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Joint contractures and acquired deforming hypertonia in older people: Which determinants?

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Abstract

Joint contractures and acquired deforming hypertonia are frequent in dependent older people. The consequences of these conditions can be significant for activities of daily living as well as comfort and quality of life. They can also negatively affect the burden of care and care costs. However, etiological factors and pathophysiologic mechanisms remain only partly understood. As a result, preventive interventions and treatments focus entirely on controlling symptoms rather than the causes. Moreover, the effectiveness of these interventions remains to be validated. The purpose of this position paper is to present current data on etiological factors contributing to the development of joint contractures and acquired deforming hypertonia in older people. The pathophysiologic mechanisms of joint contractures in animal models are also presented.

Introduction

The aging process starts as early as 25 years of age and inevitably continues until death. Thus, humans spend approximately 70% of their life undergoing age-related decline. Aging is a multifactorial process often characterized by progressive degeneration of organ systems and

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tissues (1). The physiological state during aging is widely influenced by genetics and exposure to environmental factors.

Beyond physiological aging, several diseases can be associated with loss of autonomy. Alzheimer disease and associated disorders, ischemic and hemorrhagic stroke, extrapyramidal diseases, degenerative diseases of the musculoskeletal system, and diabetes and its vascular and neurological complications are the main pathologies increasing the dependence level in older people. Loss of autonomy in older people is typically associated with decreased mobility, which results in further functional decline. Moreover, abnormal postures or joint deformities affecting the upper and lower limbs can develop when combined with motor, articular, or periarticular disorders (2). Usually, the term “joint contractures” is used to describe the development of joint deformities in this context.

Although the decrease in joint range of motion (ROM) is the most commonly reported clinical characteristic of contractures, this term lacks a standard definition. For some authors, contractures are only the result of changes in periarticular tissues, whereas for others, both intra- and extra-articular components are involved (3, 4). The lack of consensual definition and the imprecision of assessment criteria to determine the presence of contractures can explain the wide prevalence range reported in the literature, from 20% to 75%, in older people (5, 6).

Recently, a new terminology, acquired deforming hypertonia (ADH), was proposed to replace the term joint contracture, with a more restrictive and precise definition. ADH was defined as any joint deformity with decreased ROM and increased resistance to passive movements, regardless of the cause, that promotes functional impairments, discomfort or any other limitation in activities of daily living (ADL). In the ADH survey in France, a multicenter cross-sectional study conducted in 39 geriatric institutions, 22% of 3,145 institutionalized older patients had ADH (2).

ADH can cause serious consequences for older people. Indeed, it increases the level of mobility limitation of the upper or lower limbs, thus maintaining the risk of new deforming hypertonia or contractures. In the ADH survey, one-third of patients had more than 5 ADH locations in the upper and/or lower limb and two-thirds had bilateral ADH (2).

ADH development can represent the harbinger of a cascade of decompensations that can exacerbate the functional decline, affecting social participation and quality of life of these older adults (7).

ADH is often associated with pain, which can be spontaneous or provoked by mobilization. This consequence, sometimes very intense, can generate or amplify behavioral

symptoms, which may lead to increased use of antalgic or psychotropic drugs, with additional iatrogenic risk. Pressure ulcers are another consequence, especially for hands with clenched fist deformities, and represent a common reason for medical consultation. To a lesser extent, maceration of skin folds (elbows, armpits, palms of hands etc.) is also frequently associated with ADH. This situation can undermine skin and lead to chronic skin wounds. Indeed, in a vicious cycle, cutaneous lesions increase pain, which can worsen the initial hypertonia by acting as a major noxious stimulus.

Basic ADL are altered by ADH. For the upper limbs, ADH of the shoulder, elbow or wrist and finger can interfere with the ability to assume self-care, eat or dress without assistance. Regarding the lower limbs, difficulties in getting dressed and putting on shoes as well as getting up and walking independently represent the negative impact of ADH. Furthermore, ADH can be an important source of difficulties for positioning in a bed or chair, with a risk of discomfort and pressure ulcers. Access to the perineum or axilla may be impeded, which can cause pain during mobilization, maceration and hygiene problems.

For caregivers, ADH increases care demands in all ADL and basic care (toilet, cutting of nails, transfers, positioning etc.). Finally, ADH also increases care costs in nursing homes and long-term care facilities (8, 9).

However, despite the important prevalence and possibly major consequences of ADH for dependent older people, its risk factors and pathophysiology remain only partially identified. Moreover, no therapeutic guideline or clear preventive strategy is currently available.

In this position paper, we present current data about etiological factors potentially involved in the development of contractures and ADH and the pathophysiologic mechanisms, including mechanical, histological, cellular and molecular changes observed during joint immobilization.

Etiological factors of ADH in older people

Muscular hypertonia in older people is most often multifactorial. Upper motor-neuron syndrome, extrapyramidal dysfunction and paratonia are frequently incriminated and associated, thus resulting in “mixed” hypertonia. The exact causes of each hypertonia often remain unknown, and currently, treatments proposed address the symptom rather than the cause. Behavioral and psychological symptoms of dementia (BPSD) and environmental factors can also contribute to the development of contracture mainly by favoring a decrease in mobility or activity.

Upper motor-neuron syndrome

The components of upper motor-neuron syndrome are both positive and negative signs, including, among others, spasticity, spastic dystonia and motor weakness (10). Immobilization and hypo-mobility induced by motor weakness and spasticity are the main contributors to the development of contracture. Spasticity is defined as a "disordered sensori-motor control … presenting as intermittent or sustained involuntary activation of muscles" (11). In older people, the most common etiology is cerebrovascular disease. The characteristics of spastic hypertonia in older people are the same as in the general population (12). However, the burden of this condition is all the greater because this population is often already affected by several other comorbidities and physical limitations (13). Furthermore, spasticity can be aggravated by concomitant medical conditions frequently encountered in older people, such as pressure ulcers, skin infections, constipation or urinary tract infections (14).

Extrapyramidal system dysfunction

Extrapyramidal lesions are source of muscular hypertonia and joint contractures. The main etiologic classes are neurodegenerative disorders (e.g., Parkinson disease), cerebrovascular disease and iatrogenic causes (medication). Clinically, damages observed in the striatum generally correspond to rather distal hypertonia (hands and feet) (15), whereas thalamic locations lead to more dystonic manifestations.

Although extrapyramidal syndrome is generally associated with Parkinson disease and parkinsonian syndromes, people with Alzheimer dementia and other dementia such as frontotemporal lobal degeneration or Lewy body disease also seem to present these symptoms (16, 17). In older people with major cognitive impairment, extrapyramidal symptomatology is correlated with the severity of cognitive decline and functional limitations. The most common signs are rigidity and bradykinesia, which have a direct impact on motor skills and increase the risk of functional impoverishment (17). Striatal deformities are often observed in older people because these deformities are more common in advanced stages of Parkinson disease (15).

Moreover, neuroleptics are by far the most frequent medication associated with extrapyramidal syndrome (18). In older people, their use is common in the treatment of neuropsychiatric and behavioral symptoms associated with dementia (19).

Paratonia

Beyond pyramidal and extrapyramidal hypertonia, paratonia represents the most singular part of the hypertonia observed in older people. Paratonia is a motor disturbance seen mostly in people with cognitive impairment. In 2006, a small group of international experts proposed a consensus definition of paratonia: "hypertonia with an involuntary variable resistance during passive movement" in any direction (20).

Paratonia is a common problem. In a recent study, paratonia was found in 58% of people with severe dementia, and its prevalence seems to increase with the progression of cognitive impairment (21). Another study suggested a prevalence of paratonia of up to 100% in people with severe dementia (22). Paratonia has been described in degenerative, vascular and mixed dementias but also in head trauma, anoxia and depression (22, 23).

As previously mentioned, several motor signs are described in dementia, whose appearance and nature vary according to the type of dementia (24). These symptoms can evolve, contribute to a loss of mobility and promote the development of contractures (22, 25). The prevalence and severity of paratonia as well as that of rigidity and hypomimia are increased in people with Alzheimer disease with more severe functional impairment (25). However, paratonia was the most consistently present form of hypertonia seen across all stages of functional impairment, with an overall prevalence of 85.7% in people with moderately severe and severe dementia. Follow-up of people with subcortical vascular disease over 6 years identified paratonia as an independent significant predictor of decline in instrumental ADL (26).

The pathogenesis of paratonia remains poorly understood, and more studies are needed to clarify the changes underlying motor signs in dementia. Some findings suggest vascular cerebral damage, and medical conditions such as diabetes that may promote vascular disease, may be part of the answer (21). Paratonia is also frequently associated with frontal release signs, which suggests a frontal lobe dysfunction (23-25).

Behavioral and psychological symptoms associated with dementia

BPSD encompass a wide variety of clinical manifestations that directly and indirectly affect mobility. they may contribute to contracture development if mobility and functional level are significantly reduced.

Apathy, whose core feature is a loss of or diminished motivation in comparison to the person's previous state (27), is a highly prevalent neuropsychiatric symptom in Alzheimer disease, affecting more than half of the individuals at some point during the disease (28). It

has also been documented frequently in older adults with Parkinson disease and other atypical parkinsonian syndromes (29), frontotemporal lobar degeneration, cerebral vascular disease (stroke and vascular dementia) and traumatic brain injury (28, 30). In most dementias, the severity of apathy increases with the disease progression (30). Apathy has been found associated with several negative outcomes.

Agitation and aggression contribute to the burden of care and caregivers' distress, which leads to the increased use of both chemical and physical restraints for older individuals. Several studies report the extensive use of antipsychotics for agitation and aggressive behaviors, whether in community, hospitalized or long-term care patients (31). Their effectiveness is modest (32), but the harmful consequences of their use are well known. The many side effects associated with antipsychotics include extrapyramidal symptoms, gait disorders and orthostatic hypotension (31), which can all lead to mobility limitations. Other drugs used to control BPSD may also have side effects with similar consequences. Benzodiazepines and other hypnotics can cause sedation and confusion and increase the risk of falling. Selective serotonin reuptake inhibitors and serotonin and norepinephrine reuptake inhibitors may cause extrapyramidal symptoms.

Physical restraints are mainly used in long-term care facilities for patients with impaired mobility function, presumably to limit the risk of falling, and in those with disruptive behaviors (33). However, a study of 264 068 nursing-home residents showed that outcomes including behavior issues, falls, walking dependence, ADL, pressure ulcers and contractures were significantly worse when physical restraints were used (34).

When in pain, people with dementia may become more agitated or aggressive (35). However, other behavioral changes and modifications in body activity such as refusal to move, decreased spontaneous motor activity and presence of muscle rigidity can also indicate the presence of pain. Pain can contribute to the appearance of contractures probably in part via these changes in body activity (9).

Environmental factors

Environmental factors may contribute to ADH development. Care given to older patients in long-term care or nursing homes often focuses on doing things for rather than with the person (36). This philosophy of care, present all over the world, prevents older people from using their remaining abilities and can lead to further deconditioning and loss of function (37).

Beyond environmental factors, older people are vulnerable to acute medical conditions with the accumulation of deficits and comorbidities with age (38). Immobility induced by

those conditions constitutes a supplementary risk of developing joint contractures and ADH (39).

Aging and potential pathophysiologic mechanisms implied in ADH development

Connective tissue

The following sections will first synthesize the knowledge of connective tissue (CT) and present an overview of the literature on the aging process of joint CT that can contribute to joint stiffness and ADH. Joint flexibility depends on an integrated system involving the viscoelastic properties and neurophysiological mechanisms of the tissues that cross that joint. Age-related modifications to this system can interfere with the ability of these tissues to lengthen or to deform. This section focuses on the non-contractile component of this system.

Macro structure of connective tissue

CT consists of cells and fibres immersed in a ground substance, also known as the extracellular matrix (ECM). On the basis of specific morphological and functional characteristics, CT can be differentiated into subtypes, proper CT being one of them. Proper CT is a very large group of tissues comprising both loose and dense CT (40). Dense CT is primarily located in fibrous load-bearing tissues such as tendons, ligaments, capsules and fasciae (40). The cells, namely fibroblasts, can be considered an "active" component of CT because they provide the metabolic properties of the tissue. Their stimulation by mechanotransduction leads to synthesis activities when the tissue experiences physiological loading or to degradation activities when the tissue experiences unloading or overloading (41, 42). In the past few decades, a particular type of fibroblast called a myofibroblast has been found in tendons, fasciae and scar tissues (43). These cells have actin fibres in their cytoplasm that allows them to contract. Some authors have hypothesized that long-lasting isometric contraction plays a role in pathological fascial contractures such as Dupuytren disease, plantar fibromatosis or frozen shoulder (44-46).

The ECM and its contents (the "inert" component) provide the mechanical and viscous properties of the tissue. It contains approximately 60% to 80% water and 20% to 40% solid material, but these distributions vary by anatomical region, tissue type, tissue function and age (47, 48). The ECM is an interlaced network that distributes mechanical stresses on the CT and provides support for the cells. The main components of the ECM are the ground substance and several types of fibres, the principal ones being collagen and elastin. The ground substance is composed of water, extracellular proteins, proteoglycans and

glycosaminoglycans (GAGs). The ground substance is responsible for providing nutrition to the cells. It also provides hydration by attracting water, which creates a viscous gel that acts as a lubricant. The ground substance also creates space between the collagen fibres at points where they cross, so that they can glide on each other when tensile force is applied on the tissue. The inter-fibrillar space may also prevent excessive cross-link formation that could decrease tissue mobility and deformation (49), two mechanisms contributing to the development of ADH. In general, each collagen fibre is made up of thread-like subunits called collagen fibrils. Each fibril, in turn, is made up of collagen molecules linearly arranged in an overlapping head-to-tail fashion. The fibril's strength is due to intra- and inter-molecular bonds. Elastic fibres are thinner and arranged in a complex 3D branching network according to the tensile force imposed on the CT. Therefore, the concentration of elastin is reflective of the amount of mechanical strain imposed on the CT and the need for that tissue to return to its original state (40). In summary, collagen and elastin fibres provide the mechanical properties of the tissue, which explains their role as being complementary from a functional point of view. Although the main role of collagen is to resist tensile stress, it is interwoven with elastin fibres to prevent tearing and facilitate the tissue's return its pre-deformed state. Finding an effective intervention that allows collagen to be deformed without being injured is one of the challenges clinicians encounter in the conservative management of ADH.

Age-related changes of CT

Although age-related mechanisms and their impact on joint flexibility are specific to each type of CT, some more general processes can be applied to most CT (for reviews see (41, 47)). For example, enzymatic modification of the structural proteins collagen and elastin following their synthesis has been reported. Acquired imbalance between the synthesis and breakdown of the ECM has been related to decreased tissue volume and accumulation of degraded molecules that affect the CT state or "quality". Collagen, elastin and the ground substance undergo changes that affect the viscoelastic properties of the tissues and therefore modify their responses to tensile stress, their ability to deform, their force transmission capacity and also, responses of cells (41) to the mechanical loading.

With aging, an increase in intramuscular lipid concentrations has been reported (50, 51). The total amount of collagen fibres of the tendon (52, 53), the capsule (54) and the intramuscular muscle's CT also increases (55, 56). More complex intermolecular cross-links between tropocollagen molecules have been reported, and all these modifications lead to more stable cross-links (57). Moreover, the wave length of the crimp structure of the collagen fibril

increases and the wave-crimp angle decreases (58). Therefore, when the collagen fibril is exposed to a load, these changes can be expressed from a temporal standpoint by using the load-deformation curve model. The fibrils spend a shorter time in the toe region of the curve to reach the linear region sooner, and once in this zone, the load increases at a faster rate. The clinical meaning of these changes is increased tissue stiffness and CT that attains its limits of deformation sooner. The reduced content of elastin fibre also interferes with the tissue's ability to deform.

Another mechanism that could explain stiffness resulting from aging is related to changes of the ground substance. Ground substance content has been shown to decrease with age (59, 60), thereby resulting in reduced hydration and a lower gel-to-fibre ratio. A decrease in this ratio can potentially reduce the space between the collagen fibrils, interfering with their ability to glide and promote binding between collagen and the GAGs that surround the fibre, thus interfering with CT lubrication. These modifications can increase the friction between the different layers of CT that surround or cross a joint and contribute to joint stiffness during aging and possibly to the development of contractures or ADH. To summarize, aging CT features greater collagen content and less water, elastin and ground substance. These histological changes contribute to CT stiffness and in some cases, ADH.

The stiffness of CT tissue and its reduced ability to deform results in decreased flexibility as people age. In turn, older people have difficulty moving joints into ranges of motion required for daily activities (e.g., reaching overhead, standing up from a chair, walking). This is particularly true for older individuals with a medical condition (e.g., stroke, dementia) that limits their capacity to move even more. The CT of individuals no longer able to move one or more joints by a previously available ROM (relative immobilization) can become unloaded. This under-stimulation causes changes in the CT that mimic those observed during absolute joint immobilization (e.g., post-injury, casting, etc.).

In summary, age-related modifications in the CT can lead to CT stiffness and loss of flexibility. When joints are no longer used to their maximum capacity, as with conditions of relative immobilization, the CT might become unloaded and under-stimulated, which can induce changes in CT. Therefore, aging and immobilization are two factors that induce decreased ROM in older individuals. In some individuals, the pathological changes in the CT will add to those changes associated with aging and immobilization, thereby resulting in the development of ADH and thus a vicious cycle that is very difficult to break.

Molecular and cellular aspects of joint contractures and ADH

Clinical research investigating molecular and cellular mechanisms of aging and immobility on human articular tissue is rare (61) and is limited by ethical issues and various factors that complicate clinical aging research (62). Animal models continue to contribute basic new data to aging research (Table 1). For ADH, the rat model of knee immobilization in flexion has allowed for studying the progression of joint contractures throughout aging, with up to 32 weeks of immobility and up to an additional 48 weeks of mobility in animals with a lifespan of 2 to 3 years (63). A temporal study on the reversibility of knee flexion contractures determined that recent-onset contractures were primarily due to muscular structures and were reversible, whereas long-lasting contractures were primarily due to articular structures and were irreversible after unassisted mobilization (63). The animal models allow for comparing and contrasting joint contractures caused by immobility or secondary to trauma, inflammatory joint diseases and central or peripheral neurological conditions causing muscle imbalance around a joint (64). In this section, we review the cellular and molecular changes associated with aging and immobility in ADH and joint contractures.

Histological and cellular changes

Sensory input provokes spasticity and can contribute to upper motor-neuron signs leading to continuous muscle activity, lack of volitional command, and lack of phasic stretch (65). The onset of spasticity may contribute to the plastic rearrangement of the central nervous system, which can result in over-active muscles and exaggerated reflex responses to external stimuli (66). Histological changes in paretic and immobilized muscles are atrophy, loss of sarcomeres, accumulation of intramuscular connective tissue and increased fat content (67). Immobilization in a shortened position further aggravates muscle contractile properties and ultimately results in myogenic joint contractures (67). Pyramidal or extrapyramidal diseases modify the neurogenic sensory and motor environment around the joint, but the resistance to passive movements can only be attributed to non-neurogenic tissues (2). Several histomorphological and cellular changes accompany the pathophysiology of joint contractures. The capsule is an important articular structure that limits ROM (63, 64). The rat model of immobilization in flexion has demonstrated a significant reduction in posterior synovial intima length (Figure) and synoviocyte proliferation, which suggests synovial adhesions rather than pannus proliferation during contractures (68). Prolonged immobilization in the same model is characterized by the replacement of articular cartilage by bone in the non–weight-bearing region of the tibia, possibly mediated by chondral vascularization (69).

Additionally, fat deposition in the bone marrow is induced by joint immobilization, characterized by hyperplasia of small adipocytes in recent-onset contractures and adipocyte hypertrophy in chronic contractures (70).

Molecular changes

Immobilized joints contain higher amounts of type I collagen and lower amounts of type III collagen in the joint capsule of immobilized legs as compared with sham treatment, which suggests that the contracture process is caused by fibrosis (71). An initial disorganization of collagen fibres followed by an increase in advanced glycation end products during immobilization is a potential mechanism contributing to the chronic stiffness of the capsule (72). Characteristic modulation of specific biochemical pathways identified by a temporal gene expression profile during immobilization-induced contracture in rat knees revealed that the joint capsule was sensitive to immobility (Table 2) (73). Along with mechanical factors in the environment of the joint, a study of different inbred rat strains provided evidence that intrinsic genetic factors contribute to the development and susceptibility to joint contractures (74). These experimental results provide insight into molecular changes relevant to the pathophysiology of joint contractures in the context of ADH.

Conclusion

An increasing number of dependent older people are living at home or in long-term care facilities. At least 20% of this population is at risk of developing joint contractures or ADH. These conditions can have significant consequences. They can contribute to functional limitations, discomfort and decreased quality of life. However, little is known about preventing and treating ADH. Better knowledge of the etiological factors and pathophysiologic mechanisms of ADH is needed and might help improve patient care and lead to new therapeutic approaches.

Legend

Figure. Histomorphological changes in the posterior side of the rat knee joint after 16 weeks of immobility. Microphotograph of a sagittal section of the rat knee joint at the medial mid-condylar plane stained with Alcian blue and direct red. A markedly reduced posterior capsule length is shown in the immobilized knee caused by obliteration of the joint recess and synovial folds. Irregularity and degeneration of articular cartilage is noticeable on both the femur and tibia as compared with the smooth and uniform articular cartilage on the

contralateral knee. A) 3.3X magnification of contralateral knee. B) 6.6X magnification enlargement of boxed region in A. C) 6.6X magnification of knee immobilized for 16 weeks. F, femur; T, tibia; M, meniscus. Dotted lines measure synovial intima length of the posterior capsule. Open circles indicate measurement from the medial horn of the meniscus to the synovial cartilage junction. Arrows indicate the degeneration and irregularity of the articular cartilage. Magnification 6.6X (Olympus BH2).

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Figure

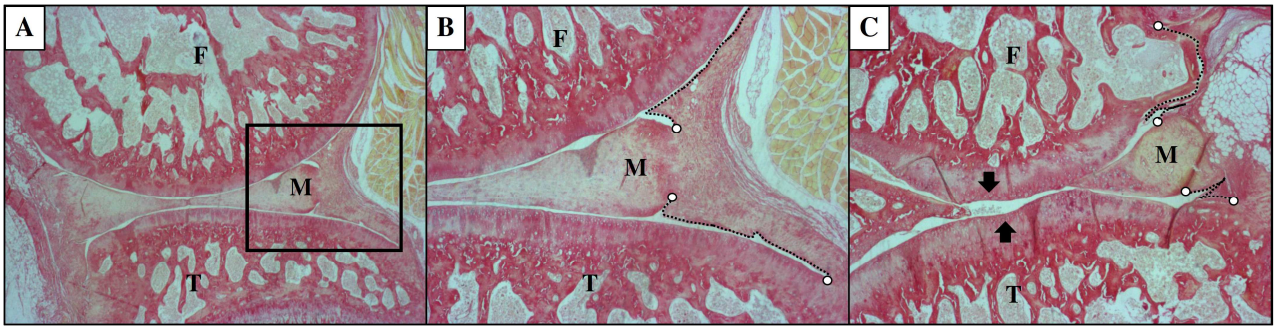

Table 1. Animal models used to study the effects of aging and immobility.

Model	Benefit	Drawback
Aging and immobility		
Senescence-accelerated mouse [a]	Premature onset of aging-related bone and joint disease. Rapid testing of hypotheses about the causes and treatments of aging-related orthopaedic complications.	Mechanisms by which senescent cells promote degeneration of bone and joint tissues is unknown.
Rat knee immobilisation [b]	Investigation of joint contractures secondary to immobility and study of its temporal progression and reversibility.	Direction of limitation of range of motion is unidirectional, and natural standing position of rat knees is in flexion.
Rabbit knee post-traumatic contractures [c]	Modelling post-traumatic joint contracture with a fracture that exposes the joint environment to a hemarthrosis with bone-marrow elements. Joint stability or congruity are not compromised.	Model is limited to flexion contractures.
Aging		
Inbred mice [d]	Genetic similarity minimizes confounding factors attributing differences to environmental or treatment effects.	Genetic uniformity of inbred strains is not representative of the human population. Limited in range of pathology.
Outbred and F1 mice [d]	Hybrid vigor, long life span, rapid growth, large size. Considered to be more representative of human population.	Heterogeneity limits the assessment of the benefits of an intervention.

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Table 2. List of differentially expressed genes and pathways in the posterior joint capsule during immobilization-induced joint contracture [73].

Gene Ontology: biochemical pathways	**Genes** [3]
Lipid biosynthetic and metabolic process [1]	Fasn, Ggat2, Acaca, Gpd1, Elov1, and Acsl1.
Extracellular structure and organization[2]	MMP3, MMP9, MMP13, Col2a1, Col10a1, Col11a1, Agt, Alb, Cdh1, Cdh2, Cfd, Chad, Ibsp, Ky, Myh11, Obp3, Pcsk6, Tf, Tnfrsf11b, Tnn, and Vit.

[1] All 7 genes showed reduced expression over the immobilization time course [93].

[2] All metalloproteinase genes (MMPs) showed a decreased expression profile over the immobilization time course [89].

[3] Fasn: fatty acid synthase; Ggat2: glutamate-glyoxylate aminotransferase 2; Acaca: acetyl-CoA carboxylase alpha; Gpd: glycerol-3-phosphate dehydrogenase 1; Elov1: elongation of very long chain fatty acids protein 1; Acs11: 1-aminocyclopropane-1-carboxylate synthase 11; MMP: metalloproteinase genes; Col: collagen type alpha chain; Cdh: cadherin; Cfd: complement factor D; Chad: chondroadherin; Ibsp: integrin binding sialoprotein; Ky: kyphoscoliosis peptidase; Myh11: myosin heavy chain 11; Obp3: odorant bind protein; Pcsk6: proprotein convertase subtilisin/kexin type 6; Tf: transferrin; Tnfrsf11b: TNF receptor superfamily member 11b; Tnn: Tenascin N; Vit: vitrin.