectivity and constrain clinical output and eventual recovery. A relatively new approach to study the brain function in neuroscience is the „functional connectivity" analysis, namely the synchrony in time of activity in anatomically−distinct but functionally−collaborating brain regions. There is increasing evidence to support the concept that brain plasticity after stroke involves distinct functional and structural components, each requiring several cellular mechanisms operating within an extremely complex framework. However, the precise relationship between functional and structural components of brain plasticity/connectivity is still unclear and its explanation represents a major challenge within modern neuroscience. It is believed that effective connectivity and optimal network structure are essential for proper information processing in the brain; indeed, functional abnormalities of the brain are found to be associated with pathological changes in connectivity and network structures. An integrated approach utilising neurophysiological techniques, including electroencephalography (EEG) and transcranial magnetic stimulation (TMS), together with biological markers and structural and functional imaging (MEG, fMRI) is a promising and non−invasive method to test these phenomena and to deliver possible rehabilitation treatment.
Disclosure: Nothing to disclose

Ability to drive in neurological disorders

FW04_1

Fitness to drive in sleepy patients

J. Mathis
Berne, Switzerland

Abstract: The judgement of an individual patient's fitness to drive is part of the general duties of all physicians in every consultation. The decision for or against granting permission to drive is based on a comparison of all risk factors combined including, but not restricted to, the risk associated with a specific disease from a patient's perspective and the accepted range of risk from a societal perspective.

With an odds ratio of 3.5 for motor vehicle accidents compared to the general population, sleepy patients rank highest among all patient groups and are the only group to rank above the accepted odds ratio of 2.0 as observed in healthy subjects with a blood alcohol concentration below 0.5 per mil. In patients suffering from sleepiness due to a specific disorder, apart from the severity of sleep pressure, the rate of motor vehicle crashes can be influenced by the effectiveness of compensation strategies, individual risk taking behaviour and the well-established general risk factors such as young age, male sex, shift work, inadequate sleep hygiene and driving at night.

It is a well-accepted and scientifically proven fact, that sleepiness at the wheel is always subjectively perceived before any driving impairment occurs. As a logical consequence, the responsibility of not driving when sleepy can theoretically be delegated from the physician to the patient, as long as the patient can be considered legally competent. Nevertheless it is the duty of the physician to inform the patient about the legal consequences of this convention, namely that any crash due to sleepiness at the wheel is considered as negligent behaviour and would be punished accordingly: In addition to the withdrawal of their licence, the driver also faces the risk of receiving a fine or a prison sentence, and their actions not being covered by insurance.

The physician also has the duty to inform his patients about the effective countermeasures against impending sleepiness at the wheel. In contrast to the frequently applied, but insufficient, measures of opening a window, listening to loud music or smoking while continuing to drive, stopping in a rest area and drinking a coffee and napping are the only effective countermeasures. Apart from the adequate treatment of any sleep-wake disorder, regular and sufficient sleep before driving is a particularly important prerequisite of safe driving in sleepy patients.

The practical procedure regarding how physicians should act depends on the legal rules of the country. In countries with a mandatory "categorial reporting", the authorities must be informed of the diagnosis, and the practical steps for judging the permission to drive will be indicated by the authorities. In countries without mandatory categorial reporting, the following procedures can be considered: Professional drivers and private drivers after any type of motor vehicle accident, with serious co-morbidities or with suspected risky behaviour should be referred to a sleep-wake centre for objective sleepiness assessment, respecting a waiting period until efficient treatment. Private drivers without the previously mentioned risk factors should be informed of their responsibility when driving and treated within 3 months, without necessarily requiring a waiting period.

Disclosure: Nothing to disclose.

FW04_2

Fitness to drive after the first epileptic seizure

T. Marson
Liverpool, United Kingdom

Abstract: Seizures are the most common medical cause of motor vehicle accidents. Following a first seizure, the risk of a subsequent seizure is highest immediately following that seizure and diminishes over time. When deriving policy to inform decisions about returning to drive, a decision has to be made as to the level of risk of a subsequent seizure that is acceptable. This was considered by an EU working group on driving and epilepsy that reported in 2005. The recommendation is that an individual can return to group one driving (ordinary motor vehicle) once their risk of a seizure in the next 12 months drops below 20%. This information was used when drafting EU legislation, which was followed by harmonisation of driving standards across EU countries. Further analysis of the Multi-centre Study of Early Epilepsy and Single Seizures (MESS) indicates that in general it takes 6 months following a single unprovoked seizure for the risk of a further seizure in the next 12 months to drop below 20%. Consequently the EU legislations would allow a return to driving once 6 months seizure free. However, first seizure populations are heterogeneous and individuals at higher risk of seizures can be identified, including those with a remote symptomatic seizures, and abnormal EEG or MRI brain scan. EU member states are allowed to implement stricter legislation, as does the UK, which requires 12 months seizure freedom for individuals with an abnormal EEG (Epileptiform) or MRI scan.

Disclosure: Nothing to disclose

FW04_3

Fitness to drive after stroke

C. Lundberg

Stockholm, Sweden

Abstract: Post-stroke conditions have the potential to affect fitness to drive and a people who have sustained a stroke should therefore be assessed medically /cognitively before resuming driving. Factors to consider include the risk of recurrence, the risk of seizures, the presence of visual field defects, or cognitive deficits. Physical limitations might require a technical adaptation of the vehicle. Guidelines regarding the time limit before returning to driving and limitations to driving vary across countries.

Studies of the performance of post-stroke drivers on in-traffic tests show that many score poorly and that they have a diversity of deficits in critical driving-related skills. There is also evidence that the site of lesion, more than laterality as such, is correlated to specific aspects of driving performance. Awareness of deficits may also be a crucial aspect related to driving performance. Cognitive tests tapping complex functions such as speed-related flexible processing, executive functioning and attention are reported to classify unsafe drivers with a high degree of accuracy.

Many post-stroke drivers with diminished driving skill may benefit from behind-the-wheel or simulator training. However, it appears that that the advantage of targeted training observed at 6 months post-stroke is not seen after 5 years.

Several investigations have found that post-stroke drivers have an increased relative risk of crashes (ranging from 1.9 to 7.7), but there is also evidence to the contrary (0.8). This may reflect the limitations of these studies, due to methodological issues.

Disclosure: Nothing to disclose.

Overarching Theme:
Familial amyloid polyneuropathy: phenotype, genetics, treatment

FW05_1

60 years of transthyretin familial amyloid polyneuropathy in Europe: epidemiology, clinical presentation and genetic basics

T. Coelho
Porto, Portugal

Abstract: Familial amyloid polyneuropathy is nowadays included in the group of ATTR amyloidoses, a group of conditions distributed worldwide, either related to the presence of transthyretin (TTR) mutations or simply to the aging process and characterised by the deposition of systemic extracellular amyloid.

Neuropathy and cardiomyopathy are the most common clinical aspects, leading always to a severe, progressive and ultimately fatal progression.

Inherited forms have autosomal dominant transmission with variable penetrance, age and gender dependent. More than 130 pathogenic mutations are present worldwide with an asymmetric distribution. TTRVal30Met mutation is the most frequent and is also related to the largest disease clusters in the world. In Europe the main foci related to TTRVal30Met mutation are Portugal, Sweden, Balearic Island and Cyprus and present a large range of age-of-onset. Otherwise many different mutations are increasingly recognized across Europe associated with isolated families or smaller clusters, such as TTRGLu89Gln in Bulgaria, Italy and Balkan area and Thr60Ala in North Ireland.

Age-of-onset may be early (<50years) and late. These categories have different pathological and clinical aspects. Early onset patients show predominantly a small fiber neuropathy, with severe autonomic dysfunction. Late onset patients present a sensory and motor axonal neuropathy frequently associated with severe heart disease and other organ involvement (kidney, eye).

Because penetrance can be extremely low many patients present as sporadic cases with no family history. In these cases misdiagnosis and delayed diagnosis can be a major problem, particularly nowadays when many different disease modifying treatments became available.

Disclosure: Nothing to disclose.

FW05_2

The course and prognostic factors

L. Obici
Pavia, Italy

Abstract: Hereditary transthyretin amyloidosis (hATTR) is characterised by high genetic and phenotypic variability, with differences in disease presentation and progression across different populations and geographical regions. The most common TTR pathogenic variant, Val30Met, clearly exemplifies such significant heterogeneity in clinical presentation and disease course, being associated with two different phenotypes, indicated as early-onset and late-onset respectively. Differences include not only the age at disease onset but also the pattern of organ involvement, with small-fibre neuropathy, severe autonomic dysfunction and nephrotic renal damage dominating in the first case, whereas in patients with the late-onset phenotype the disease is heralded by bilateral carpal tunnel syndrome and usually manifests with early involvement of larger sensory and motor nerve fibres and mild autonomic neuropathy. Moreover, a progressive cardiomyopathy with a hypertrophic phenotype typically occurs in late-onset patients but it is not observed in the early-onset population. Finally, differences occur also in response to treatment, with higher beneficial effect from liver transplantation and treatment with tafamidis in early-onset patients, resulting in better outcome. Neuropathy progression occurs relentlessly in the absence of treatment, with walking impairment and wheel-chair requirement within a few years. The rate of disease progression and outcome may vary according to the underlying TTR mutation. The nutritional status at diagnosis also impacts on prognosis. In particular, early onset of diarrhoea is associated with shorter survival, malnutrition, and increased mortality after liver transplantation. Additional prognostic factors include the serum cardiac biomarkers NT-proBNP and troponin.

Disclosure: Nothing to disclose.

FW05_3

Recent advances in therapy

I. Conceicao

Lisbon, Portugal

Abstract: Hereditary amyloidosis related to transthyretin (hATTR) is a multisystemic disease with a wide range of genotype/phenotype variability follow-on from deposition of insoluble ATTR amyloid fibrils in various organs and tissues.

Treatment options for FAP focus on stabilising or decreasing the amount of circulating amyloidogenic protein (transthyretin). Orthotopic liver transplantation, the first approved therapy for hATTR, reduces mutant TTR levels, with improved survival reported in patients with early-stage ATTRV30M. The enthusiasm for liver transplantation for hATTR was dampened by poor outcomes among patients with mutations other than V30M, late stages disease, mortality and morbidity subjacent to the procedure.

The TTR stabilizers as tafamidis and diflunisal have been proved to slow the rate of disease progression, being tafamidis the only approved drug therapy in early-stage hATTR. However disease progresses in some patients besides treatment, as well late stages disease patients have not available treatments, highlighting the need for new, disease-modifying treatment options for hATTR.

The reduction of the amyloidogenic protein (TTR), wild type and mutated, have been recently showed to be possible with Inotersen an antisense oligonucleotide, or Patisiran a small interference RNA. Positive results on 2 phase III trials on these TTR gene modifiers, have been recently released. Synergistic effect of doxycycline and tauroursodeoxycholic acid on dissolution of amyloid is under investigation. Furthermore, immunotherapies targeting the amyloid deposits are being explored.

The evolving treatment landscape for ATTR amyloidosis brings hope for further improvements in clinical outcomes for patients with this debilitating disease.

Disclosure: Nothing to disclose

Sunday, June 17 2018

EAN/MDS-ES: Management of Parkinson's disease in non-routine circumstances

FW06_1

Fasting during Ramadan

P.G. Damier[1], J. Al-Hashel[2], W.A. Kamel[2]
[1]Nantes, France, [2]Kuwait city, Kuwait

Abstract: Most Parkinson's disease (PD) patients need regular multiple daily administration of dopamine-replacement medication to control the symptoms. Although thousands of Muslims with PD around the world fast during the Ramadan, to our knowledge there are no published analyses on the medical management of the disease during this period.

The Islamic practice of fasting during Ramadan is not mandatory in the case of chronic disease but many believers still want to fast even at the risk of damaging their health.

In case of PD, interrupting treatment might worsen motor symptoms and even lead to a severe withdrawal syndrome. Although no specific studies on this topic have led to formal recommendations, there are some options for adapting the treatment for patients who fast during Ramadan. The general principle is based on switching most of the patient's PD treatment to an equivalent dosage of a dopamine agonist that can be administered once daily or by transdermal patch, and on having an intake of L-DOPA before dawn and one after dusk. However, such an option is only feasible for patients who require a moderate amount of PD treatment and can tolerate dopamine agonist therapy.

We applied this principle in a prospective study conducted in 20 PD outpatients in Kuwait city. Six patients were able to abstain from drug intakes from dawn to dusk; the others needed 1 or 2 intakes of L-DOPA during the day. There were no serious side effects reported during the Ramadan period.

Disclosure: Nothing to disclose

FW06_2

Travelling Abroad

E. Ruzicka
Prague, Czech Republic

Abstract: Travelling on medium and long distance trips is now part of the lifestyle. Even patients with chronic neurodegenerative diseases such as Parkinson's disease (PD) should not be excluded from travel, whether for work, family or for relaxing touristic reasons. Traveling, however, involves a number of difficulties and risks that are increasing in people with PD.

On the road, daily routines change and sometimes completely disrupt. Travellers are confronted with unusual external conditions such as time zone changes and temperature shifts. Insufficient water intake is almost a rule, as well as irregular feeding and irregular medication intake with an increased risk of under- or overdose. There is a risk of general health complications such as venous thrombosis, cardiovascular events, and infections. A common travel event such as lost luggage may represent an additional problem due to the loss of antiparkinsonian drug supply.

PD-specific signs can increase during the trip due to dehydration, lack of sleep, missed medication doses, etc. On the other hand, side effects of drugs may appear, including dyskinesias, impulsive and compulsive behaviors, hallucinations or delusions particularly in PD patients with cognitive dysfunction.

The risks associated with urgent medical care on a trip include non-recognition of PD. This may result in withdrawal of anti-PD drugs or prescription of neuroleptics and other contraindicated medications. In addition, unavailability or different names of antiparkinsonian drugs can lead to problems, especially in less developed countries. Patients treated with deep brain stimulation or infusions of Duodopa or Apomorphine are exposed to additional risks.

Travel Tips for Patients with Parkinson's Disease (PD)
1. Choose the right destination for your vacation trip, corresponding to your state of health. Talk to your doctor (GP, neurologist or PD nurse).
2. Make sure to have a full health insurance and valid travel insurance in all countries on your trip. Specific vaccinations may be needed in advance when traveling to certain countries.
3. Take care to book the corresponding travel and accommodation conditions (air, car or rail; ground floor, stairs or lift, regular or disabled room).
4. Take with you and always carry a card with brief information about your disease in English and the language of the final destination, as well as your medication list and daily schedule. A medical certificate for diagnosis and medication may be needed in some countries.
5. Ask your doctor about the prevention of deep vein thrombosis during long flights.
6. Prepare for baggage loss - during air travel, keep the drug supply for the entire trip in the carry-on baggage and during the entire trip, always keep the drug supply for at least 48 hours on you (e.g., in a belt pocket).
7. Pay attention to appropriate clothing to avoid overheating or cold during the trip and at the final destination
8. Drink enough fluid (= more than usual) and avoid alcohol, especially during long flights.
9. Keep the medication as close as possible to your usual schedule. During long flights and when traveling across time zones, maintain the usual intervals between drug doses (i.e. you may need taking an extra dose). Since the next day, switch the dosing schedule to the new time zone.

Travelling Abroad Evžen Růžička, Dept. of Neurology, Charles University, Prague
Focused Workshop EAN Congress Lisbon 2018 "EAN/MDS-ES: Management of Parkinson's disease in non-routine"

Travel Tips for Patients with Parkinson's Disease

Disclosure: Nothing to disclose

FW06_3

Undergoing a surgical procedure

H. Reichmann

Dresden, Germany

Abstract: Both patients and caregivers but also treating physicians are concerned about complications along with surgical interventions. A major problem is abrupt cessation of anti-Parkinson medication, which leads to manifold disturbances, sometimes even to an akinetic crisis. There are several means to guarantee continuous dopaminergic stimulation even in patients that are not allowed to take medication orally before they undergo surgery. Amongst others rectally applied levodopa, amantadine infusions, and especially the use of a rotigotine patch are good means to overcome oral intake. Perioperative management is important due to the fact that in Germany alone each year more than 10,000 PD patients undergo surgery. Main reasons for this are fractures, but also elective interventions. Further emergency situations that cause treatment as an inpatient are psychosis, motoric disability, but also pneumonia and cardiovascular disturbances. In contrast PD patients suffer less often from cancer.

Disclosure: Professor Reichmann was acting on Advisory Boards and gave lectures and received research grants from Abbott, Abbvie, Bayer Health Care, Bial, Boehringer/Ingelheim, Brittania, Cephalon, Desitin, GSK, Lundbeck, Medtronic, Merck-Serono, Novartis, Orion, Pfizer, TEVA, UCB Pharma, Valeant, and Zambon

FW06_4

Can people with PD drive?

J. Ferreira

Lisbon, Portugal

Abstract: Although there are many factors affecting a person's fitness to drive, it has been reported that people with Parkinson's Disease (PD) have driving impairments, stop driving earlier than non-PD controls and have a higher rate of cancellation of their driving license. Likewise, driving capabilities also decline with disease progression.

Due to the risks associated with on-road driving, practitioners need to have criteria to identify at-risk patients. Although robust predictors of fitness to drive are missing in PD, the best data available associates aggravation of driving performance with a cognitive deterioration, aggravation of motor function and impairments in visual perception. Like with other motor tasks in PD, the effects of distraction on driving performance should also be considered.

Interestingly symptomatic treatment and DBS seems to have a beneficial effect on driving ability.

Currently, there are no PD-specific recommended tests to evaluate driving ability and predict on-road driving safety in persons with PD.

In addition to the anticipated factors related to cognition and motor impairment, drivers with PD may be also at risk for unsafe driving in low-contrast visibility conditions such as during fog or twilight. For this reason, contrast sensitivity screening may be added to the screening tests of potentially at-risk drivers with PD.

Disclosure: Nothing to disclose

Epilepsy surgery in 2018: Has anything changed in the last decades?

FW07_1

Update on the concept of drug resistance. When should pediatric and adult patients be referred for epilepsy surgery?

E. Hirsch
Strasbourg, France

Abstract: In 2010, Kwan P et al. published a New Definition: "Drug resistant epilepsy may be defined as failure of adequate trials of two tolerated and appropriately chosen and used AED schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom. Trials of two tolerated and appropriately chosen and used AED schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom". "New" drug resistance definition does not seems to change patients' referrals. But development of minimally invasive procedures, had influence patient referral until they seems to have limited sides effects. Thermo-coagulation, destruction/disorganisation of "Epileptogenic zone" or" network" became part of therapeutic surgical procedure. This could done by using, Laser MRI guided and SEEG guided radiofrequency lesioning. New definitions (Fischer R et al., 2014) and classification of epilepsies (Scheffer I et al, 2017) influenced referral and strategy of patients with drug resistant focal epilepsies. More and more, epilepsy surgery teams try to improve not only epileptic seizures frequency but cognitive-psychiatric status, risk of sudden death, epileptic encephalopathies. Knowledge that multiples etiologies participate to epileptogenesis influence patient referral. However, precision individualised epilepsy surgery is far to be already a realistic goal, even if Genetic and Immunologic status are routinely evaluated during pre-surgical workup even in patients with structural epilepsies. So patient referral changed probably because epilepsy surgery has improved outcomes over time with less side effects and reduction of the invasiveness of surgical procedures. Such surgical techniques influence patients' selections depending of medico-surgical teams' experiences and mentalities.
Disclosure: Nothing to disclose

FW07_2

Common and not so common surgically remediable syndromes

C. Baumgartner
Vienna, Austria

Abstract: Epilepsy surgery is a valuable treatment option for patients with medically refractory epilepsy. The two goals of epilepsy surgery are (1) seizure-freedom by resection of the epileptogenic tissue through an exact delineation of the epileptogenic zone and (2) avoidance of neuropsychological or neurological deficits by localisation of eloquent cortex. Recent improvements in epilepsy surgery include (1) a better understanding of the natural history of epilepsy, i.e. recognition of epilepsy syndromes with low probability of successful medical treatment, but high surgical success rates, (2) technical advances of presurgical evaluation with a better delineation of the epileptogenic zone providing a surgical option for more patients and a better identification of eloquent cortex facilitating exact counseling of patients at risk for postoperative (neuropsychological) deficits, (3) improvement of surgical techniques and development of alternative surgical approaches, and (4) surgery early in life (epilepsy surgery in childhood) and in the disease process (early referral). The following surgically remediable epilepsy syndromes can be distinguished: (1) syndromes with focal pathology amenable to restricted (unilobar) excisions including mesial temporal lobe epilepsy with hippocampal sclerosis, malformations of cortical development - focal cortical dysplasia, benign/low grade tumors, cavernous angiomas, other pathologies (postencephalitic and posttraumatic lesions etc.) and focal epilepsy with normal MRI (MRI negative epilepsies), (2) conditions that may require more extensive, multilobar excisions or hemispherotomy including extensive cortical dysplasia, hemimegalencephaly, Sturge-Weber syndrome, pre- and post-natal vascular lesions, Rasmussen's syndrome etc., and (3) conditions amenable to disconnective surgery including patients with frequent drop attacks and Landau-Kleffner syndrome.
Disclosure: Nothing to disclose.

Impact of technology in neuro-rehabilitation

FW08_1

Rehabilitation of hand function post-stroke: Application of research based technology

V. Dietz

Zurich, Switzerland

Abstract: In recent years it has become evident that, in a number of functional movements, synergistically acting limbs become task-specifically linked by a soft-wired 'neural coupling' mechanism (e.g. both hands during cooperative hand movements. Experimentally this mechanism became evident by the analysis of reflex responses as a marker for a neural coupling during cooperative hand movements. It is reflected by the task-specific appearance of reflex EMG responses to non-noxious nerve stimulation, not only in muscles of the stimulated arm, but also, with the same long latency, in muscles of meaningful coupled (contralateral) forearm. After a stroke, nerve stimulation of the unaffected arm during such cooperative tasks is followed by EMG responses in muscles of the (contralateral) coupled paretic arm, i.e. unaffected motor centres support synergistically acting movements of the paretic limb. In contrast, following stimulation of the affected arm, no contralateral responses appear due to defective processing of afferent input. As a consequence, it may be therapeutically possible to strengthen the influence of unaffected motor centres on the performance of affected limb movements through training of cooperative limb movements using a device ('opening a bottle') that allows the training of tasks required during activities of daily living.
Disclosure: Nothing to disclose.

FW08_2

Robotic support for cognitive therapy of hand function

O. Lambercy

Zurich, Switzerland

Abstract: In this lecture, I will review and discuss novel approaches in robot-assisted therapy of hand function after stroke, which aim at maximally exploiting the potential of robotics. In addition to increasing exercise intensity, therapeutic robots also allow to precisely control interaction with the patient. Sensors embedded in robots can be used not only to control the device, but also to provide an objective and continuous evaluation of sensorimotor deficits. As a result, the nature and difficulty of the therapy exercises can be automatically adapted to the current capabilities of the patient in order to maximize active participation and motivation. In particular, I will share our experience from a randomised controlled trial on neurocognitive robot-assisted rehabilitation that focused on the integration of motor, cognitive and somatosensory aspects of movement into therapeutic exercises.
Disclosure: Nothing to disclose.

FW08_3

Robotic technology in the rehabilitation of gait after a stroke and spinal cord injury

K. Jahn

Bad Aibling, Germany

Abstract: Improving gait after a structural lesions in brain and spinal cord requires (1) the ability to keep the body upright and (2) training of the cyclic quadrupedal movement patterns that characterise locomotion. The best way to improve gait abilities is training of natural overground locomotion in demanding environments. However, in severely affected patients this is not possible. Using robotic assisted systems allows many repetitions of step cycles and step-wise adaptation of external support. About 75% of stroke patients show impairment of stance and gait. The majority of them re-learns how to walk after intensive neurorehabilitation, but full recovery is rare. Further, 75% of stroke patients fall >1x in the first 6 month after the event; the risk for fractures is highly elevated. There is high evidence for interventions favoring intensive high repetitive task-oriented and task-specific training in all phases post stroke. Effects are mostly restricted to the actually trained functions and activities. During this presentation the technology available to support gait rehabilitation using exoskeletons and endeffector systems will be reviewed. Scientific evidence shows that robotics do support motor recovery, e.g. via high repetition rates and high motivation of patients. Robotics further support the therapist, but they are only one part in the rehabilitation program of stroke patients. For the future, quantitative data, e.g. sensors from robotic devices, should be used better to improve rehabilitation programs. Mathematical models might also help improving technology and protocols in the future.
Disclosure: Nothing to disclose

Overarching theme: Novel genetic techniques in neurological practice – time for responsible clinical and research implementation

FW09_1

What should the general neurologist know about Next Generation Sequencing (NGS)?

H. Houlden
London, United Kingdom

Abstract: Next-generation sequencing (NGS) is increasingly being applied to clinical testing and gleaning knowledge on the application, interpretation and shortcomings are essential for the all neurologists. This practice is only predicted to grow especially in neurology clinics because many of the patients with monogenetic causes and the significant heterogeneity.

The cost of sequencing has been steadily decreasing, but the cost of DNA sequencing is a minor part of the total cost of the patient journey. Downstream data analysis, storage, and interpretation account for most of the expense. In patients with nonspecific neurologic disorders in which an extensive number of genetic differential diagnoses exist, whole-genome sequencing (WGS) or whole-exome sequencing (WES) has shown promise in the identification of genetic causes. However, coverage and ethnicity often create unexpected findings in genes unrelated to the initial sequencing indication. Targeted-panel NGS starts with the capture of a set of disease-focused genes, followed by massive parallel sequencing. For many genetically heterogeneous neurologic disorders, a genetic panel that is disease focused yet inclusive of a large genetic differential diagnosis can be defined to reduce cost and optimize performance. There are still drawbacks to the current sequencing technologies and the future may hold other methods such as long read and nanopore technology.

In this talk, I provide an overview of WGS, WES, and targeted-panel NGS in the practical neurogenetics clinic and the utility in clinical testing for general inherited neurologic diseases with examples and videos.

Disclosure: Nothing to disclose

FW09_2

Interpretation of NGS test: neurological disease and beyond

T. Gasser
Tübingen, Germany

Abstract: Genetic testing for mutations causing inherited neurologic disorders has become an important part of the modern diagnostic work-up. The results of genetic tests were still relatively easy to understand also for the general neurologist, when single-gene Sanger sequencing was used to identify missense or nonsense mutations in clearly defined clinical syndromes. Since next-generation sequencing (NGS) technology has in most instances replaced Sanger sequencing, the interpretation of test results have become much more challenging. NGS tests interrogate not a single, but usually dozens or even hundreds of genes, or the entire coding sequence of the human genome (exome). This usually results in the identification of numerous genetic variants and their potential pathogenetic role in the disorder under investigation needs to be carefully examined. The situation is complicated further by the fact that the widespread use of sequencing has shown that most human disease genes can result in a wider spectrum of clinical manifestations than previously recognised (a phenomenon called "pleiotropy"), and that, conversely, mutations in a large number genes can contribute to most clinical phenotypes ("genetic heterogeneity"). In order to make sense of NGS test results, the neurologist needs a thorough understanding of these clinico-genetic correlations. It is also necessary to understand the major determinants of pathogenicity of a genetic variant, the contribution of common and rare genetic variability to the total genetic risk, as well as the use of genetic databases and pathogenicity prediction programs in the process of interpretation of genetic tests.

Disclosure: Nothing to disclose

FW09_3

The use of genetic information in the context of clinical trials

C. Sampaio

Lisbon, Portugal

Abstract: There is a wealth of information on the use of genetic markers in the context of oncologic clinical trials, mostly as stratifiers or predictors of response. Oncology trials have several specificities that set them apart. We will not include them in this discussion. We are also excluding from this framework gene therapy trials, which by definition imply the manipulation of a gene what involves genetic information.

Genetic information (GI) in non-oncologic, neurology trials have two main, current uses: 1) Definition of target population either by diagnostic or predictive testing or subtyping; 2) Risk Stratification. GI may potentially be used for hypothesis testing of genotype X environment (drug or intervention) interactions and, as in all prospective, human studies GI can be the matter of "incidental findings". In any of the four circumstances here defined (population targeting, risk stratification, hypothesis testing or incidental finding) there is a critical ethical dimension related to the use of GI. The ethical discussion is especially complex1 when predictive testing is a requisite for trial participation (e.g., Huntington's Disease (HD), Familial Alzheimer's Disease (FAD), FrontoTemporal Dementia (FTD)). This complexity will be addressed.

Technically, trial designs that involve subtyping or risk stratification (Stereoisomer oligonucleotides in HD, Ibiglustat in PD, Exon-skipping therapy in Duchenne) imply several statistical, operational and regulatory challenges that deserve commentary.

Sampaio, C. Levey, J. and Klitzman, R. (2018), Predictive testing and clinical trials in Huntington's disease: An ethical analysis. Mov Disord., 33: 243-247. doi:10.1002/mds.27247

Lost in space - clinical and neurobiological aspects of topographagnosia

FW10_1

The map cannot be explored - disorders of spatial exploration in neglect (perceptive topographagnosia)

M. Husain
Oxford, United Kingdom

Abstract: One of the most striking disorders of space exploration observed in humans is that associated with the neglect syndrome. In particular, patients with left-sided neglect following right hemisphere stroke often suffer from a profound unawareness of space to their left and fail to explore leftwards.

In many conceptualisations of this deficit, researchers have envisaged the problem to be one of mapping egocentric space (space with respect to body co-ordinates such as the trunk, head or direction of gaze). In addition, others have also presented evidence in favour of a deficit in the brain's ability to remap space after movements of body parts, including – crucially – that of the eyes. These formulations have led to a model in which the right posterior parietal cortex plays a crucial role in mapping the external world with respect to the body.

Other evidence suggests that rather than a sector of space being neglected – and unexplored – the key deficit in neglect is a directional impairment. According to this view, damage to one parietal lobe leads to an imbalance in attention, with items on the ipsilesional side of space winning in the competition for attention.

In this talk I shall present the evidence for these points of view as well as data which shows how the degree of neglect – and the extent of space exploration – can be modulated by dopaminergic and noradrenergic drugs.

Disclosure: My research is supported by The Wellcome Trust.

FW10_2

The map is distorted - disorders of the perceptual analysis of space (apperceptive topographagnosia)

W. Heide
Celle, Germany

Abstract: Topographagnosia, also known as topographical or spatial disorientation, is an inability to orient oneself in one's surroundings ("lost in space"), read maps, draw plans, or perform similar functions, often associated with focal damage to the right parietal or temporal lobe. Associative topographagnosia is an inability to use selective spatial information (e.g. landmarks) for orienting in familiar surrounds and to associate the preserved perception of spatial relations with the stored knowledge of them ("spatial map"). However, this lecture will be about apperceptive topographagnosia, which is a failure of the perceptual analysis of space, even though the basic visual functions and other mental processing, such as spatial memory are preserved. These patients are impaired in integrating spatial features such as lines, orientations, angles, distances, 3D objects, and coordinates (vertical, horizontal, straight ahead) unto a stable percept of egocentric space (the map is "distorted", but preserved in memory). As a result, they cannot perform tasks requiring copying, matching, or drawing figures ("visuo-constructive apraxia"). This lecture will particularly review deficits of maintaining spatial constancy, - the important ability to continuously update ("remap") the percept of egocentric (gaze- or body-centered) visual space by correcting for intervening eye, head or body movements, using visual, vestibular and efference copy signals about these active movements. The critical cerebral site for these functions is the posterior parietal cortex around the intraparietal sulcus, which has been demonstrated not only in monkey experiments, but in numerous lesion, fMRI or MEG/EEG studies in humans during the last 20 years.

Disclosure: Nothing to disclose

FW10_3

The map is lost - disorders of spatial memory (associative topographagnosia and topographical amnesia)

J. Laczó
Prague, Czech Republic

Abstract: Orientation in one's environment requires effective spatial exploration and perceptual analysis of space. As the next step, acquired spatial information has to be encoded, stored and later retrieved. This process called spatial memory is a key process for spatial navigation, the ability of knowing where you are and knowing how to get to places that you want to get. Generally, two frames of reference are used to specify the remembered locations of objects. The egocentric frame of reference defines the location of an object relative to the observer's body (subject-to-object relation – viewpoint dependent). The allocentric frame of reference defines location of an object relative to the location of other objects (object-to-object relation – viewpoint independent). Spatial memory and spatial navigation depend on neural networks, within which the lesion, electrophysiological and functional imaging studies have identified the most important brain areas including the hippocampus, entorhinal, perirhinal, retrosplenial, posterior parietal and prefrontal cortices. Impairment of spatial memory and spatial navigation is common in many neurodegenerative diseases, especially in those primarily causing dementia including Alzheimer's disease, and may accompany many neurological disorders including epilepsy, developmental, traumatic and vascular diseases. Therefore, assessment of spatial memory and spatial navigation abilities may be beneficial for obtaining a comprehensive cognitive profile of patients with impairment of higher cortical functions. Recently, there have been introduced neurorehabilitation training programs aiming to improve navigation abilities in neurological patients with brain lesions.

Monday, June 18 2018

CGRP Inhibition for Migraine Prevention – hype or hope?

FW11_1
Rationale of blocking CGRP

M. Ashina
Copenhagen, Denmark

Abstract: Calcitonin gene-related peptide (CGRP) is widely distributed in the central and peripheral nervous system including in the trigeminovascular system. It is expressed in perivascular trigeminal sensory afferents and dilates human cerebral arteries. Furthermore, CGRP is released upon activation of trigeminal ganglion and causes migraine like attacks in patients with migraine with and without aura. Taken together, these studies demonstrated that CGRP is a key signaling molecule in migraine pathophysiology and that CGRP receptor antagonists and antibodies against CGRP and its receptor are a new target in migraine treatment.
Disclosure: Nothing to disclose.

FW11_2
Clinical Results

U. Reuter
Berlin, Germany

Abstract: Monoclonal antibodies (mAbs) targeting CGRP will most likely be available for prescription in several European countries late 2018/2019. One of these mAbs is directed against the CGRP receptor (erenumab), while three mAbs are targeting the CGRP peptide (eptinezumab, galcanezumab, fremanezumab). These antibodies have advanced to randomized placebo controlled phase III trials for the prevention of migraine. We will demonstrate the design and character of these phase III trials for all mAbs and show primary endpoint data. Results for the secondary endpoint such as quality of life data, the reduction of monthly acute anti migraine medications will be illustrated and so will be long term data if available. In addition, we intend to discuss data which are specific for mAbs such as onset of efficacy or treatment results in treatment failure subjects. It is our goal to provide the audience with a comprehensive overview of this new substance class.
Disclosure: Nothing to disclose.

FW11_3
Clinical interpretation

M. Ferrari
Leiden, Netherlands

Abstract: Calcitonin Gene-Related Peptide (CGRP) is a vasoactive neuropeptide involved in neurogenic inflammation and neuronal pain signalling. CGRP is released during migraine attacks. Experimental infusion of CGRP may provoke migraine-like attacks in migraineurs but not in people without migraine. Recently published phase 2 & 3 trials with four different monoclonal antibodies (MABs) against CGRP or its receptor, have all shown prophylactic efficacy in episodic and chronic migraine. The tolerability was excellent. The emerging picture is that while the average therapeutic gain versus placebo is limited (only a few days greater reduction from baseline), in a subgroup of patients the reduction in attack frequency is clinically highly relevant. Moreover, compared to historical data from existing migraine prophylactic agents, the tolerability of this new class of drug appears to be considerably better. Head-to-head comparator trials versus current migraine prophylactics should be conducted to assess the relative efficacy and tolerability profile of CGRP (receptor) MABs and to determine their potential role in the management of migraine. A major challenge will be how to identify responders for patient specific "precision medicine". Finally, as CGRP release is one of the rescue mechanisms in cerebral and cardiac ischaemia, it will be crucial to study cardiovascular safety in patients getting CGRP (receptor) MABs.
Disclosure: Nothing to disclose.

Overarching Theme:
Neurogenetic avenues and new
directions on risk factors in dementia?

FW12_2

Large data bases, big science?

P.J. Visser
Maastricht, Netherlands

Abstract: Alzheimer's disease (AD) is the most common form of dementia. There is yet no treatment available and many clinical studies investigate the underlying pathophysiology, prognosis, and diagnosis of AD. Collaborations between individual studies will increase sample size and this will likely foster progress in clinical AD research. The European Medical Information Framework for Alzheimer's disease (EMIF-AD, www.emif.eu) was set-up to facilitate combining and re-using AD-related data. Aim of this presentation is to briefly outline the structure of EMIF-AD and to present findings from two collaborative studies initiated by the project. The first study is the EMIF-AD biomarker discovery study. Aim was to develop diagnostic and prognostic markers for predementia AD. We selected 1221 individuals from 11 European longitudinal cohort studies and performed central proteomic, metabolomic, genomic, epigenomic and imaging analyses using existing MRI scans and plasma and cerebrospinal fluid samples. The second study is the Amyloid Biomarker Study Group. This initiative is a subject-level meta-analysis of over 10.000 individuals from over 50 cohorts worldwide. The study has provided estimates of the prevalence of predementia AD, information on riskfactors for amyloid pathology, and information on the effect of amyloid pathology on cognition in non-demented individuals. Both studies demonstrate the power and efficiency of reusing existing data and samples. Future plans of EMIF-AD will be discussed.

Autoimmune encephalitis in the Intensive Care Unit (ICU)

FW13_1

New concepts in etiology and disease mechanisms in autoimmune encephalitis

H. Prüss
Berlin, Germany

Abstract: The various clinical manifestations of autoimmune encephalitis made this disease group an exciting new field in Neurology and Psychiatry. Identification of numerous pathogenic auto-antibodies against neuronal tissue resulted in unprecedented diagnostic and therapeutic opportunities. This has led to a critical reappraisal also of symptoms in patients in the intensive care unit (ICU), and in some instances resulted in re-classification of disease.

We could recently show that patient-derived monoclonal autoantibodies against neuronal surface proteins are sufficient to cause receptor internalization and synaptic changes underlying clinical disease. This has immediate implications for ICU patients: given their pathogenicity, the primary goal of treatment must be the removal of auto-antibodies using sufficiently aggressive state-of-the-art immunotherapy. The technological achievement of recombinant generation of disease-causing human auto-antibodies will allow in the future (i) to clarify the specific role of a given auto-antibody for the disease mechanisms, including down-regulation of synaptic proteins or membrane receptors; (ii) to identify novel antibodies targeting yet unknown epitopes on neuronal or glial surfaces; (iii) to explain immunological triggers for better understanding of disease etiology; and (iv) to provide molecular tools for improved research into autoimmunity by using these human antibodies for high-resolution molecular imaging and animal models.

Findings from these studies will likely change the current diagnostic concepts in ICU patients. It has become clear that the perpetual discovery of novel antibodies will continue and ultimately result in a better understanding of pathomechanisms and therapies
Disclosure: Nothing to disclose

FW13_2

"Established" and experimental treatments of refractory autoimmune encephalitis

S. Rüegg
Basel, Switzerland

Abstract: Autoimmune encephalitis (AE) has emerged as an important cause for patients to be admitted in an intensive care unit (ICU). Treatment of AE is dependent on different essential factors: it may be restricted to immunomodulatory therapies in the case of non-paraneoplastic AE. When AE is caused by a paraneoplastic antineuronal autoantibody (ANAB), comprehensive treatment includes detection and antitumoral therapy of the underlying neoplasm beyond the immunological.approaches. Although large controlled randomized, double-blind prospective studies for the treatment of the different types of AE are lacking, there is broad consent on an algorithm of sequential measures and drug applications. It is important to note that the treatment regimen for the various forms of AE is almost always the same („one size fits it all"), independent fo their causing ANAB. Ancillary treatments include the application of antiseizure drugs and neuroleptics or other drugs targeting structures of the central nervous system. Many immunomodulatory drugs approved for other autoimmune disorders or even antitumoral compounds enlarge the armamentarium to control AE and special emphasis is given to these interesting avenues during this activity.
Disclosure: The author received commercial support by CSL-Behring, Desitin, Novartis, and UCB for the organisation of the 1st, and 2nd meeting on „Inflammation, Immunity, and Epilepsy"(IIE), held at the Mario Negri Insitute, Milan, September 16-18, 2010, and October 13-15, 2016, respectively.

FW13_3

Epileptic seizures and status in autoimmune encephalitis

S. Demeret

Paris, France

Abstract: Autoimmune encephalitis associated with antibodies against neuronal cell-surface antigens is an emerging cause of diffuse or limbic encephalitis that frequently presents with seizure or status epilepticus. Some entities are particularly associated with epileptic manifestation: the anti-LGI1 encephalitis is characterised by faciobrachial dystonic seizures; the anti-GABA A and anti GABA B Receptor encephalitis are associated with a high rate of generalised seizure and status epilepticus; the prevalence of seizure is up to 80% in the anti-NMDAR encephalitis. Early recognition of the autoimmune origin of new onset epilepsy is of paramount importance since early immunotherapy is known to induce a better prognosis.

New Onset Refractory Status Epilepticus (NORSE) is a rare and very severe condition. In up to 60% of cases of NORSE, an extensive diagnostic workup fails to reveal the cause of status epilepticus. There is currently no specific therapy for cryptogenic NORSE, and conventional anti-seizure medications show very limited success. The hypothesis of either an autoimmune origin, with not yet known antibodies, or worsening by immune activation, suggests that early immunotherapy should be considered, even when a definite immune etiology has not been identified.

Autoimmune encephalitis open a broad field of basic and therapeutic research in the field of epilepsy, with the hope to better understanding, and better treating some refractory status epilepticus and perhaps drug-resistant epilepsy.

Disclosure: Nothing to disclose.

EAN/MDS-ES: Evidence-based medicine and beyond in neuropsychiatric complications of Parkinson's diseases

FW14_1

Treatments of depression in Parkinson's disease

O. Rascol

Toulouse, France

Abstract: Depression is a common and important non-motor aspect of Parkinson's disease (PD). Its treatment has been an especially troublesome problem for clinicians, in part because there are so many treatment modalities from which to choose and so little definitive information available for guidance. The management of depressive symptoms in PD has been indeed largely based until very recently on poor evidence and empirical experience, extrapolating to PD patients findings obtained in other non-PD populations. The research in this area has been delayed because of insufficient interest in non-motor symptoms in PD, lack of appropriate animal models, limitations of clinical scales insufficiently validated in PD patients and paucity of good quality placebo-controlled double-blind randomized controlled trials (RCTs).

Recent systematic reviews and meta-analysis of published RCTs have assessed the effectiveness of pharmacologic treatment but also non-pharmacologic approaches such as cognitive behavioral therapy or repetitive transcranial magnetic stimulation (rTMS) for the treatment of depressive symptoms in PD. Their conclusion is that both antidepressants (including selective serotonin reuptake inhibitors and imipraminics) and cognitive behavioral therapy are efficacious or likely efficacious in the management of depression in individuals with PD. Very few (if any) data are available to compare the relative efficacy of different therapeutic approaches or of their combination. These reviews also provide incentive to researchers by illustrating the need for more extensive and definitive study of this very important aspect of PD.

Disclosure: Nothing to disclose.

FW14_2

Therapeutic approaches of cognitive decline and dementia

D.J. Burn

Newcastle upon Tyne, United Kingdom

Abstract: This focussed workshop will address several key non-motor symptoms that frequently complicate the course of Parkinson's, or may even predate the motor features. In part, these symptoms may be precipitated or exacerbated by drugs used to treat motor impairments. But undoubtedly the genesis of depression, cognitive impairment, psychosis and impulse control disorder relates to underlying neuropathological and neurochemical changes in strategic brain areas. Treatments used to manage these challenging symptoms are generally inadequate, despite their de facto logical focus on neurotransmitter placement and/or receptor stimulation. Furthermore, despite the availability of several agents in class, such as antidepressants, the evidence base to guide treatment of many of these symptoms is poor. Neuropsychiatric symptoms associated with Parkinson's are therefore an area of major unmet need. This session will review current treatments for depression, cognitive impairment, psychosis and impulse control disorder and will also consider future possible therapeutic approaches.

Disclosure: Nothing to disclose.

FW14_3

Therapeutic approaches of hallucinations and psychosis

M. Emre

Istanbul, Turkey

Abstract: Hallucinations and psychosis are frequent features in patients with Parkinson's disease (PD), in particular in those with PD dementia (PDD). Hallucinations are usually visual, well-formed images of humans or animals, auditory hallucinations may seldomly occur, hallucinations in other modalities are rare. Along with hallucinations other psychotic features include delusions, feeling of presence and phantom boarder phenomenon, psychotic agitation and aggression may occur occasionally. The first step in management of psychosis is to assess its etiology; concomitant diseases or conditions should be investigated, in particular if the onset is acute. Medications that can induce psychosis (such as anti-cholinergics, dopamine agonists) should be discontinued. In case hallucinations or other psychotic features persist after potential triggering factors have been excluded or treated, the next step is to decide if the severity and frequency of these symptoms justify a pharmacological treatment. Typical neuroleptics such as haloperidol are contraindicated as they can worsen motor symptoms or result in severe neuroleptic-induced akinetic-rigid crisis. The most robust evidence for efficacy exists for clozapine, its use necessitates periodic monitoring of leucocyte count as it may rarely induce agranulocytosis. Among the other atypical or second-generation antipsychotics, quetiapine may be considered although evidence-base is weak. Other atypical neuroleptics such as risperidone, olanzapine and aripiprazole may all worsen motor symptoms and are not recommended. A new atypical antipsychotic, pimavanserin, a selective serotonin 5-HT2A inverse agonist, has recently been developed specifically for the treatment of hallucinations and delusions associated with PD psychosis.

Disclosure: Nothing to disclose

Guillain-Barré Syndrome: new developments in immunology, electrophysiology and treatment

FW15_1

Understanding the auto-immune attack

H.J. Willison
Glasgow, United Kingdom

Abstract: Guillain-Barré syndrome (GBS) is the prototypic autoimmune neuropathy and the foremost cause of neuromuscular paralysis worldwide. Studies in animal models of experimental allergic neuritis over many decades have been crucially important in developing concepts for the immunopathological basis of GBS. In human disease, studies conducted during the last 20 years have focused on humoral effector arms, mainly serum anti-ganglioside antibodies. Gangliosides are a family of ~50 structurally distinct sialic acid-containing glycosphingolipids. Anti-GM1 and -GD1a antibodies characterise the motor axonal form of GBS and anti-GQ1b/GT1a antibodies characterise Miller Fisher syndrome (MFS). Antibodies arise through molecular mimicry with sialic acid containing bacterial lipopolysaccharides (LOS) and are the principle pathogenic mediators of the disease. Using in vivo and ex vivo mouse model systems, we have shown complement-dependent destructive effects induced by anti-ganglioside antibodies at clinical, physiological and morphological levels. Neural injury can be exaggerated or attenuated by manipulating the levels of the ganglioside target, and complement inhibition can attenuate the pathological procession. Recent work has focused on novel complement therapeutics, now available for use in man. These studies are helping us to unravel the pathophysiological events mediated by anti-ganglioside antibodies in models of GBS and thereby design and test improved treatments. The major unsolved question for the future remains the nature of the antigen(s) that mediate the common-or-garden demyelinating forms of GBS that typify the usual clinical and pathological phenotype, and much effort is being put into this exciting area. This presentation reviews some of the experimental highlights in this field.
Disclosure: Nothing to disclose.

FW15_2

Unravelling the electrophysiological diagnostic challenges

P. van den Bergh
Brussels, Belgium

Abstract: Electrophysiology plays a crucial role in the characterisation and diagnosis of peripheral neuropathies. It provides insight in the type and mechanism of peripheral neuropathy by giving information on the spatial pattern (generalised, multifocal, focal), the fibre type involved (motor, sensory), pathology (axonal, demyelinating), and the severity and time course (acute, ongoing, chronic).
Guillain-Barré syndrome (GBS) is a post-infectious inflammatory neuropathy. A proper diagnosis as early as possible is very important because timely immune treatment can largely reduce morbidity and disability. The diagnosis is based on a constellation of clinical and laboratory features, including electrophysiological studies, spinal fluid examination, and in serological studies.
Electrophysiological studies are an important tool in the early detection and characterisation of GBS. Much effort has gone into developing criteria which can distinguish axonal and demyelinating subtypes. The discovery of reversible conduction failure (RCF) has led to the concept of nodopathy/paranodopathy, where conduction slowing and conduction block are due to the immune attack mainly at the nodal axolemma level. There is no actual demyelinisation as defined pathologically and if the immune attack continues, conduction failure may not reverse and axonal degeneration will ensue. Recent electrophysiological studies shed light on this pathophysiological mechanisms and show that the dichotomous distinction between axonal and demyelinating in GBS based on electrophysiology is not tenable (Muscle nerve, 2018).

Unraveling the electrophysiological diagnostic challenges

Disclosure: Nothing to disclose

FW15_3

Novel treatment methods

P.A. van Doorn
Rotterdam, Netherlands

Abstract: Guillain-Barré syndrome (GBS) is a heterogeneous acute polyneuropathy for which a standard dosage of intravenous immunoglobulin (IVIg) or plasma exchange (PE) are proven effective. This treatment however is insufficient for many patients. Therefore, new treatment modalities are eagerly awaited. Times are now changing.

Why? It is now possible to predict outcome adequately early in the course of disease using prediction models like the modified Erasmus GBS Outcome Scale (mEGOS). This enables to select patients with a poor prognosis for more aggressive treatment.

New trials are currently being conducted. The second dose IVIg RCT investigates whether a second IVIg course administered one week after start of the first IVIg course is effective in GBS patients with a poor prognosis, based on mEGOS. This study is now almost finished. The International GBS Outcome Study (IGOS) group studied this effect in a prospective non-randomized study (I-SID-GBS study). There is evidence that complement activation plays an important role in GBS. A new treatment approach for GBS using the complement C5 inhibitor Eculizumab has been initiated by Willison (Glasgow). The recent small RCT by the Japanese Eculizumab Trial (JET) study group indicates that Eculizumab indeed may be a promising treatment.

Studies on small volume plasma exchange, a very simple and non-expense procedure to improve outcome of GBS are being conducted in Bangladesh. This potentially could be attractive especially in countries with limited resources.

The new EAN/Peripheral Nerve Society (PNS) guideline on diagnostics, treatment and outcome of GBS is expected in 2019.

Disclosure: Nothing to disclose.

Precision medicine in stroke

FW16_1

Do we need precision medicine in stroke?

D. Bereczki
Budapest, Hungary

Abstract: Stroke is a major public health issue for the coming decades in Europe. To decrease morbidity and mortality, and to improve outcome, the most efficacious and least harmful interventions should be offered both in acute care and in prevention for those who are affected by the disease or its risk factors. Evidence based clinical guidelines help the practicing physician to make the best decision in routine patient care. Guideline recommendations are based mostly on results of large randomised controlled trials (RCT) and their systematic reviews, therefore reflect the conclusions of statistical evaluation of a large number of patients. Entering patients to such RCTs is limited by predefined inclusion and exclusion criteria. Due to these strict study criteria, the majority of patients in everyday practice cannot be included in these trials. For this reason, although guideline recommendations can be applied in general, this is certainly not the case for every individual patient. Patients often differ in important characteristics from those who were included in the large randomized trials. Such features could be age (either too young or too old), pregnancy, certain co-morbidities, short life expectancy, severe cognitive dysfunction, attitude to treatment adherence, or even some socioeconomic features. For these patients guideline recommendations are not necessarily valid or obviously cannot be applied, therefore there may be need for individual considerations when deciding on their best treatment. Whereas guideline recommendations can be used in the majority of stroke patients, individual considerations – "precision medicine" – are often needed in patient care.
Disclosure: Nothing to disclose

FW16_3

What to expect in the future?

J. Montaner
Barcelona, Spain

Abstract: Blood biomarkers measurement could add in acute stroke management, in both selecting patients at the pre-hospital level, as well as guiding reperfusion therapies to evaluate efficacy and safety. In acute stroke, blood biomarkers to distinguish between real strokes and stroke-mimics would be useful at pre-hospital level and differentiation between ischemic and hemorrhagic subtypes would permit administration of pre-hospital reperfusion therapies. Retinol-binding protein 4 (RBP-4) is as a promising biomarker to distinguish IS from ICH and when complemented with glial fibrillary acidic protein (GFAP) the discrimination of both stroke subtypes improves.
Also, specific biomarkers that selectively evaluate response to tPA, predict the appearance of secondary intracranial hemorrhages and identify patients with unsuccessful tPA-induced recanalisation have gained in importance during the last few decades. Identification of patients resistant to tPA-thrombolysis would be of great interest in deciding whether stroke patients may benefit from endovascular thrombectomy. Hence, pre-treatment levels of fibrinolytic inhibitors such as plasminogen activator inhibitor-1 (PAI-1) or thrombin activatable fibronolysis inhibitor (TAFI), as well as other molecules related with coagulation, such as factor seven activating protease or A Disintegrin And Metalloproteinase with a ThromboSpondin type-1 motif, member-13 (ADAMTS13) have been associated with a poor tPA response in terms of recanalisation.
Beyond the acute phase, prediction of stroke outcome and the occurrence of post-stroke complications such as stroke-associated infections and assessment of stroke etiology to guide further studies or even therapeutic measures in cases of stroke of undetermined cause represent the main indications for the use of blood biomarkers in precision medicine.
Disclosure: Nothing to disclose.

Special Session

Sunday, June 17 2018

EAN/MDS-ES: European Basal Ganglia Club

SPS01_1

David Marsden Award Lecture

M. Hallett
Bethesda, USA

Abstract: The etiology of the syndrome of dystonia has always been difficult. While in some patients, such as those with post-hemiplegic dystonia, there is an obvious lesion, in most patients there is no obvious lesion. In the mid-twentieth century, there was a very strong feeling that most such dystonia, particularly the most common, adult onset focal dystonias were functional. One of David Marsden's lasting contributions to Neurology was to make clear that most such patients had an organic disorder. His voice was sufficiently powerful, that for some time, no patient presenting with focal dystonia was considered functional. However, it was subsequently recognised that a minority of such cases are indeed functional. There are many etiologies of dystonia syndromes and functional is one of them. While there are some clinical clues to separate organic and functional, many patients cannot be diagnosed easily. This has led, for example, to some functional patients getting DBS. It would be good if there were laboratory tests that could differentiate these two classes of etiology, but another conundrum is that many such abnormal clinical neurophysiological tests are abnormal in both entities. Tests that might be useful include the blink reflex recovery curve and paired associative stimulation to assess plasticity. More work is needed in this area for both understanding and help with clinical diagnosis.
Disclosure: Nothing to disclose.

EAN/EFAS: Autonomic dysfunction as early markers in rare and neurodegenerative diseases

SPS03_2

Biomarkers in MSA, a prerequisite for disease modification

A. Fanciulli
Innsbruck, Austria

Abstract: Multiple system atrophy (MSA) is a rare, adult-onset, fatal neurodegenerative disease. Several interventional trials with putative neuroprotective agents have been completed in the past decades. Despite pre-clinical evidence in favour of neuroprotection, thus far, no disease-modifying candidate proved effective.

Among the several reasons that may have accounted for such failure, it has been hypothesised that a putative neuroprotective compound might be effective in early stages of the disease, but will not generate disease-modifying benefit later on, when much of the neuronal reserve has already been lost. Assessment of early MSA-specific biomarkers has therefore become of pivotal importance for planning future neuroprotective trials.

Early, widespread and progressive autonomic failure distinguishes the parkinsonian variant of MSA from Parkinson's disease. Additional clinical red flags, like early postural instability, rapid progression, abnormal postures, bulbar and respiratory dysfunction and emotional incontinence, point towards a MSA diagnosis. In patients presenting with idiopathic late-onset cerebellar ataxia, the presence of REM behaviour disorders, autonomic failure or parkinsonism helps differentiating the cerebellar variant of MSA from other ataxias. At present, there's no single MSA-specific wet biomarker, while recent advances in diffusion-weighted and automated, observer-independent volumetric MRI yield high diagnostic accuracy for a MSA diagnosis.

Combination of multiple clinical, wet and instrumental biomarkers in a scoring system may support an earlier identification of patients with a high-probability of suffering from MSA.

Disclosure: Nothing to disclose

SPS03_3

Can autonomic dysfunction differentiate early neurodegenerative diseases including Dementia, Parkinson and MSA ?

W. Struhal
Tulln, Austria

Abstract: The quest for a biomarker for neurodegenerative diseases is also extending to the autonomic field. Of all organ systems in autonomic dysfunction cardiovascular, sudomotor dysfunction, and urogenital dysfunction are employed for serving as biomarker, gastrointestinal function being rather difficult to assess.

Concerning tauopathies and alpha-synucleinopathies autonomic involvements show differences.

Alpha-synucleinopathies

In alpha-synucleinopathies autonomic dysfunction may be of central (multiple system atrophy (MSA)) or of peripheral (e.g. Parkinson's Disease (PD), pure autonomic failure) origin. A number of systems may be involved including the cardiovascular and the sudomotor system.

MIBG-SPECT may help to differentiate MSA from PD, other techniques have been described as well including skin biopsy or clonidine stimulation tests.

Urogenital dysfunction in PD is rather urge incontinence while in MSA rather rentention and incontinence. Sexial dyfunction is in MSA early while in PD multifactorial and at any stage of the disease.

In Lewy Body Dementias (LBD), autonomic involvement is often present, but not as prominent as in MSA. However, the prevalence rate for orthostatic hypotension (OH) is known to be high. In patients suffering LBD, a recent small study revealed the skin to be a possible biomarker.

Tauopathies

In tauopathies including Alzeimer's disease (AD) as well as Frontotemporal dementia, behavioural variant (FTDbv), a considerable frequency of cardiovascular autonomic dysfunction is reported (around 40%), of those 20% suffer OH. In AD, sympathetic dysfunction plays a crucial for cardiovascular dysregulation.

In AD as well as FTDbv, the peripheral sudomotor function is intact, available data suggest central origin of autonomic dysfunction.

Disclosure: Nothing to disclose

SPS03_4

Autonomic dysfunction in hereditary sensory and autonomic neuropathies and Fabry disease

M.J. Hilz

Erlangen, Germany

Abstract: Autonomic dysfunction can appear early in hereditary sensory and autonomic neuropathies (HSAN) and Fabry disease.

The five HSANs have different inheritance, pathology, disease-progression, biochemical, neurophysiological and autonomic abnormalities. HSAN I patients show low normal sensory and motor nerve conduction velocities, but abnormal warm, cold and heat-pain perception thresholds and distal anhidrosis. Sensory symptoms are slowly progressive and symmetrical. Patients develop acral mutilations of the feet with plantar ulcers, stress fractures, osteomyelitis, and osteolysis.

HSAN II patients have severely impaired sensory perception including elevated vibratory and thermal perception thresholds. Sensory nerve conduction is highly abnormal, motor nerve conduction is almost normal. Already during infancy, patients show acral anhidrosis, tonic pupils, eating and swallowing difficulties, constipation and apneic episodes. They develop deformed distal phalanges, paronychia, finger and plantar ulcers, unrecognised fractures and mutilating acropathy.

The autosomal-recessive HSAN III or Familial Dysautonomia afflicts Ashkenazi Jewish children, is characterised by pronounced central and peripheral autonomic dysregulation, including severe orthostatic hypotension and autonomic crises. HSAN IV manifests as congenital insensitivity to pain with anhidrosis with episodes of high fever, unnoticed injuries, fractures and limb mutilation. HSAN V presents as selective loss of pain perception.

Neurological manifestations of Fabry disease include episodes of severe lancinating pain and burning paraesthesias in the extremities, often triggered by temperature changes.

Assessment of somatic and autonomic small nerve fiber dysfunction requires testing of temperature perception, vibratory perception, sudomotor function, limb and superficial skin blood-flow and vasoreactivity. Early diagnosis and enzyme replacement therapy may improve autonomic dysfunction in Fabry disease.

Disclosure: Nothing to disclose

EAN and European involvement in Rare Neurologic Diseases (European Reference Networks and other activities)

SPS04_1

Introduction: EAN's activity for Rare Neurologic Diseases

A. Federico
Sienna, Italy

Abstract: Since the beginning of EAN's activity, a special interest has been focused by the Board and the Scientific Committee to Rare Neurologic Diseases, with the organisation of a Task Force formed by members of all the EAN scientific Panels, with a management committee, that tried to develop within the European Neurology the attitude and knowledge of rare neurologic diseases, that are the most frequent conditions present in all rare diseases, sometime poorly diagnosed and followed. We will report all the activities, showing a growing interest by general neurologists to the topics, with an increased number of proposals to the EAN congresses dedicated to Rare Neurologic Diseases, and by a large number of young neurologists and the very intensive collaboration with the ERNs dedicated to Rare Neurologic Diseases (Neuromuscular ERN, Neurologic ERN, Epicare ERN dedicated to Epilepsy, Metabern dedicated to Metabolic Diseases).

Finally we are collecting data about the organisation of care of rare neurologic diseases in the different European countries and the therapeutic facilities.

Disclosure: Nothing to disclose.

SPS04_3

NMD-ERN: The European Reference Network for Neuromuscular Diseases

T. Evangelista
Newcastle upon Tyne, United Kingdom

Abstract: EURO-NMD is the European Reference Network for rare neuromuscular diseases (NMDs), a broad group of related disorders that represent a major cause of mortality and lifelong disability in children and adults. NMDs are difficult to recognise, and patients experience long delays in diagnosis. There are no curative treatments and their rarity and diversity pose specific challenges for healthcare and research, and for the development and marketing of therapies.

NMDs collectively affect an estimated 500,000 EU citizens and result in significant costs for families and the healthcare system. EURO-NMD unites 61 of Europe's leading NMD clinical and research centres in 14 Member States and includes highly active patient organisations. The network addresses harmonising and implementing standards for clinical and diagnostic best practice, improving equity of care provision across Member States, decreasing time to diagnosis, increasing cost efficiency through better care pathways, access to specialist training and education, application of eHealth services, development and application of care guidelines, facilitating translational and clinical research, harmonising data and samples for research reuse, and sharing of high-quality data.

EURO-NMD is now an operational network with active participation from our Health Care Providers (HCPs) in all disease and diagnostic working groups. The working groups have designed a number of questionnaires that were sent to all HCPs aiming to identify were the main expertise in each area was located across Europe. A series of GAP analysis of published guidelines was done by each group. The guidelines in need of development or updating were identified. We have established connections with the learned societies, with the other ERNs and have also been instrumental in shaping the political decisions of the European Commission. As we move into year two, our priorities are to strength the ERN; planning a more direct participation of the HCPs and patient representatives, endorse or develop the guidelines, develop an educational training programme, act on the existing research plan, deliver the first EURO-NMD training school and begin using the Clinical Patient Management System for e-Consultation.

ERNs are an interesting health-care model based on the dissemination of the best available information, education and e-Health. Due to their structure networks will be able to reach a greater number of stakeholders and have a good geographic coverage unlike traditional models where HCPs work for more confined communities.

Disclosure: Nothing to disclose.

SPS04_4

RND-ERN: The European Reference Network for Rare Neurologic Diseases

H. Graessner

Tübingen, Germany

Abstract: ERN-RND is a network of 32 Healthcare Providers from 13 EU member states. ERN-RDN builds on existing expert centres and mature networks dedicated to rare neurological diseases (RND) as well as established rare disease infrastructures such as Orphanet, EURORDIS and RD-Connect. Through coordination and knowledge transfer, ERN-RND is about to establish a patient-centred network to address the needs of patients with RND of all age groups, with or without a definite diagnosis, by implementing an infrastructure for diagnosis, evidence-based management, treatment and collection of patient data.

The network is active in three main areas: (i) knowledge generation, transfer and dissemination in order to harmonise quality of diagnosis and treatment provided in the network and beyond; (ii) introduction, piloting and role-out of the Clinical Management System (CPMS), an e-health platform provided to the ERNs by the European Commission, to consult on complex cases applying multidisciplinary expert panels; and (iii) contribution to Solve-RD (www.solve-rd.eu), a H2020 funded diagnostic research flagship project. According to these three areas of activity, ERN-RND's most important operational current targets are: Consensus on diagnostic flowcharts for all RND covered by ERN-RND, Identify disease groups specific most important care needs for RND in the EU, Establish ERN-RND web-site as THE RND information hub and use it as the core of a ERN-RND information strategy, Introduction and piloting of CPMS in ERN-RND for e-consultation of clinical cases based on well-defined use cases, and Contribute to Solve-RD utilising the existing patient cohorts.

Sunday, June 17 2018

Neurological disorders of famous composers

SPS05_1

Maurice Ravel's fatal neurological illness

V. Demarin
Zagreb, Croatia

Abstract: French famous composer, of paternal Swiss and maternal Basque descent, wrote orchestral, chamber, piano and vocal music together with operas and ballets. In the last decade of his life he suffered from a slow but progressive neurological disorder that has impoverished his creativity but also has been subject of medical debate which continues to this day. Renowned French neurologist Dr. Theophile Alajouanine evaluated and followed him during his illness and we owe him precious clinical observations of Ravel's disease. He describes - „ a Wernicke aphasia of moderate intensity, without any trace of paralysis, without hemianopia, but with an ideomotor apractic component". He noted oral and written language diffusely impaired, without any noticeable intellectual weakness or memory, judgment and affectivity impairment. Ravel's recognition of tunes and musical themes, musical thinking together with artistic sensitivity was well preserved, but he showed loss of musical expression (written and instrumental), difficulties with note reading and musical writing. Alajouanine concludes that because of aphasia and simultaneous apraxia, musical reading with piano playing and use of musical signs were much more impaired than expression and recognition of musical themes. Differential diagnosis of Ravel's neurological disorder will be discussed – brain tumour, systemic, vascular, infectious or endocrine chronic disease, heredity influence, sequels of traumatic head injury, Alzheimer's disease, corticobasal degeneration, primary progressive aphasia, frontotemporal dementia and Pick's complex. No conclusive diagnosis can be made - possibly several pathologies were superimposed. Ravel died after craniotomy. The autopsy was not obtained. So his neurological disorder remains mysterious, like his music.
Disclosure: Nothing to disclose

SPS05_2

Joseph Haydn - a case of subcortical vascular encephalopathy

H. Bäzner
Stuttgart, Germany

Abstract: Joseph Haydn died in 1809, aged 77, as the most famous composer of his time. With increasing age, he complained of progressive forgetfulness preventing him from composing for about the last 8 years of his life. He spent his days increasingly immobilised and inactive, suffering from a disabling gait disturbance. Still, most biographers quote the diagnosis of the composer's final illness and a reason for his death as diffuse atherosclerosis and congestive heart failure (CHF). A more sophisticated pathography, however, can be referred to detailed analysis of documents and sources, which lead to a diagnosis of subcortical vascular encephalopathy (SVE). SVE is caused by progressive cerebral microangiopathy presenting with two main types of pathological changes: recurrent lacunar strokes and widespread diffuse white matter changes. "Subcortical vascular dementia" is rather a misnomer for the syndrome, since important and predominant features as mood changes, urinary symptoms, and in particular a characteristic gait disturbance are not incorporated in this term while dementia is often rather mild. All of these manifestations which most probably result from ischemic interruption of subcortical network structures can be found in the famous composer. Haydn was severely disabled by the symptoms of SVE for several years. For instance, he often reported difficulties in finishing his last oratorio 'Die Jahreszeiten' due to the various disease symptoms. Subsequently, the disease prevented him from composing another large oratorio which had been already drafted. Finally, the progress of SVE stopped his long career as a composer at the age of 73 years.
Disclosure: Nothing to disclose

SPS05_3

Stroke in famous composers

T. Breitenfeld
Zagreb, Croatia

Abstract: Creatvity is a highly appreciated, remarkable and uniquely human skill defining the ability to use imagination or original and unusual ideas to create something new or imaginative. The quick advancement of neuroscience has enabled us to observe creativity not only as mystery but also in the context of science. Stroke is one of the most common of all neurological diseases, one of the leading causes of death and leading cause of disability. This was true historically as well as now. The goal of biopathographies is to investigate lives and creativity of famous composers from psychological as well as medical point of view. Last decades gave us a whole new insight into famous composers' creative lives. Looking at musical history, nearly a quarter of those considered "great composers" suffered from vascular disease. The most prominent renaissance composers were stroke victims, like Orlando di Lasso (Orlande de Lassus) and Giovanni Pierluigi da Palestrina as well as German Baroque giants – Heinrich Schutz, Johann Sebastian Bach, Georg Friedrich Handel and Christoph Willibald Gluck. Further on Felix Mendelssohn, Giuseppe Verdi, Hector Berlioz, Antonin Dvorak, Igor Stravinski, Sergej Prokofiev, Jean Sibelius and Benjamin Britten among others, are also famous composers that suffered or died of stroke. These composers all had wide talent, success, importance, and ultimately, stroke. Cerebrovascular disorders of famous composers will be discussed in this presentation, together with their influence on composers' creativity.
Disclosure: Nothing to disclose

SPS05_4

Breaking barriers in Neuro-musicology: Beethoven's deafness, Schumann's madness, Porter's pain, Gershwin's uncinate seizures

P.L. Pearl
Boston, USA

Abstract: The impact of neurological disease has led to an enhanced understanding of the lives and creative output of the great musical masters.

Presentations with live demonstration of the great composers' music will cover the differential diagnosis of a sampling of artists from various genres throughout history. In these cases, aspects of misunderstood pathophysiology will be explored.

Topics to be included are the differential diagnosis explaining the early onset and catastrophic deafness of Beethoven yet with preserved mental status and musical genius and output (1770-1827); overuse syndrome that presaged the discipline of performance arts medicine, erratic productivity, and early death of Robert Schumann (1810-1856); inexorable dementia with effects on compositional output of Maurice Ravel (1875-1937); progressive neuromuscular syndrome unexplained in his lifetime of Dmitri Shostakovich (1906-1974) with eponymic implications for all neurology; complex orthopedic and neurological course, from nerve injuries to phantom limb pain, of Cole Porter (1891-1964); and clinicopathologic correlation of the misdiagnosed tumor of George Gershwin (1898-1937).

We discover the role of neurology and its effects on the humanities through the lens of the great masters and our own appreciation of each genre. Enhanced understanding of the neurological vulnerabilities and struggles of legendary figures, and misdiagnoses in their histories, leads to increased appreciation for their contributions and serves as an important exercise in diagnostic formulation.
Disclosure: Nothing to disclose.

EAN Resident and Research Fellow Section Round Table Discussion: Learn about clinical work and research (clinical and laboratory) around Europe

SPS06_1

Table 1

J.M.M.C. Ferro
Lisbon, Portugal

Abstract: Participants will have opportunity to ask me questions about my own career, clinical and research activities. I will also explain how medical undergraduate and postgraduate education is organized in Portugal. Information on how internship, specialty residency and the PhD-resident program work will be provided. Currently available careers and job opportunities in clinical, research, industry, education and management related to health care, both public and private will be detailed.
Disclosure: Nothing to disclose.

SPS06_2

Table 2

K.V. Toyka
Würzburg, Germany

Abstract: Professor Klaus V. Toyka. MD, FRCP, FEAN, FAAN, University of Würzburg, Germany: "How to become a clincial-scientist?" In this session I will discuss the category of a clinician-scientis in an academic neurology department with integrated experimental research facilities and neuroimaging. This is based on my experience in Europe and the US with various international academic appointments. How can one start a double-carrier? What are the obstacles? How long should one have had cliical training in neurology before getting into a research field? How can one apply from the outside? What is the communication langage - with patients or with researchers? What degree can one earn? What kind of training and expertise should one have before applying to a clinician-scientist program? The main categories for a clinician-scientist are 1- patient-orientated research including treatment trials, epidemiology, genetics of defined disorders; 2- studies into disese mechanism, action of drugs and other therapeutic factors and the like through use of cell or organ culture systems or via experimental rhodents (rats and mice) that are specially made for laboratory studies. How does one get into these main systems? What kind of infrastructure is needed? How is the funding provided? Next, the way of presening research data at acdaemic meetings or through publications is discussed. The key question is what type of carrier one aims at long-term.
Disclosure: Until 2011 advisory board and consultant appointments and research funding with some pharmaceutical companies not related to the subject of this session. All funding was controlled and permitted by governmental public service agencies.

SPS06_3

Table 3

H. Cock
London, United Kingdom

Abstract: Prof. Cock qualified from and completed her post-graduate and research training in and around London. Having started her consultant career at the National Hospital for Neurology, she moved to St George's in 2003 where she is Consultant Neurologist at Atkinson Morley Regional Neuroscience Centre, and Professor of Epilepsy and Medical Education in the Institute of Medical & Biomedical Education at St George's, University of London. From a background in mitochondrial diseases including molecular biology, cell culture and biochemical techniques, but developing a clinical interest in epilepsy, she established a research group working on mechanisms of seizure-related neuronal damage gaining additional in vivo experience in the process. Personal circumstances influenced a decision to close her laboratory group, and expand a developing portfolio of clinical studies, as well as embracing an established interest in education. She was the initiator, and is now a co-investigator on one of the largest ever status epilepticus clinical trials running in the USA (ESETT), was chair of the UK epilepsy research network Interventions & treatment clinical study group 2010-2014, and is currently the epilepsy Lead for the London South Research Network. Specific interests include functional non-epileptic attacks, status epilepticus and epilepsy comorbidities and consequences. Prof Cock is also the education lead for the European Academy of Neurology, a fellow of the Higher Education Academy and EAN, and member of the International League Against Epilepsy Epilepsy Certification task force, and has been involved in all aspects of undergraduate medical and post-graduate neurological education throughout her career.
Disclosure: Prof. Cock reports personal fees from Sage Pharmaceuticals Ltd, personal fees from Eisai Europe Ltd, personal fees from UCB Pharma Ltd, personal fees from European Medicines Agency, personal fees from UK Epilepsy Nurse Specialist Association, non-financial support from Special Products Ltd, grants from U.S NIH Institute of Neurological Disorders and Stroke, non-financial support from International League Against Epilepsy, Status Epilepticus Classification Task Force, non-financial support from International League Against Epilepsy, Epilepsy Certification (education) Task Force, outside the submitted work.

SPS06_4

Table 4

E. Havrdova

Prague, Czech Republic

Abstract: My primary intention was to help persons with multiple sclerosis. My tutor prof. Jedlicka believed in autoaggressive processes taking place in MS pathogenesis many decades before this idea was officialy accepted and used immunosuppression since 1970. When biological treatment was introduced in MS, it was clear that only part of patients responds well and we needed to better characterize treatment response. As one of the first groups in the world we started to measure brain volume and volume of brain lesions on MRI with ultrathin slices and slowly developed program for measurement of brain regions, white and grey matter and started to co-operate with Buffalo Neuroimmaging Analysis Center. We have now plenty of publications on quatitative MRI in MS and we moved to correlations with working capacity and cognitive decline in MS. We try to keep the science useful and applicable for clinicians to enable early and effective change of MS treatment to stop MS activity. Therefore we also moved back to biomarkers like neurofilaments to enrich our ability to predict MS course. We have build a team of dedicated clinicians, radiologists and postgradual students to continue this effort.

Disclosure: Nothing to disclose.

EAN Corresponding Members of the Mediterranean Area - Clinical Neuroimmunology

SPS07_1

NMO Devic's disease

A. Awada

Neurology, Hotel Dieu de France Hospital, Beirut, Lebanon

Abstract: Since the description of Devic in 1894, the spectrum of Neuromyelitis Optica (NMO) has expanded considerably. The discovery of anti-aquaporin-4 antibodies in 2004, associated with NMO in 70-80% of cases, and advances in medical imaging, have changed the nosology of this syndrome.

Besides the classical extensive myelitis & optic neuritis, 4 "encephalic" subtypes of NMO spectrum are now individualised: 1) incoercible vomiting associated with area postrema lesions; 2) clinical picture of narcolepsy with hypothalamic lesions; 3) Acute brainstem syndrome, and 4) encephalopathy with diffuse white matter lesions resembling "ADEM"

More recently, another antibody, the anti-MOG, was found in about 20% of the AQP-4 seronegative cases. Patients with anti-MOG tend to have more limited and less severe disease (conus terminalis myelitis for example) or an "ADEM"-like picture, especially in children.

Disclosure: Nothing to disclose.

SPS07_2

Neurological complications of Behcet's disease

M. Benabdeljlil

Rabat, Morocco

Abstract: Behçet's disease (BD) is a chronic multisystemic inflammatory disease, predominant within the Mediterranean countries, characterised by oral and genital mucous ulcers and uveitis. It commonly affects young male adults. Its exact etiology remains unknown. Neurological involvement is one of the most serious complications of BD.

Central Nervous System (CNS) manifestations of BD can be categorised in two main types. Parenchymal involvement or "neuro-Behçet's disease" (NBD) represents 74% of our 161 cases and includes hemispheric, brain-stem, spinal and multifocal presentations. It is due to small vessel disease and mostly presents as a subacute brainstem syndrome with hemiparesis, but a chronic progressive type is also described with slowly progressive dementia, ataxia and dysarthria. The second type, non-parenchymal CNS involvement is essentially represented by cerebral venous thrombosis. Cerebral arterial involvement is rare, only 4 cases in our series including 3 intracranial aneurysms. Peripheral nervous system involvement is extremely rare.

Diagnosis is based on the International Study Group of BD clinical criteria, with suggestive neurological and radiological features. Most common lesions are located at the mesodiencephalic junction, followed by pontobulbar, thalamic and basal ganglia areas. CSF analysis can show inflammatory changes. Diagnosis could be quite challenging, particularly with MS, other inflammatory diseases and CNS infections.

Neurological complications of BD can be a remarkable cause of morbidity or even mortality at the acute phase. Management should associate steroids with long-term immunosuppressive treatment in NBD. The use of anticoagulants is controversial in case of venous thrombosis due to the bleeding risk of a coexisting aneurysm.

Disclosure: Nothing to disclose.

SPS07_3

Autoimmune encephalitis

M.J. Titulaer

Rotterdam, Netherlands

Abstract: The evolution of Autoimmune Encephalitis (AIE) has been a major breakthrough. Anti-NMDA receptor encephalitis (NMDARE) is the most frequent, while over 10 new antibodies were discovered in the last years. It has fueled interest in recognising AIE outside the field of classic limbic encephalitis, like patients with epilepsy. The identification of antibodies (and AIE) is important as the antibodies are likely pathogenic, and treatment with immunotherapy is often very rewarding.

Anti-NMDARE is a severe disease, affecting patients of all ages. Often initially seen by psychiatrists, most patients end up in ICU. Disease course is protracted, and half the patients fail initial immunotherapy. Nevertheless, outcome is good in most patients in the long term. In a third of the patients, anti-NMDARE is paraneoplastic (mainly ovarian teratomas in females 12-45 years old), while it is preceded by HSV1 encephalitis in 5-10%. Vice versa, anti-NMDARE occurs within 3-6 weeks in ~25% of HSV1 encephalitis patients.

Anti- GABAbR encephalitis is a limbic encephalitis, marked by refractory seizures. Half the patients have a small cell lung cancer, often unknown to the patients at the time of AIE.

Originally known as VGKC-encephalitis, it was shown in 2010 that VGKC-antibodies do not exist. Patient can have antibodies against LGI1 or Caspr2 (and incidentally Contactin-2). Recent studies question the additional value of a positive VGKC-test when LGI1 and Caspr2 are negative. Anti-LGI1 encephalitis is marked by faciobrachial dystonic seizures or focal seizures with memory loss, while Caspr2 encephalopathy can show a combination of core symptoms.

Disclosure: MT has filed a patent for methods for typing neurological disorders and cancer, and devices for use therein, and has received research funds for serving on a scientific advisory board of MedImmune LLC, for consultation at Guidepoint Global LLC, and an unrestricted research grant from Euroimmun AG.

SPS07_4

Neurological complications of Lupus and anti-phospholipid antibodies

J.-M. Vallat

Limoges, France

Abstract: Systemic lupus erythematosus (SLE) is a multisystemic, chronic autoimmune disease with production of autoantibodies and the development of tissue injury. The etiology of SLE is not known. 30 to 40% of SLE patients present an anti-phospholipid syndrome (APS), 30 to 40% of this group develop thrombotic complications. About 50% of patients with SLE have neurological manifestations during the course of their disease, which are associated with impaired quality of life, and high morbidity and mortality rates. In 1999, the American College of Rheumatology has identified nineteen neuropsychiatric syndromes associated with SLE (NP-SLE) involving central nervous (CNS) and/or peripheral nervous systems (PNS). Peripheral neuropathy is said to occur in 1.5–27.8% of SLE cases. Various mechanisms explain the direct effects of SLE on CNS and PNS structures. Otherwise, toxic effects of drugs (e.g. steroids, thalidomide,anti-coagulants etc…) and infections may induce neurological complications.

This presentation will review major NP-SLE and APS and will discuss their mechanisms, clinical features, radiological findings and treatment options. As various physio-pathogenic mechanisms may induce NP-SLE, it may be necessary to use a combination of drugs (sometimes in the same patient): "symptomatics" (anticonvulsants, antipsychotics, anti-coagulants…), high dose steroids (pulse methylprednisolone) and immunomodulators (antimalarials, statins, cyclophosphamide, azathioprine, methotrexate, mycophenolic acid etc…). Plasmapheresis also may be useful, as IV immunoglobulins and rituximab, due to the role of potentially pathogenic autoantibodies. Long-term remission is plausible, although symptoms persist in 3%–20% of cases; most require steroids and the recurrence rate is 21%–47%. Mortality can be high (≥18%).

Disclosure: Nothing to disclose.

Monday, June 18 2018

History of Neurology: Lessons from Portuguese Clinical Neurosciences

SPS08_3

From pioneers to interventional angiography

V.A.R. Oliveira
Lisbon, Portugal

Abstract: Cerebral angiography was presented, for the first time, by Egas Moniz at Societé Neurologique in Paris in July 1927. It was the corollarium of about seven years of investigations aiming to find a method able to identify intracranial space-occupying lesions, mainly tumours.

Egas Moniz designed an elegant method in four steps: First: to identify an opaque substance to be seen on X- ray film through the skull. Second: to inject constrast media in the cerebral vessels of a corpse (then the first angiograms came to light). Third: to inject carotids in living animals (dogs). The fourth step was to inject a patient. No one had considered such an audacious procedure of delivering a chemical agent directly into the cerebral circulation. But he did. After a first failure he succeded. It was the case of an hopeless patient with focal signs and advanced intracranial hypertension. Now the angiogram was done without complications. Moniz collected the films and a few days later, he was in Paris presenting his discovery. The acceptance of angiography was not immediate: many centers kept faithful to pneumoencephalography introduced by Walter Dandy in 1919. But Moniz made a step forward understanding that cerebral vessels were not only a way to identify space-occupying lesions but the vessels, themselves, deserved investigation. For example, he described carotid occlusions, a phenomenon unknown until then, while performing angiograms in cases suspicious of intracranial tumor. Many other vascular abnormalities were then identified, one after another. The amazing recent advances in interventional angiography reinforced the value of the pioneer work of Moniz 90 years ago.
Disclosure: Nothing to disclose.

EAN/EBC/EFNA: The Value of Treatment (VoT) of brain disorders

SPS09_1

Brain disorders in Europe: unmet needs

W. Oertel
Marburg, Germany

Abstract: About a third of the European population suffers of a brain disorder. Psychiatric and neurological disorders represent an enormous burden on both individuals and societies and threaten the quality of life of millions of European citizens with important implications on economic growth.

In respect to neurology the disciplines neurology, child neurology, neurosurgery – and pain and sleep experts – diagnose and treat individuals who suffer from a neurological disorder. Depending on the health system and economic situation in the different European countries 1) the number of specialists in the disciplines listed above, 2) the degree of their education and qualification, 3) the access to and degree of reimbursement of pharmacotherapy and neurosurgical interventions and 4) the availability of a specialized infrastructure for certain neurological disorders (i.e. stroke units, monitoring units for epilepsy, neurological intensive care units) varies throughout Europe. Thus most of the current healthcare systems in Europe don't adequately respond to the need of patients with brain disorders, especially with chronic brain disorders.

In order to reemphasise the unmet needs and dramatic burden of neurological diseases to society and to the individual, EAN – under the umbrella of the European Brain Council – has launched a new program called Value of Therapy (VOT). In this project teams of experts of EAN and EFNA have analysed the costs for society if you do NOT treat neurological disorders (such as dementia, epilepsy, headache, Multiple Sclerosis, Parkinson's disease, restless legs syndrome, stroke). This Special Session will present the results of this study.
Disclosure: Nothing to disclose.

SPS09_2

The value of early diagnosis and treatment. A patient journey

J. Jaarsma
Amsterdam, Netherlands

Abstract: The Value of Treatment Project initiated by the European Brain Council is one excellent example of patient participation in research. The project addresses the burden of disease and the issues in the current healthcare system, and proposes evidence-based and cost-effective solutions to achieve high value for patients. By describing ("mapping") the patient journey in full detail (by both patients and health care professionals), treatment gaps were identified for eight neurological diseases. These results will be addressed in the policy recommendations resulting from this project.

The journey of patients in the healthcare systems in a number of European countries and the socio-economic burden resulting from late detection, diagnosis and treatment, will be presented.
Disclosure: Nothing to disclose.

SPS09_3

The Value of Treatment: using economic modelling to assess costs and outcomes associated with healthcare interventions

M. Tinelli

London, United Kingdom

Abstract: Improving health-outcomes should not simply be seen as a matter for health policy. Better health can make a very important contribution to economic and social goals through longer working lives, greater productivity, reduced disability, better educational outcomes, and reduced social exclusion. The Value-of-Treatment (VoT) Project is a timely and ground-breaking initiative of the European-Brain-Council (EBC) in collaboration with the European-Academy-of-Neurology (EAN), European-Federation-of-Neurological-Associations (EFNA), the London-School-of-Economics (LSE) and other EBC partner institutions. It argues that optimizing interventions in neurological and mental health diseases can bring both positive outcomes for patients and socio-economic gains for society. The economic case studies aimed at producing economic evidence on the value of closing treatment gaps for brain disorders to inform decision-making (at potentially many levels). The economic analyses sourced evidence in previously published studies and administrative datasets, with inputs from a wide range of experts over many months. Two or more interventions (eg policies, strategies, services, treatments) were compared looking at a wide a range of costs and outcomes, and for the longest time periods possible. The baseline scenario included treatment/care as usual where it represented a 'gap' (e.g. delayed diagnosis, poor adherence). The perspective adopted was health-and-social-care system, or, pending on the data, the whole public sector/society. They looked at whether the interventions on offer were cost-saving and, if not, whether they were nevertheless cost-effective. The economic findings showed that closing treatment gaps is widely beneficial for patients, families, providers, payers, policy-makers. Fundamental to treatment is the planning of coordinated, multidisciplinary, patient-centered care.

Tuesday, June 19 2018

Population, migration and neurological disorders

SPS11_1

Migration as a reality of today

A. Federico

Sienna, Italy

Abstract: In recent years important political social and health problems in Europe was the migration phenomenon mainly in the southern countries (Greece, Turkey, Italy). The presence of people from other countries requires that the doctors may be informed on the different pathological conditions, that may have different presentation, and sometime are not normally present in the hosting country.
We will discuss the topic following three main approachs: The number of migrants and the main pathologic neurologic disorders, reporting some epidemiologic data collected in several hospitals. The use of migration data for understanding the physiopathology of some neurologic disorder (Multiple Sclerosis, stroke and other diseases), the different phenotypic presentations of several genetic conditions, etc; The relationship of migrants' lifestyle and its correlation with the neurologic disorders.
Disclosure: Nothing to disclose.

SPS11_2

Changing risk factor profile and migration. Health indicators - who cares?

S. Öztürk

Konya, Turkey

Abstract: Noncommunicable diseases (NCDs) are the leading cause of death. Forced displacement, the deterioration of living conditions and the interruption of regular medical treatment can all affect the health of people living with NCDs. The current crisis in Syria and the related health burden shouldered by displaced people in refugee camps and urban settings in neighbouring countries. Turkey is a leading country which has an important amount of refugees. Approximately 30% of refugees lived in refugee camps in 2010, including 52% of children and 49% of women. Studies on cerebrovascular diseases and risk factors for refugees reported important findings. According to the demographic data, education lewel was low, unemployement rate was 23.8 %, avarage income was 366 USD. 38.3% of the Syrian refugees currently smoke a tobacco product, consume fruit 2.9 days a week. In both sexes physical activity was at the lowest level in the age group 60-69 years, CVD history of 14.7%. Overall 79.8%, i.e., close to four fifths, of Syrian refugees have never had their blood sugar measured. Overall, for both sexes, 4.1% of individuals have been diagnosed with high blood sugar in the past 12 months. Overall, 60.0%, i.e. close to three fifths, of Syrian refugees have never had their blood pressure measured. A 2.8% of women were diagnosed with high blood pressure more than 12 months ago. BMI was high as overweight and obesity (32.6%, 27.7%). Effective prevention strategies must be considered for this very special population to decrease (NCDs) and related burden.
Disclosure: Nothing to disclose.

SPS11_3

Neurologic infections in immigrants

M. El Alaoui Faris

Rabat, Morocco

Abstract: The geopolitical factors that influence human migration are complex and subject to change often influenced by regional conflicts. In addition to the political and economic impacts, the health conditions of the immigrant population must also be taken into consideration. Migrants and refugees are particularly vulnerable to infectious diseases because they have often traveled in difficult and challenging conditions. These stressful circumstances can lead to the activation of latent infections such as tuberculosis or the human immunodeficiency virus (HIV) infection. Some communicable diseases are very frequent in immigrants such as respiratory or gastrointestinal infections, other are rare such as Malaria or Chagas disease, specially among Latin American immigrants.
Neurologists must be aware to the neurological manifestations of infections diseases among immigrant pupulation. Neuro-tuberculosis or Neuro-HIV should be diagnosed quickly to avoid serious complications such as meningoencephalitis, seizures, paralysis or cognitive impairment.
In host countries, a public health policy based on vaccination to prevent the spread of communicable diseases, and screening for sexually transmitted infections and diseases such as tuberculosis, viral hepatitis and the human immunodeficiency virus, coupled with targeted screening by country of origin, is quite justified and valid economically. Beyond these measures, the fear of the introduction of exotic infectious diseases seems to be unfounded among immigrant populations, all the more, most of whom are generally in good health.
Disclosure: Nothing to disclose.

Tournament

Sunday, 17 June 2018

Tournament Basic

TBASIC01

A missense mutation in the Low Complexity Domain of endogenous TDP43 induces gain of splicing function and neurodegeneration in the mouse

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A. Isaacs[2], P. Stanier[2], M. Lythgoe[2], Y. Gondo[8],
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United Kingdom,* [4]*UCL, London, United Kingdom,* [5]*ICGEB,
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La Laguna, Spain*

Background and aims: TDP43 is a highly conserved protein involved in multiple processes of Ribonucleic Acid (RNA) metabolism including alternative exon splicing and regulation of gene expression, together with regulation of its own protein levels.

Missense mutations clustering in TDP43's Low Complexity Domain (LCD) cause Amyotrophic Lateral Sclerosis (ALS). Additionally, cytoplasmic inclusions of cleaved, polyubiquitylated and hyperphosphorylated TDP43 constitute the major histopathological hallmark of ALS.

The mechanism leading from TDP43 dysfunction to neurodegeneration has remained elusive since both over-expressor models using wild-type or mutant TDP43 or conditional deletion models lead to neurodegenerative phenotypes.

We have characterised Ethyl-Nitrosurea (ENU) Tardbp mouse mutants in order to dissect whether TDP43 gain or loss of function is sufficient cause neurodegeneration.

Methods: ENU mutagenesis, mouse phenotyping, cell culture, Polymerase Chain Reaction, RNA Sequencing, Western Blotting, Electrophysiology, Histology

Results: A mutation in the second RNA binding domain of TDP43 (F210I) leads to loss of splicing function, mimicking TDP43 depletion. Contrastingly, a mutation in the LCD (M323K, referred to as LCDmut) leads to gain of splicing

function, with effects in alternative exon splicing opposite to the F210I at the transcriptome-wide level and, in addition, novel splicing events involving skipping of constitutive exons, not previously reported.

Homozygous LCDmut developed late-onset decrease in grip strength, accompanied by a reduction in muscle strength and in surviving motor units together with widespread p62 and ubiquitin positive inclusions in the spinal cord (figure 1).
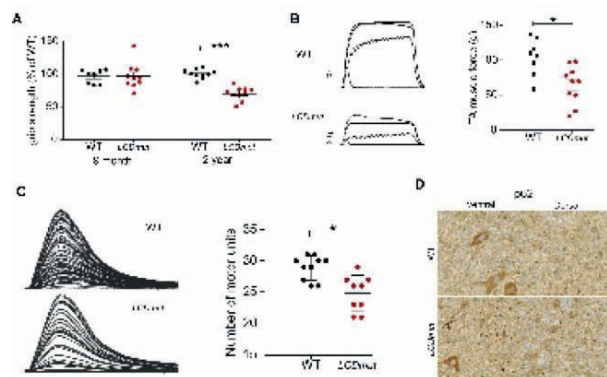
Homozygous LCDmut develop neurodegenerative phenotypes including a) decreased grip strength and b) muscle force, together with c) reduced number of surviving motor units and d) positive p62 inclusions in the spinal cord

Conclusion: Mutation-induced gain of splicing function in TDP43 is sufficient to cause neurodegeneration and could constitute an early process in pathophysiology of ALS.

TBASIC02

Parkinson's disease motor symptoms are linked to red nucleus volume and cerebellar metabolism

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Background and aims: Numerous studies have shown that the cerebellum is involved in Parkinson's Disease (PD). However, it remains unclear whether it has a compensatory or a pathological role in PD. As the Red Nucleus (RN) is intricately connected to the cerebellum, this structure has also been hypothesized to be involved in PD. Our aim was to investigate the involvement of the RN and cerebellum in the motor symptoms of PD.

Methods: We retrospectively examined 72 patients with PD. All patients had undergone whole-brain T1-weighted (T1w) and T2w MRI and 18F-fluorodeoxyglucose PET (18F-FDG PET). For each patient, RN volume was automatically estimated from the T2w MRI scan, and cerebellar metabolism was extracted from the 18F-FDG PET scan for each of the lobes. We assessed the correlations between RN volume, cerebellar metabolism and PD motor symptoms, as measured by the Unified Parkinson's Disease Rating Scale Part III off medication (UPDRS-III OFF).

Results: We observed a significant positive correlation between the RN volume and the UPDRS-III OFF score ($r2=0.11$, $p=0.009$), and between left anterior cerebellar lobe metabolism and the UPDRS-III OFF score ($r2=0.09$, $p=0.028$). In addition, we found a significant positive correlation between RN volume and left anterior cerebellar lobe metabolism ($r2=0.07$, $p=0.025$).

Conclusion: These results indicate that cerebello-rubral pathways play a compensatory role in PD, and demonstrate the need to target these structures with therapies such as transcranial magnetic and direct-current stimulation.

Disclosure: This study was funded by a grant from the Rennes Clinical Neuroscience Institute (INCR).

TBASIC03

Salivary Alpha-Synuclein and tau in Parkinson's Disease and Progressive Supranuclear Palsy

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Background and aims: Alpha-synuclein (a-syn) aggregation and tau deposition are respectively the pathological hallmarks of PD and PSP. The aim of this study is to measure a-syntotal, a-synolig and total tau concentration in the saliva of patients affected by PD and PSP in order to test whether they can be used as biomarkers for differential diagnosis.

Methods: 100 PD patients, 20 PSP patients and 80 healthy subjects were recruited. Samples of saliva were collected following previous protocol (Vivacqua et al., 2016). ELISA analysis was performed using three specific ELISA kits: SensoLyte 55550 for a-syntotal, MyBioSource MBS043824 for a-synolig and Life Technologies KHB0041 for total tau. Statistical significance was evaluated by Mann-Whitney U test. Spearmann Rank correlation coefficient was used for clinical correlations and Receiving Operating Analysis (ROC) was applied to determine sensitivity and specificity.

Results: A-syntotal is significantly lower in PD patients confronting to healthy subjects, whereas a-synolig is significantly higher ($p<0.05$). Conversely, in PSP patients salivary a-syntotal is comparable to healthy subjects. Salivary tau total is significantly higher in both PD and PSP patients confronting to healthy subjects ($p<0.05$) but no significant differences were detected between PD and PSP patients ($p>0.05$). Salivary a-syntotal is able to differentiate PD from PSP with a sensitivity of 100% and a specificity of 96,51%. Conversely, salivary tau total is able to distinguish PD and PSP patients from healthy subjects, but it cannot differentiate PD from PSP.

Conclusion: Our data support salivary a-syn detection as a promising biomarker for differential diagnosis between PD and PSP.

Disclosure: Nothing to disclose

TBASIC04
A novel gene causing primary familial brain calcification: JAM2

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Background and aims: Primary Familial Brain Calcification (PFBC) or Fahr's disease constitutes a heterogeneous neurodegenerative disorder presenting with calcium deposits in the brain and neuropsychiatric symptoms. Usually dominantly inherited, although recessive families have been reported. Genes linked to dominant PFBC are: SLC20A2, PDGFRB, PDGFB, XPR11.

We aim to investigate the cause of PFBC in 2 recessive families.

Methods: Five subjects were genotyped on Illumina-HumanCytoSNP-12v2-1_H array, and analysed by homozygosity mapping. We performed exome-sequencing (ES) on Illumina Hi-Seq-2000.

Fibroblasts were obtained from skin biopsies of one subject and his parent. Protein lysates were separated on SDS-PAGE gels and western blotted for JAM2.

We also developed a JAMB (ortholog of human JAM2) knock-out (KO) mouse model. We investigated the phenotype of these mice with behavioural tests and we analysed the histopathology of their brain compared to wild-type.

Results: Patients presented in childhood or their forties with movement disorders and neuropsychiatric symptoms and had widespread calcification on brain scans. They were consanguineous travellers.

Three homozygous regions were detected and WES identified a novel nonsense variant; c.C685T:p.R229X; in the gene JAM2 encoding for Junctional Adhesion Molecule 2 (JAM2). Segregation was confirmed.

There was no expression of JAM2 in homozygous state compared to heterozygous and controls on western blot.

The JAMB-KO animals exhibited significant difficulties in beam walking and gait, and presented brain vacuolization with glial activation.

Conclusion: We identified mutations in JAM2 causing PFBC in two recessive families. We confirmed the absence of the protein in patient's fibroblasts and demonstrated impaired gait and histopathological abnormalities in mice.

Disclosure: Nothing to disclose

TBASIC05

Subcortical anatomy of the default mode network: a functional and structural connectivity study

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Background and aims: Resting-state functional connectivity has been providing maps anatomically consistent with task-related networks. Default Mode Network (DMN) is the most studied functional network. However, its precise neuroanatomy, its structural connections and the reasons for its involvement in a wide range of brain diseases, remain elusive. In group analysis, small critical subcortical structures may be misaligned and not reach significance due to misalignment between functional territories, even with excellent anatomical registration.

We aimed to create an improved model of the DMN anatomy using an innovative approach of functional alignment. We hypothesised that basal forebrain nuclei and limbic thalamus belong to the DMN.

Methods: We collected resting-state fMRIs and diffusion-weighted imaging tractography from 20 healthy subjects(22-42 years-old, 11 female). Seeds previously reported were employed to create DMN maps, using BCBtoolkit (http://toolkit.bcblab.com). The seeded images were functionally aligned in a functional space, through iterative diffeomorphic transformations using Advanced Normalization Tools (http://stnava.github.io/ANTs/;Fig.1). Tractography was registered to the same space.
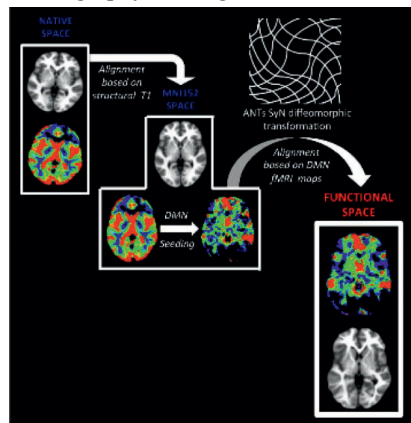
1st) Images were structurally registered to the MNI space through linear and diffeomorphic deformations; 2nd) resting state fMRI data was seeded to DMN areas; 3rd) individual DMN maps were functionally aligned in a new functional space through iterative diffeomorphic transformations. ANTs – Advanced Normalization Tools.

Results: DMN map demonstrated higher correlations in the functional space than in the MNI space, with significant difference in the hypothesised areas (Fig.2). This map overlapped anterior and mediodorsal thalamic nuclei, nucleus accumbens and basal forebrain cholinergic nuclei. Tractography identified tracts supporting their structural connectivity (Fig.3).
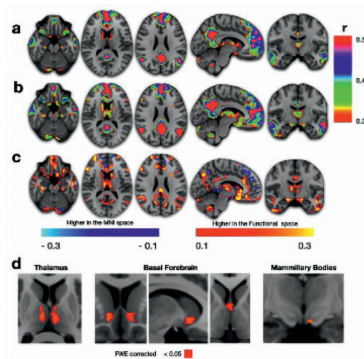
Comparison of functional and structural methods of alignment: a) DMN map based on structural alignment in the MNI152 space; b) DMN map based on alignment in the functional space; c) subtraction of the two maps; d) paired t-test between two maps in the hypothesised regions. FWE – Family-wise error.
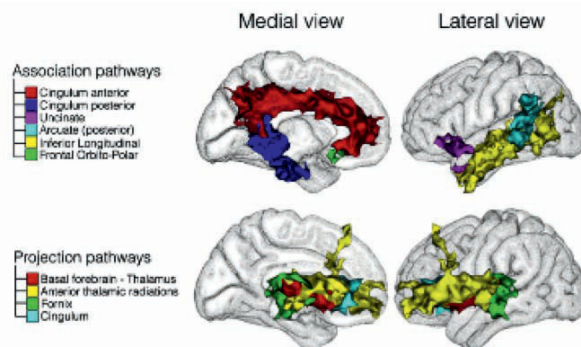
Tractography: tracts identified between the regions of interest of the new DMN map. Besides the association pathways between cortical regions, projections pathways were identified supporting the structural connectivity of basal forebrain and thalamic regions in the network.

Conclusion: Our method provides a more advanced model of the DMN including the basal forebrain and thalamus. The neurochemical diversity of these regions and its involvement in limbic processes of memory and emotion clarify the reason of the DMN involvement in various brain diseases, such as Alzheimer's disease, schizophrenia and depression.

TBASIC06

A passive transfer animal model of CASPR2 antibodies

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Background and aims: Antibodies to CASPR2 have been associated with limbic encephalitis and a wide range of central and peripheral nervous system disorders. However, their pathogenicity has not yet been established by a classic animal passive transfer model.

Methods: 19 C57Bl6 male mice were injected intraperitoneally (ip) with either CASPR2- (n=10) or healthy control (HC, n=9)- purified immunoglobulin G (IgG). Basal behavioural tests were performed between days -6 and -1, IgG injections given from day 1 to 8, with LPS injected ip on day 3. Behavioural testing was then performed from day 5 to 10. At day 11, animals were sacrificed and tissue collected for analysis. Brain sections were stained for bound human IgG, CASPR2 and cfos expression, neuronal loss, astrocytosis, microglia activation, and complement C3.

Results: The spontaneous continuous alternation test showed an impaired working memory in CASPR2-IgG injected mice. In a social behaviour task, CASPR2-injected mice displayed longer latency to start interacting and more freezing behavior compared to HC-IgG injected mice. CASPR2-IgG exposed mice showed the presence of CASPR2-IgG in sera and the presence of human IgG bound to the brain parenchyma. Purkinje cell loss and astrocytosis were present in the cerebellum of CASPR2-IgG mice, as well as diffuse microglia activation, increased complement C3 expression on astrocytes in the hippocampus and increased cfos expression in the piriform cortex and hypothalamus.

Conclusion: Using LPS to disrupt the blood-brain barrier, CASPR2 antibodies were able to access the brain and produce behavioural and histological changes. The precise mechanisms need to be addressed in further experiments.

Disclosure: Nothing to disclose

Monday, 18 June 2018

Tournament Clinical

TCLIN01

Assessment of diabetic medication in ~8,000 dementia patients with diabetes mellitus. A study from the Swedish Dementia Registry.

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Background and aims: Dementia patients concurrently diagnosed with Diabetes Mellitus (DM) receive a plethora of medication. Certain drugs used in DM treatment have been associated with reduced mortality and better cardiovascular outcomes, though it is unclear whether this applies to DM patients with dementia. We aimed to determine how specific diabetic medication affects all-cause mortality, incidence of stroke, Myocardial Infarction (MI) and Heart Failure (HF) in patients with DM and dementia.

Methods: We designed a longitudinal registry-based study focused on pre-dementia diabetic drug usage and post-dementia mortality, incident strokes, MIs and HFs. We merged four registries – the Swedish Dementia Registry, the Swedish National Patient Register, the Swedish Prescribed Drug Register, and the Swedish Cause of Death Register. We identified 8328 patients with DM and dementia with valid information on baseline covariates, diabetic drug usage, mortality, incidence of stroke, MI and HF. We used propensity score matching with subsequent Cox-regression to determine Hazard Ratios (HR) and 95% Confidence Intervals (CI) for all-cause mortality, stroke, MI and HF.

Results: Metformin usage was associated with lower mortality (HR 0.85, [95% CI - 0.80-0.90]), whereas the insulin users had higher mortality (1.12 [1.04-1.20]). Insulin users had higher hazard of heart failure (1.28 [1.03-1.59]), and DPP-4 inhibitor users had higher hazard of MI (2.50 [1.09-5.72]). We found no association between the studied medication and stroke.

Conclusion: Metformin use is associated with prolonged survival in DM patients with dementia. Patients using insulin could benefit from more frequent check-ups regarding hypoglycemia and cardiovascular status.

Disclosure: Nothing to disclose

TCLIN02

Cerebrovascular events after surgery versus conservative therapy for moyamoya disease: a meta-analysis

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Background and aims: To determine the effect of a neurosurgical intervention in patients with Moyamoya Disease (MMD) on the risk of cerebrovascular events.

Methods: We included studies with at least 10 MMD patients in either intervention or control group which investigated cerebrovascular events during a minimal follow-up period of one year after a neurosurgical intervention vs. conservative therapy. The primary outcome was any stroke and we prespecified three subgroups: adult, ischemic and hemorrhagic moyamoya patients. Secondary outcome events were ischemic stroke, hemorrhagic stroke and mortality. We performed a random effects meta-analysis to calculate Odds Ratios (OR).

Results: We included 2484 patients from 10 studies. The rate of any stroke was 14.1% in surgical treated compared to 30.0% in non-surgical treated patients (OR 2.63, 95%CI 1.57-4.39, NNT 6.3). In subgroup analyses we identified this beneficial effect of surgery in patients presenting with hemorrhagic, but not ischemic MMD. The secondary endpoint of hemorrhagic stroke was present in 4.6% of the patients who underwent a surgical intervention compared to 18.6% of the conservatively treated patients (OR 3.71, 95%CI 1.89-7.28, NNT 7.1). In addition, we observed a reduction in mortality, 2.9% vs. 0.6% (OR 3.12, 95%CI 1.30-7.47, NNT 42.8), but did not identify an association between surgical treatment and the outcome of ischemic stroke (10.0% vs. 13.5%; OR 1.41, 95%CI 0.92-2.16, NNT 28.1).

Conclusion: Surgical intervention in MMD is associated with a decreased risk of stroke most striking in patients presenting with hemorrhagic MMD. The relationship was present between surgical treatment and the outcome of hemorrhagic, but not ischemic stroke.

Disclosure: Nothing to disclose

TCLIN03

Pediatric and adult MS: a longitudinal multimodal MRI study to explore the substrates of the different clinical courses

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[1]San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Neuroimaging Research Unit, Milan, Italy, [2]San Raffaele Scientific Institute, Vita-Salute San Raffaele University, Department of Neurology, Milan, Italy, [3]Ospedale di Gallarate, Multiple Sclerosis Center, Gallarate, Italy, [4]Università Vita-Salute San Raffaele, Neuroradiology, Milan, Italy

Background and aims: At short-medium term, pediatric Multiple Sclerosis (pedMS) patients have a more favorable clinical course than adult ones (adMS). Against this background, this study investigates the pathobiological basis of such a different clinical outcome by applying structural and functional MRI techniques.
Methods: Using a 3T scanner, brain dual-echo, 3DT1-weighted and Resting State (RS) functional MRI (fMRI) scans were acquired from 31 pedMS and 30 adMS patients at baseline and after a 3.2 years mean follow-up. 26 pediatric and 30 adult healthy controls (HC) were also enrolled in order to estimate age-related differences. Voxel-based and tensor-based morphometry were used to assess regional patterns of volume changes, while RS fMRI analysis was performed to explore functional connectivity (FC) in the main networks. Correlations between MRI and clinical variables were explored using multiple regression models.
Results: PedMS experienced a more favourable clinical course. During the follow-up, compared to adMS, pedMS showed more significant GM atrophy in several frontal and parietal regions, with sparing of bilateral cerebellum and precentral gyrus and left supplementary motor area. During the follow-up period, compared to adMS, pedMS showed brain regions with increased and decreased RS FC in the networks explored. Disability measures correlated with RS FC modifications, but not with volumetric GM changes.
Conclusion: The onset of MS during childhood is likely to increase vulnerability to neurodegenerative processes, especially for brain regions with a maturation during adolescence. Functional brain plasticity is likely to contribute to protect pedMS patients from clinical disability accrual.

TCLIN04

Safety and efficacy of percutaneous pulsed radiofrequency at the C1-C2 level in Chronic Cluster Headache: a retrospective analysis of 21 cases.

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Background and aims: Chronic Cluster Headache (CCH) patients are often resistant to pharmacological management. We performed an audit of the safety and efficacy of Percutaneous Pulsed Radiofrequency (PRF) directed at the nerve root and ganglion of the C1 and C2 level, performed at our local pain clinic on the basis of trigeminocervical convergence.
Methods: 21 patients with CCH underwent percutaneous PRF treatment (240sec, max. 45V, max. 42°C) directed at C1 and C2 ipsilateral to attacks. Data on demographic variables, onset and duration of the headache, mean attack frequency and prior pharmacological treatment were collected by retrospective chart review. We evaluated safety and reduction of attack frequency in the three months following the first PRF treatment.
Results: Patients were between 25 and 62 years old. Ten suffered from primary CCH, 11 from secondary CCH. All had been treated with at least two prophylactic drugs and 19 (90%) had previously been treated with verapamil, lithium and topiramate. Ten patients (47,6%) reported no meaningful effect after PRF treatment, 4 patients (19%) reported a meaningful reduction in headache burden of less than 50% and 7 patients (33,3%) reported a reduction in headache burden of more than 50% in the three months following treatment. Two patients reported occurrence or increase in frequency of contralateral cluster attacks. No other adverse events were reported or detected at follow-up.
Conclusion: Percutaneous PRF treatment at the C1-C2 level is a safe procedure in experienced hands. It could prove effective in the treatment of refractory CCH patients; a controlled study is warranted.
Disclosure: Nothing to disclose

TCLIN05

Has deep brain stimulation changed the natural history of Parkinson's Disease? A case control longitudinal study

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Background and aims: Deep Brain Stimulation (DBS) is often regarded as the second therapeutic breakthrough after L-Dopa in the history of Parkinson's Disease (PD) therapies. However, the impact of DBS on the long-term course of PD has not yet been evaluated in a controlled manner.

Methods: We collected retrospective information on key disease milestones (recurrent falls, psychosis, dementia, and nursing-home placement) and death from clinical notes of PD patients treated with chronic subthalamic DBS >10 years (1999–2007) at our centre. A control group of PD patients similar in age at onset and age at baseline was extracted from a registry study (EuroPa) performed in 2003/2004 with corresponding retrospective data collection on long-term outcomes. Cox regression models were used to calculate hazard ratios (HR), adjusted for potential confounding variables.

Results: 54 patients with DBS and 54 patients without DBS at baseline were included. Groups were not significantly different with respect to age at onset, age at baseline, sex-distribution, and number of comorbidities at baseline. Compared to patients without DBS, patients treated with DBS were at lower risk of recurrent falls (HR=0.6; p=0.035) and of psychosis (HR=0.4; p=0.031). There was no significant difference in risk for dementia (HR=1.2, p=0.67), nursing home placement (HR=0.6; p=0.26), or death (HR=1.1; p=0.73).

Conclusion: Treatment with chronic subthalamic DBS was associated with longer intervals to recurrent falls and onset of psychotic symptoms. There was no evidence for beneficial effects of DBS on the long-term evolution of dementia, need for nursing home placement, or on overall survival.

Disclosure: Nothing to disclose

TCLIN06

Neuromyelitis optica spectrum disorder and Rituximab: a multi-center analysis

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Background and aims: Rituximab is often used as a first-line therapy for neuromyelitis optica spectrum disorder (NMOSD). Aim of the study was to evaluate, in a multicenter real life Italian dataset, Annualized Relapse Rate (ARR), disability (measured with expanded disability status scale, EDSS) and Adverse Events (AE) in NMOSD patients as main outcome measures to determine Rituximab efficacy and safety profile.

Methods: Uncontrolled retrospective multicentre observational study including all the patients with NMOSD treated with Rituximab in 17 Italian centers. Baseline demographics, outcome data and Adverse Events (AE) over the follow up were summarised.

Results: 80 patients were included in the analysis. Median follow up was 2.03 (range 0.1-11.7) years. Mean pre-treatment EDSS was 4.5. 41 (51%) patients were treatment naïve at Rituximab administration, 27 (34%) patients were treated with other immunosuppressive therapies and 12 (15%) with other disease modifying therapies approved for Multiple Sclerosis. ARR was 1.85 (95% Confidence Interval (CI): 1.56-2.18) in the year before Rituximab start, it decreased to 0.13 during the whole follow up, that is further reduced to 0.11 excluding relapses occurred in the first 6 months after Rituximab induction. AE or serious AE were experienced, respectively, in 27 and 6 patients. Proportion of patients without evidence of disease reactivation after 2 years was 85%.

Conclusion: Rituximab induced disease remission in most patients with NMOSD without occurrence of relevant AE o SAE. Results of this retrospective multi-center study are in line with others published reports on CD20+ B-cells targeting therapy in NMOSD.

Disclosure: Nothing to disclose

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