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**Emotions modulate subthalamic nucleus activity: new evidence in obsessive-compulsive disorder
and Parkinson disease patients**

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Abstract

Background: Subthalamic nucleus (STN) deep brain stimulation (DBS) alleviates obsessive-compulsive disorder (OCD) symptoms, suggesting that this basal ganglia structure may play a key role in integrating limbic and motor information. We explored the modulation of STN neural activity by visual emotional information under different motor demands.

Methods: We compared STN local field potentials acquired in 7 obsessive-compulsive disorder (OCD) and 15 Parkinson's disease (PD) patients Off and On-levodopa while patients categorized pictures as unpleasant, pleasant or neutral, and pressed a button for one of these 3 categories depending on the instruction.

Results: During image presentation, theta power increased for unpleasant compared to neutral images in both OCD and PD patients. Only in OCD patients was theta power also increased in pleasant compared to neutral trials. During the button-press in OCD patients, no modification of STN activity was seen on average but theta power increased when the image triggering the motor response was unpleasant. Conversely in PD patients, a beta decrease was observed during the button press unrelated to the valence of the stimulus. Finally, in OCD patients, a significant positive relationship was observed between the amplitude of the emotionally-related theta response and symptom severity (measured using Yale Brown OCD scale [YBOCS]).

Conclusion: We highlighted modulations of STN theta band activity related to emotions that were specific to OCD and correlated with OCD symptoms severity. STN theta induced activity might therefore underlie dysfunction of the limbic STN and its related network leading to OCD pathophysiology.

Introduction

Obsessive compulsive disorder (OCD) is characterized by repetitive intrusive thoughts (obsessions), and behaviors (compulsions) (1). Forty to 60% of patients have persistent symptoms despite cognitive behavioral therapy and selective serotonin reuptake inhibitors (SSRIs) and 20% of patients are considered refractory (2,3). In line with experimental (4–6) and clinical findings (7) that OCD results from dysfunction of the limbic cortico-basal ganglia-thalamo-cortical loop (8), deep brain stimulation (DBS) of the limbic part of various basal ganglia nuclei has been proposed to treat severe OCD patients with resistant symptoms (9,10), with two recent meta-analyses reporting that 60% of OCD patients respond to DBS whatever the target (11,12). The multiplicity of targeted structures and the absence of significant differences between them highlights the need to better characterize the specific involvement of various regions of the complex limbic cortico-basal ganglia circuitry in the pathophysiology of OCD (8,13,14).

At rest, STN single-unit neuronal recordings in OCD patients indicate that average firing rate is similar to that of normal monkeys but with less beta and more low frequency (1-4 Hz) oscillations compared to PD patients (15,16), with a correlation between low frequency power and OCD severity (16). During doubt and before checking behaviors, increased STN spiking activity has also been observed (17). Using STN local field potential (LFP) recordings, increased oscillatory activity in alpha/beta bands was recorded in two OCD patients during acute symptoms (18), and theta (6.5-8 Hz) power in the ventral STN of one patient was negatively correlated with OCD symptom severity (19). In the STN of PD patients, low-frequency oscillatory activity has been involved in emotional processing (20,21) and subjective value coding (22,23). All together, these data suggest that emotion-related modulation of theta oscillatory activity within the STN could represent a pathological biomarker for OCD. Outside of OCD pathophysiology, the basal ganglia have been implicated in action selection (24), with a potential role for the STN in delaying decision and action especially in high-conflict situations (25,26). It seems therefore important to study how STN emotion-related activity evolves in relation to upcoming actions.

To further explore the role of the STN in emotional processing and better understand the link between emotional processing and action in OCD, we recorded STN-LFP activity while OCD patients perform an emotional categorization task that combined emotional processing with motor responses

(27). We compared the results obtained with those recorded in the same condition in PD patients without and with dopaminergic treatment, with a posterior dorsolateral position in PD (28) *versus* an anterior ventromedial in OCD (29).

MATERIALS AND METHODS

Patients

Fifteen patients with PD and 7 patients with OCD participated to the study and signed informed written consent. The protocol was approved by the local ethics committee for biomedical research and supported by INSERM and APHP (RBM C07-42, STOC Study Clinical trials NCT00169377). Inclusion criteria for DBS surgery in the two groups of patients were previously published (29,30). Demographic and clinical features of the patients are listed in the Tables 1 and 2.

Surgical procedure and location of definitive DBS electrodes

We targeted the STN using a combination of a direct T1 and T2 MRI visualization and an indirect method using our validated 3D histological and deformable atlas of the basal ganglia (YeB atlas, (31,32). We used a Leksell frame (Elekta Instruments, Inc) to bilaterally implant quadripolar electrodes (3389-28; Medtronic, Minneapolis, Minn., USA), combining intra-operative microelectrode recordings and stimulation tests.

The definitive DBS electrode locations were determined using the YeB atlas. As we performed bipolar recordings between two adjacent contacts on the electrode, the location of the dipoles was computed as the inter-contact positions. Dipole coordinates were normalized and expressed in AC-PC coordinates.

Experimental design

Stimuli

Complex pictures were selected from the International Affective Picture System (33) and the Internet. Stimuli valence and arousal were assessed in 80 control subjects (20–70 years old; mean age 40 ± 15 years) using the Self-Assessment Manikin Scale (34). The pictures were separated into pleasant (mean $\pm$ SD: valence= 6.6 ± 1.3 , arousal= 4.1 ± 2.2), unpleasant (valence= 2.5 ± 1.2 , arousal= 5.6 ± 2.0) and

neutral (valence= 5 ± 0.9 , arousal= 1.7 ± 1.2) valences.

Task

Each trial consisted of a fixation point (random time from 1 to 3s), followed by image presentation (1s), followed by a question mark (3s) initiating the response phase (Figure 2A, (27)). The task comprised two active (A and B) and one passive (C) condition. In A, the patient had to evaluate the unpleasantness/pleasantness of the pictures according to their own feelings and indicate unpleasant/pleasant pictures by pressing a button during the response phase. In B, the rules were inverted and patients had to indicate neutral pictures. In C, patients passively looked at the pictures. This design generated 'emotional motor' and 'neutral non-motor' trials (A), 'emotional non-motor' and 'neutral motor' trials (B), 'emotional passive' and 'neutral passive' trials (C). Blocks of 100 trials containing 50% neutral and 50% emotional stimuli (either pleasant or unpleasant, none containing both pleasant and unpleasant pictures) were assigned to each condition, for a total of 50 trials per valence and condition, with the same trial duration for each condition, and equal mean luminance and mean spatial frequency content between blocks. Each picture was presented only once during the experiment. The sequence of pictures within blocks, the association between block and condition, and the order of active conditions (A and B) were randomized between patients. All patients first performed the passive condition without being informed of the upcoming categorization task to avoid explicit categorization and motor preparation in passive trials.

Procedure

We recorded STN-LFPs 3 to 4 days after surgery. All PD patients completed the task Off dopaminergic medication and 7 completed the task On medication. The Off-dopa recordings were made after an overnight withdrawal of dopaminergic medication. The On-dopa recordings were made 1 hour after the intake of the patient's morning dosage. For all patients, the experiment started with a 3-minute recording at rest. The emotional categorization task was then performed using a 15-inch screen displaying the stimuli and a button pad on which patients responded with their right hand. Due to fatigue and the postoperative state, not all patients completed the full experiment. All patients (n=22) performed the unpleasant task but 3 patients did not perform the pleasant task (2 PD-Off, 1 PD-On).

Recordings

Local field potentials (LFPs) were recorded bilaterally using definitive stimulating electrodes, which have four platinum-iridium cylindrical contacts (1.27mm in diameter, 1.5mm in length) separated by 0.5mm. Bipolar recordings were made between adjacent contacts of the electrode, yielding six recordings channels per patients. For 19 patients, signals were amplified and digitized at 512Hz using an EEG amplifier (Digital EEG-EP Multifunction System, EBNeuro, Italy). For the 3 remaining patients (OCD patients), signals were digitized at 2048 Hz using a different EEG amplifier (Porti systems, TMSI, Netherlands). Signals sampled at 2048Hz were resampled to 512Hz prior to analysis.

Data analysis and statistics

Behavior

We assessed patient performance (ability to categorize pictures as unpleasant, pleasant or neutral) by comparing their categorization with healthy controls (27). A trial was correct if the patient attributed to the image the valence previously defined and responded during the question mark. Reaction times (RT) were computed from picture offset. Behavioral performance and RTs were compared between patient groups (OCD, PD-Off, PD-On) and between emotional valences (negative, positive and neutral) using mixed-effect models. The models included fixed-effects for patient group, emotional valence and the interaction between the two, as well as random intercepts by subject.

Analyses

Analyses were performed using Matlab (MATLAB 2019b, The MathWorks, Inc., Natick, Massachusetts, United States) and R (version 3.6.1, R Core Team, 2014).

Seventeen out of 174 recording channels were excluded due to excessive noise (PD-Off: 8 channels in 3 patients, PD-On: 6 channels in 2 patients, OCD: 5 channels in 2 patient). The remaining continuous bipolar recordings were high-pass filtered at 1.5Hz using a FIR filter and included for spectral analysis.

Recordings at rest were divided into contiguous 4 seconds segments, and artifactual segments were rejected through visual inspection (0 to 25%). For each segment, the power spectrum was

estimated using a multitaper algorithm (35) with 9 orthogonal tapers and a time-bandwidth product equal to 5, resulting in a frequency half-bandwidth of 1.25Hz. Estimates were log-transformed, averaged across segments and normalized by subtracting the power averaged across the 85 to 95Hz frequency band. We chose this frequency window as no peak in these frequencies could be detected for any patient group. Power was then averaged across 5 frequency bands: theta (3-8Hz), alpha (8-12Hz), low-beta (12-25Hz), high-beta (25-35Hz) and gamma (40-80Hz). Differences were tested using linear mixed-effect models that included a fixed effect for patient group (PD-Off or PD-On or OCD) with random intercepts by patient.

Recordings during the task were divided into 4s epochs, starting 1s before to 3s after stimulus onset. Artifacts segments were rejected through visual inspection (0 to 39% of trials, mean $\pm$ SD number of trials per patient valence and condition =25 $\pm$ 8). Time-frequency maps were estimated using the multitaper algorithm, on 500ms sliding window stepped by 50ms, using 5 orthogonal tapers with a time-bandwidth product equal to 3, resulting in a frequency half-bandwidth of 6Hz. Log transformed power was baseline normalized for each trial using a 500ms pre-stimulus window [-750 to -250ms]. The same baseline period was used for cue-induced and motor-related responses.

We analyzed time-frequency data by fitting linear mixed models to predict estimated power at each time-frequency point. When testing cue-induced modulations we included fixed effects for patient group (PD-Off or PD-On or OCD), emotional valence (negative or positive or neutral), trial type (motor or non-motor or passive), and the interaction between these three variables. We also included fixed effects for hemisphere (left or right) and dipole position (mediolateral, anteroposterior and dorsoventral). When testing motor-induced modulations we included fixed effects for patient group, emotional valence, and the interaction between these two variables. We also included fixed effects for hemisphere, dipole position, and reaction time. All models included random intercepts by patient. We fit the linear mixed models using the R package lme4 (version 1.1, (36)), and assessed significance using Satterthwaite's approximation for the denominator degrees of freedom of the F-statistic. To examine emotional and motor demand specificity, we computed estimated marginal means contrasting emotional and neutral trials, separated by patient group and motor condition. We adjusted multiple comparisons to control for the false discovery rate (37).

To summarize comparisons between patient groups and motor demand, we used the same linear mixed models as described previously, modelling the average power in five frequency bands (theta, alpha, low beta, high beta, gamma). For each frequency band, we modeled cue-induced and motor-related activity averaged over a 750ms time window, [0 to 750ms] post stimulus onset for cue-induced activity, [-250 to 500ms] around the button press for motor-related activity.

RESULTS

Electrode localization in OCD and PD patients

Figure 1 illustrates the recording locations in OCD and PD patients. Dipoles were located more medially and anteriorly in OCD compared to PD. The mean AC-PC coordinates were laterality (X, mm±SD): OCD: 10.0±1.61, and PD: 10.72±1.70 ($p<10^{-4}$); anteroposteriority (Y): OCD: 9.35±1.34 and PD: 9.24±1.57 ($p=.06$), and depth (Z): OCD: 3.06±1.71 and PD: 3.19±1.95 ($p=.70$).

Task performances and reaction times

OCD and PD categorized pictures correctly in 81±4% of trials, with no difference between OCD and PD but a significant difference between PD-Off and PD-On (Figure 2B, estimated mean performance in %±SE for OCD =87±3.7, PD-Off =81±3.4, PD-On =76±4.2; OCD *versus* PD-Off: $p=.24$; OCD *versus* PD-On: $p=.09$; PD-Off *versus* PD-On: $p=.005$). Looking at different valences, we observed higher performance for both OCD and PD-Off when compared to PD-On in unpleasant trials only (OCD *versus* PD-On: $p=.0073$; PD-Off *versus* PD-On: $p=.003$). Patients responded with a mean RT±SE = 786±51ms with no difference between OCD and PD (Figure 2C, estimated mean RT±SE in ms for OCD =827±54, PD-Off = 729±37, PD-On =803±39; OCD *versus* PD-Off: $p=.22$; OCD *versus* PD-On: $p=.71$), but significantly faster RT in PD-Off compared to PD-On ($p=.0009$). Looking at different valences, we observed faster RT in both OCD and PD-Off when compared to PD-On in unpleasant trials only (OCD *versus* PD On: $p=.003$; PD-Off *versus* PD-On: $p=.007$).

STN neuronal activity in OCD and PD patients

Resting state activity

We first evaluated if STN activity at rest differed between OCD and PD-Off and On. STN-LFP power was lower in the alpha, low- and high-beta bands in OCD compared to PD-Off and only lower in the high-beta in OCD compared to PD-On. PD-On power in the alpha and low-beta bands was lower compared to PD-Off (Figure 3).

Cue-induced activity

We examined how average STN activity to cue presentation differed from baseline by visualizing mean effects marginalizing over all task conditions (Figure 4). In OCD, cue onset induced increased theta power that was not significant (Figure 4, left panel). In PD Off- and On-dopa, cue onset also induced significantly increased theta power (Figure 4 middle and right panels). The cue-induced theta increase was followed by a decrease in alpha/beta power that was maintained through the response window, which was significant only in PD Off-dopa.

Cue-induced unpleasant modulations

We then looked at the effect of unpleasant emotion and motor context on cue-induced activity. Figure 5A illustrates cue-aligned time-frequency maps of the mean effect of unpleasant versus neutral images, separated by trial type (motor, non-motor, passive). In OCD, we found significantly higher power centered in the theta band only during motor trials (Figure 5A, left panels). We also observed weaker clusters of increased power in the high beta/low gamma bands in both motor and passive trials. In PD Off-dopa, we also observed increased power centered in the theta band in both motor and non-motor trials, with an additional decrease in alpha/low-beta power during non-motor trials (Figure 5A, middle panels). In PD On-dopa, we also observed an increase in theta power although it did not reach significance in any of the motor conditions (Figure 5A, right panels).

We compared the effects of unpleasant emotion between patient groups using averaged STN activity (0 to 750ms after cue onset) within five frequency bands (Table 3). Cue-induced theta power during motor and non-motor trials was not significantly different between OCD and PD, nor between PD Off and On-dopa. On passive trials, a small difference in theta power was observed between OCD and PD Off-dopa ($p=.036$). We observed few significant differences in the rest of the frequency spectrum, with weak differences between OCD and PD-Off in the alpha band in non-motor trials

($p=.048$), and between OCD and PD both On and Off-dopa in the low-beta in motor trials (OCD vs PD-Off: $p=.048$; OCD vs PD-On: $p=.052$).

Cue-induced pleasant emotional processing

We then looked at the effect of pleasant emotion and motor context on cue-induced activity. Figure 5B illustrates cue-aligned time-frequency maps of the mean effects of pleasant versus neutral images, separated by trial type (motor, non-motor, passive). In OCD, we found significantly higher power centered in the theta band (Figure 5B, left panels), which was strongest for motor trials, when a button press was required for categorizing a pleasant image, and weakest for the passive trials when no explicit categorization was required for any image. In PD, we did not observe significant changes in theta band power, and changes in other frequency bands were extremely weak (alpha power increase in PD-Off motor trials and PD-On passive trials).

As for unpleasant trials, we compared the effects of pleasant emotion between patient groups (Table 3). Cue-induced theta and alpha power was larger in OCD compared to PD both On and Off-dopa. These differences were significant in both motor and non-motor trials, but not in passive trials. We also observed a smaller difference between PD-Off and PD-On in the alpha band for non-motor trials ($p=.043$), between OCD and PD both On and Off in the high-beta for motor trials (OCD *versus* PD-Off: $p=.046$; OCD *versus* PD-On: $p=.046$) and between OCD and PD-Off in the gamma band for passive trials ($p=.033$).

Movement-related activity

We examined how average STN activity at the time of the button-press differed from baseline by visualizing mean effects marginalizing over all task conditions (Figure 6). In OCD, movement induced small changes in STN-LFP activity that did not reach significance (Figure 6 left panels). In PD, movement induced decreased alpha and low-beta band activities with increased gamma band activity, both Off- and On-dopa (Figure 6 middle and right panels).

Movement-related emotional processing

We then looked at the effect of emotion on movement-related activity. Figure 7A and B illustrates movement-aligned time-frequency maps of the mean effect of unpleasant or pleasant versus neutral images, respectively. In OCD, we observed increased theta power for unpleasant *versus* neutral trials around the time of movement (Figure 7A left panel), with no significant changes for pleasant *versus* neutral trials (Figure 7B left panel). Conversely in PD, we observed smaller changes during the button press (Figure 7A and B middle and right panels), limited to two small significant clusters in the alpha/low beta band in pleasant *versus* neutral trials (Figure 7B middle panel).

We compared the effects of emotion between patient groups using averaged STN activity around the button press (-250 to 500ms around movement detection) within five frequency bands (Table 4). The theta increase observed in unpleasant trials was higher in OCD compared to PD both On and Off-dopa (OCD *versus* PD-Off: $p < .0001$, OCD *versus* PD-On: $p = .0001$). No other differences were seen in any other frequency band or in pleasant *versus* neutral trials.

Interaction between emotion-related theta activity and OCD severity

To explore the link between task-induced theta activity and OCD symptoms, we evaluated whether emotional modulations were moderated by OCD severity (measured using YBOCS score). We augmented our linear mixed model of theta activity to test for an interaction between emotion and YBOCS score following the cue and during the motor response. For the unpleasant task, we found that the interaction between emotion and YBOCS was not significant during cue presentation ($p > .05$, Figure 8A upper panel), although there was a significant main effect with unpleasant images evoking larger theta responses compared to neutral images ($p < .001$) consistent with our prior analyses (cf. Figure 5). During the motor response, we observed a significant interaction between emotion and YBOCS ($p < .001$, Figure 8A lower panel), with larger theta responses with increasing OCD severity in unpleasant trials. In contrast, during the pleasant task, we observed a significant interaction between emotion and YBOCS ($p < .001$, Figure 8B upper panel), with pleasant images evoking larger theta responses with increasing OCD severity. During the motor response we did not observe any effect of YBOCS (Figure 8B lower panel), consistent with the lack of theta response for this condition in OCD patients (cf. Figure 7). We tested for an effect of dorsal-ventral dipole localization by adding the dorsal-ventral position of each dipole for each patient (mm in AC-PC coordinates). There was no significant effect of dorsal-ventral

localization for predicting the theta response during either the cue or movement periods (likelihood ratio test, $p > .05$ for all comparisons).

Discussion

We showed that emotional images modulate STN activity in OCD patients, and that these modulations differ markedly from those observed in PD patients, and were moderated by OCD severity. Emotional modulation of LFP power during image presentation was largely restricted to low frequencies (2-8 Hz) including the theta band. For OCD patients, this theta modulation was similar in sign and magnitude for both positively and negatively valenced images only for OCD patients. In PD, emotional modulation was only observed for negative images. Emotional modulation of LFP power was also observed at the time of the button-press in negative trials in OCD patients only. In PD, the motor response was marked by a decrease in beta power that was not modulated by the emotional context.

Pathological STN emotional processing in OCD

The differences of STN activity in relation to emotion observed between OCD and PD patients could be related to different electrode positions in these two groups of patients and/or to disease condition. The first hypothesis would be consistent with the anatomo-functional organization of the STN, with anterior and posterior STN territories receiving projections from limbic and sensorimotor pallidal territories (38) and cortical areas (39,40), respectively. This would imply that different valences are encoded in distinct neuronal populations (41,42), which would be difficult to resolve using LFP recordings. The positive correlation between the amplitude of the emotional effect and the YBOCS favors however the possibility that emotional processing within the limbic cortico-basal ganglia loop is pathological in OCD patients (43). The implication of low frequency activity including theta band in OCD pathophysiology is consistent with single-unit recordings showing a positive correlation between low frequency (1-4 Hz) activity and YBOCS (16). However, a recent study showed that decreases in symptoms severity were accompanied by increased theta (6.5-8 Hz) power at rest measured in one patient over the course of several months (19). These authors also showed decreased theta power during the presentation of OCD provocative images. The apparent discrepancy between our results and this study might be related to the fact that they studied STN activity at rest or using images that directly provoked symptoms whereas

we examined task-induced activity using images that had no direct relationship with OCD symptoms. Our results compliment these by showing that both unpleasant and pleasant stimuli lead to similar modulation of anterior STN activity in OCD, which may indicate the absence of selective modulation in these patients.

For unpleasant pictures in both OCD and PD patients, we found that STN modulation depended on impending motor demands, with increased theta activity for emotional images being significantly stronger when a motor response was instructed. Increased theta activity could reflect a precocious step of action selection, with the STN filtering or modulating the threshold to let an action emerge (25) depending on the emotional context. In this framework, the presence of an emotional modulation at the time of the action performed in an unpleasant context could also represent a pathological signal in OCD, eventually leading to action repetition.

STN activity in PD

Modulations of STN theta activity were also observed in PD patients both On and Off-dopa for unpleasant images, suggesting that STN modulation for negative valence could be a physiological pattern of activity. This is in line with previous studies in PD patients reporting modulations of STN activity in emotional tasks using visual images (27). Interestingly, others authors also reported alpha power modulation for pleasant pictures in the STN of PD patients but this change occurred later (1 to 2 sec after stimulus onset) and in a passive task (21).

During movements, we observed a significant decrease in alpha and beta band power and an increase in gamma band power in PD patients. Such modulations are well-documented in PD patients (44–46), where low-beta activity is consistently decreased after dopaminergic medication or STN-DBS (47–50).

Limitations

The targeted STN anatomo-functional territories are different between patients. We targeted the anterior associative-limbic STN in OCD patients and the posterior associative-motor STN in PD patients. This difference could be responsible for some of the differences observed in the electrophysiological results during our task, possibly related to the normal functioning of the different anatomo-functional

STN territories. We also note that our sample of OCD patients was smaller than our sample of PD patients, and that our sample of PD patients On-dopa was smaller than our sample of PD patients Off-dopa. This could have limited our power to detect differences between these groups. Future comparative studies with a larger group of OCD patients may detect differences outside of those we observed in the current study. Finally, the lower valence and arousal scores for pleasant relative to unpleasant pictures could have accentuated the changes in STN activity obtained with unpleasant *versus* neutral pictures.

Conclusion

Our results highlight different patterns of STN activity during emotional processing in OCD and PD patients. Theta activity observed in the STN could represent aberrant local or network processing that is related to OCD symptoms. This suggests that task-related theta activity may be useful as a biomarker for developing more specific and adapted DBS strategies to alleviate OCD. The identification of biomarkers, in relationship with others structural and functional imaging approaches (51,52,53) might help in understanding the networks mediating DBS efficiency.

References

1. Ruscio AM, Stein DJ, Chiu WT, Kessler RC (2010): The epidemiology of obsessive-compulsive disorder in the National Comorbidity Survey Replication. *Mol Psychiatry* 15: 53–63.
2. Skapinakis P, Caldwell DM, Hollingworth W, Bryden P, Fineberg NA, Salkovskis P, *et al.* (2016): Pharmacological and psychotherapeutic interventions for management of obsessive-compulsive disorder in adults: a systematic review and network meta-analysis. *Lancet Psychiatry* 3: 730–739.
3. Hirschtritt ME, Bloch MH, Mathews CA (2017): Obsessive-Compulsive Disorder: Advances in Diagnosis and Treatment. *JAMA* 317: 1358–1367.
4. Ahmari SE, Spellman T, Douglass NL, Kheirbek MA, Simpson HB, Deisseroth K, *et al.* (2013): Repeated cortico-striatal stimulation generates persistent OCD-like behavior. *Science* 340: 1234–1239.
5. Burguière E, Monteiro P, Feng G, Graybiel AM (2013): Optogenetic stimulation of lateral orbitofronto-striatal pathway suppresses compulsive behaviors. *Science* 340: 1243–1246.
6. Burguière E, Monteiro P, Mallet L, Feng G, Graybiel AM (2015): Striatal circuits, habits, and implications for obsessive-compulsive disorder. *Curr Opin Neurobiol* 30: 59–65.
7. Menzies L, Chamberlain SR, Laird AR, Thelen SM, Sahakian BJ, Bullmore ET (2008): Integrating evidence from neuroimaging and neuropsychological studies of obsessive-compulsive disorder: the orbitofronto-striatal model revisited. *Neurosci Biobehav Rev* 32: 525–549.
8. Robbins TW, Vaghi MM, Banca P (2019): Obsessive-Compulsive Disorder: Puzzles and Prospects. *Neuron* 102: 27–47.
9. Nuttin B, Wu H, Mayberg H, Hariz M, Gabriëls L, Galert T, *et al.* (2014): Consensus on guidelines for stereotactic neurosurgery for psychiatric disorders. *J Neurol Neurosurg Psychiatry* 85: 1003–1008.
10. Kohl S, Schönherr DM, Luigjes J, Denys D, Mueller UJ, Lenartz D, *et al.* (2014): Deep brain stimulation for treatment-refractory obsessive compulsive disorder: a systematic review. *BMC Psychiatry* 14: 214.

11. Kisely S, Hall K, Siskind D, Frater J, Olson S, Crompton D (2014): Deep brain stimulation for obsessive-compulsive disorder: a systematic review and meta-analysis. *Psychol Med* 44: 3533–3542.
12. Alonso P, Cuadras D, Gabriëls L, Denys D, Goodman W, Greenberg BD, *et al.* (2015): Deep Brain Stimulation for Obsessive-Compulsive Disorder: A Meta-Analysis of Treatment Outcome and Predictors of Response. *PLoS ONE* 10: e0133591.
13. Rotge J-Y, Langbour N, Jaafari N, Guehl D, Bioulac B, Aouizerate B, *et al.* (2010): Anatomical alterations and symptom-related functional activity in obsessive-compulsive disorder are correlated in the lateral orbitofrontal cortex. *Biol Psychiatry* 67: e37-38.
14. Velikova S, Locatelli M, Insacco C, Smeraldi E, Comi G, Leocani L (2010): Dysfunctional brain circuitry in obsessive-compulsive disorder: source and coherence analysis of EEG rhythms. *Neuroimage* 49: 977–983.
15. Piallat B, Polosan M, Fraix V, Goetz L, David O, Fenoy A, *et al.* (2011): Subthalamic neuronal firing in obsessive-compulsive disorder and Parkinson disease. *Ann Neurol* 69: 793–802.
16. Welter M-L, Burbaud P, Fernandez-Vidal S, Bardinet E, Coste J, Piallat B, *et al.* (2011): Basal ganglia dysfunction in OCD: subthalamic neuronal activity correlates with symptoms severity and predicts high-frequency stimulation efficacy. *Transl Psychiatry* 1: e5.
17. Burbaud P, Clair A-H, Langbour N, Fernandez-Vidal S, Goillandeau M, Michelet T, *et al.* (2013): Neuronal activity correlated with checking behaviour in the subthalamic nucleus of patients with obsessive-compulsive disorder. *Brain* 136: 304–317.
18. Bastin J, Polosan M, Piallat B, Krack P, Bougerol T, Chabardès S, David O (2014): Changes of oscillatory activity in the subthalamic nucleus during obsessive-compulsive disorder symptoms: two case reports. *Cortex* 60: 145–150.
19. Rappel P, Marmor O, Bick AS, Arkadir D, Linetsky E, Castrioto A, *et al.* (2018): Subthalamic theta activity: a novel human subcortical biomarker for obsessive compulsive disorder. *Transl Psychiatry* 8: 118.
20. Kühn AA, Hariz MI, Silberstein P, Tisch S, Kupsch A, Schneider G-H, *et al.* (2005): Activation of the subthalamic region during emotional processing in Parkinson disease. *Neurology* 65: 707–713.

21. Brücke C, Kupsch A, Schneider G-H, Hariz MI, Nuttin B, Kopp U, *et al.* (2007): The subthalamic region is activated during valence-related emotional processing in patients with Parkinson's disease. *European Journal of Neuroscience* 26: 767–774.
22. Zénon A, Duclos Y, Carron R, Witjas T, Baunez C, Régis J, *et al.* (2016): The human subthalamic nucleus encodes the subjective value of reward and the cost of effort during decision-making. *Brain* 139: 1830–1843.
23. Al-Ozzi TM, Botero-Posada LF, Rios ALL, Hutchison WD (n.d.): Single unit and beta oscillatory activities in subthalamic nucleus are modulated during visual choice preference. *European Journal of Neuroscience* n/a. <https://doi.org/10.1111/ejn.14750>
24. DeLong M, Wichmann T (2009): Update on models of basal ganglia function and dysfunction. *Parkinsonism Relat Disord* 15: S237–S240.
25. Frank MJ, Samanta J, Moustafa AA, Sherman SJ (2007): Hold your horses: impulsivity, deep brain stimulation, and medication in parkinsonism. *Science* 318: 1309–1312.
26. Cavanagh JF, Wiecki TV, Cohen MX, Figueroa CM, Samanta J, Sherman SJ, Frank MJ (2011): Subthalamic nucleus stimulation reverses mediofrontal influence over decision threshold. *Nat Neurosci* 14: 1462–1467.
27. Buot A, Welter M-L, Karachi C, Pochon J-B, Bardinet E, Yelnik J, Mallet L (2013): Processing of emotional information in the human subthalamic nucleus. *J Neurol Neurosurg Psychiatr* 84: 1331–1338.
28. Zaidel A, Spivak A, Shpigelman L, Bergman H, Israel Z (2009): Delimiting subterritories of the human subthalamic nucleus by means of microelectrode recordings and a Hidden Markov Model. *Mov Disord* 24: 1785–1793.
29. Mallet L, Polosan M, Jaafari N, Baup N, Welter M-L, Fontaine D, *et al.* (2008): Subthalamic nucleus stimulation in severe obsessive-compulsive disorder. *N Engl J Med* 359: 2121–2134.
30. Welter ML, Houeto JL, Tezenas du Montcel S, Mesnage V, Bonnet AM, Pillon B, *et al.* (2002): Clinical predictive factors of subthalamic stimulation in Parkinson's disease. *Brain* 125: 575–583.

31. Yelnik J, Bardinet E, Dormont D, Malandain G, Ourselin S, Tandé D, *et al.* (2007): A three-dimensional, histological and deformable atlas of the human basal ganglia. I. Atlas construction based on immunohistochemical and MRI data. *Neuroimage* 34: 618–638.
32. Bardinet E, Bhattacharjee M, Dormont D, Pidoux B, Malandain G, Schüpbach M, *et al.* (2009): A three-dimensional histological atlas of the human basal ganglia. II. Atlas deformation strategy and evaluation in deep brain stimulation for Parkinson disease. *J Neurosurg* 110: 208–219.
33. Lang PJ, Bradley MM, Cuthbert, B.N. (n.d.): International affective picture system (IAPS): Affective ratings of pictures and instruction manual. Technical Report A-8. University of Florida, Gainesville, FL.
34. Bradley MM, Lang PJ (1994): Measuring emotion: the Self-Assessment Manikin and the Semantic Differential. *J Behav Ther Exp Psychiatry* 25: 49–59.
35. Mitra P (2007): *Observed Brain Dynamics*. Oxford University Press.
36. Bates D, Maechler M, Bolker B, Walker S, Christensen RHB, Singmann H, *et al.* (2016): *Lme4: Linear Mixed-Effects Models Using “Eigen” and S4*, version 1.1-12. Retrieved May 19, 2016, from <https://cran.r-project.org/web/packages/lme4/index.html>
37. Benjamini Y (2010): Discovering the false discovery rate. *Journal of the Royal Statistical Society: Series B (Statistical Methodology)* 72: 405–416.
38. Karachi C, François C, Parain K, Bardinet E, Tandé D, Hirsch E, Yelnik J (2002): Three-dimensional cartography of functional territories in the human striatopallidal complex by using calbindin immunoreactivity. *J Comp Neurol* 450: 122–134.
39. Haynes WIA, Haber SN (2013): The organization of prefrontal-subthalamic inputs in primates provides an anatomical substrate for both functional specificity and integration: implications for Basal Ganglia models and deep brain stimulation. *J Neurosci* 33: 4804–4814.
40. Temiz G, Sébille SB, Francois C, Bardinet E, Karachi C (2020): The anatomo-functional organization of the hyperdirect cortical pathway to the subthalamic area using in vivo structural connectivity imaging in humans. *Brain Struct Funct* 225: 551–565.

41. Breyse E, Pelloux Y, Baunez C (2015): The Good and Bad Differentially Encoded within the Subthalamic Nucleus in Rats(1,2,3). *eNeuro* 2. <https://doi.org/10.1523/ENEURO.0014-15.2015>
42. Sieger T, Serranová T, Růžicka F, Vostatek P, Wild J, Štastná D, *et al.* (2015): Distinct populations of neurons respond to emotional valence and arousal in the human subthalamic nucleus. *Proc Natl Acad Sci USA* 112: 3116–3121.
43. Figeé M, Luigjes J, Smolders R, Valencia-Alfonso C-E, van Wingen G, de Kwaasteniet B, *et al.* (2013): Deep brain stimulation restores frontostriatal network activity in obsessive-compulsive disorder. *Nat Neurosci* 16: 386–387.
44. Kühn AA, Williams D, Kupsch A, Limousin P, Hariz M, Schneider G-H, *et al.* (2004): Event-related beta desynchronization in human subthalamic nucleus correlates with motor performance. *Brain* 127: 735–746.
45. Cassidy M, Mazzone P, Oliviero A, Insola A, Tonali P, Di Lazzaro V, Brown P (2002): Movement-related changes in synchronization in the human basal ganglia. *Brain* 125: 1235–1246.
46. Williams D, Kühn A, Kupsch A, Tijssen M, van Bruggen G, Speelman H, *et al.* (2005): The relationship between oscillatory activity and motor reaction time in the parkinsonian subthalamic nucleus. *Eur J Neurosci* 21: 249–258.
47. Kühn AA, Kupsch A, Schneider G-H, Brown P (2006): Reduction in subthalamic 8-35 Hz oscillatory activity correlates with clinical improvement in Parkinson's disease. *Eur J Neurosci* 23: 1956–1960.
48. Levy R, Ashby P, Hutchison WD, Lang AE, Lozano AM, Dostrovsky JO (2002): Dependence of subthalamic nucleus oscillations on movement and dopamine in Parkinson's disease. *Brain* 125: 1196–1209.
49. Doyle LMF, Kühn AA, Hariz M, Kupsch A, Schneider G-H, Brown P (2005): Levodopa-induced modulation of subthalamic beta oscillations during self-paced movements in patients with Parkinson's disease. *Eur J Neurosci* 21: 1403–1412.
50. Weinberger M, Mahant N, Hutchison WD, Lozano AM, Moro E, Hodaie M, *et al.* (2006): Beta oscillatory activity in the subthalamic nucleus and its relation to dopaminergic response in Parkinson's disease. *J Neurophysiol* 96: 3248–3256.

51. Senova S, Clair A-H, Palfi S, Yelnik J, Domenech P, Mallet L (2019): Deep Brain Stimulation for Refractory Obsessive-Compulsive Disorder: Towards an Individualized Approach. *Front Psychiatry* 10. <https://doi.org/10.3389/fpsyt.2019.00905>
52. Tyagi H, Apergis-Schoute AM, Akram H, Foltynie T, Limousin P, Drummond LM, *et al.* (2019): A Randomized Trial Directly Comparing Ventral Capsule and Anteromedial Subthalamic Nucleus Stimulation in Obsessive-Compulsive Disorder: Clinical and Imaging Evidence for Dissociable Effects. *Biological Psychiatry* 85: 726–734.
53. Baldermann JC, Melzer C, Zapf A, Kohl S, Timmermann L, Tittgemeyer M, *et al.* (2019): Connectivity Profile Predictive of Effective Deep Brain Stimulation in Obsessive-Compulsive Disorder. *Biological Psychiatry* 85: 735–743.

Figure Legends

Figure 1. Localization of STN LFP recordings in OCD and PD patients. Views of the left (A) and right (B) STN. Each sphere represents one dipole recorded with DBS electrodes in OCD (orange) and PD (green) patients. STN axes are represented in yellow (mediolateral), green (anteroposterior) and pink (dorsoventral).

Figure 2: Emotional categorization paradigm.

A. Design of the task: Pictures were presented for 1s, preceded by a fixation cross, and followed by a question mark indicating the response phase. In each task (pleasant and unpleasant), 50% of emotional (pleasant or unpleasant) and 50% of neutral pictures were presented. **B.** Performance (% of good responses with mean and SD values) in OCD and PD patients Off- and On-dopa. **C.** Reaction time (mean and SD values) in OCD and PD patients Off- and On-dopa.

Figure 3. Subthalamic resting state activity in OCD and PD patients.

A. Power spectra of rest STN activity averaged across all electrodes for OCD (yellow line) and PD patients Off-(dark green line) and On-dopa (light green line), expressed in decibel. **B.** Mean power spectrum (decibels) in the five frequency bands (theta, alpha, low-beta, high-beta and gamma). Significance code: * $p < .05$, ** $p < .01$ between patient groups (OCD, PD Off- and On-dopa). The error bars represent the sem.

Figure 4. Cue-induced activity in the STN of OCD and PD patients

Average time-frequency maps aligned on cue onset normalized relative to pre-stimulus activity. Effects are plotted marginalizing over emotion and motor context. For each panel, the two vertical lines represent the onset and the offset of the stimulus, the grey violin plots represent the distributions and median reaction times for all trials, and the contours represent significance at $\alpha=0.05$ (FDR-corrected) for the test against baseline (zero).

Figure 5. Emotion-dependent activity following image presentation

Time-frequency maps of estimated effects of unpleasant (A) or pleasant (B) images compared to neutral images. The rows correspond to estimated effects for each of the trial types (motor, non-motor, passive). For each panel, the two vertical lines represent the onset and the offset of the stimulus, and the contours represent significance $\alpha=0.05$ (FDR-corrected) for the test against baseline (zero).

Figure 6. Motor related activity in the STN of OCD and PD patients

Average time-frequency maps aligned on button press normalized relative to pre-stimulus activity. Effects are plotted marginalizing over emotion. For each panel, the grey violin plots represent the distributions and median cue offset times for all trials and the contours represent significance $\alpha=0.05$ (FDR-corrected) for the test against baseline (zero).

Figure 7. Emotion-dependent activity during movement

Time-frequency maps of estimated effects of unpleasant (A) or pleasant (B) images. For each panel, the two vertical lines represent the onset and the offset of the stimulus and the contours represent significance at $\alpha = 0.05$ (FDR-corrected) for the test against baseline (zero).

Figure 8. Interaction between the emotional effect and the YBOCS

Estimated increase in theta power as a function of YBOCS for unpleasant (left panels), pleasant (right panels) and neutral stimuli, during cue presentation (top row) and at the time of the movement (bottom row). Shaded areas represent the 95% confidence interval.

Table 1. Demographic and clinical characteristics of PD patients

N°	Age	Gender	Disease	UPDRS III ^a Off-	UPDRS III On-dopa	^b LEDD	MDRS ^c	Frontal	UPDRS I.3 ^e	Treatment for
01	51	M	8	21	2 (90)	1200	141	55	0	Off
02	57	M	10	MS ^f	MS	MS	138	52	MS	Off + On
03	64	F	19	26	7 (73)	1200	136	48	1	Off + On
04	70	M	8	32	7 (78)	1550	140	54	0	Off
05	77	M	11	21	5 (76)	1100	135	51	0	Off + On
06	74	F	17	24	10 (58)	1062	MS	MS	0	Off + On
07	71	M	14	9	0 (100)	750	143	58	0	Off
08	53	M	5	12	0 (100)	970	MS	MS	0	Off + On
09	57	M	12	26	6 (77)	950	143	56	0	Off + On
10	53	M	12	17	4 (76)	1000	136	54	0	Off
11	44	M	10	48	1 (98)	1050	144	58	2	Off
12	61	F	15	50	21 (58)	450	142	56	0	Off
13	66	F	8	13	0 (100)	660	142	53	1	Off
14	66	M	12	38	4 (89)	800	141	58	0	Off
15	60	M	8	26	3 (88)	980	142	49	0	Off + On
Mean ±	62±9	11 M/4 F	11±4	26±12	5±5 (88%±14%)	980±266	140±3	54±3	[0 – 2]	15 OFF/7 ON

^aUPDRS III=Unified Parkinson's disease rating scale, part III (motor disability, max:108); ^bLEDD=levodopa-equivalent dosage; ^cMDRS= Mattis dementia rating scale

(max:144); ^dFrontal score (max:60); ^eUPDRS item I.3 (max:4); ^fMS=missing data.

Table 2. Demographic and clinical characteristics of OCD patients

N°	Age (yrs)	Gender	Y-BOCS ^a total	Y-BOCS Obsessions	Y-BOCS Compulsions	Medical drug treatment
16	39	F	31	17	14	Fluvoxamine
17	47	F	36	17	19	Hydroxyzine, Buspirone, Venlafaxine
18	41	M	29	14	15	Risperidone, Diazepam, Fluoxetine, Clomipramine
19	43	F	26	12	14	None
20	50	M	33	17	16	None
21	35	F	32	14	18	Clonazepam, Aripiprazole, Escitalopram
22	41	M	29	14	15	Seroplex, Xeroquel, Atarax
Mean ± SD	42±5	2 M/4 F	31±3	15±2	16±2	

^aY-BOCS=Yale-Brown obsessive compulsive scale (max:40); SD=standard deviation.

Table 3: Comparisons of mean activity during cue presentation between groups

		Motor trials			
Frequency	Groups	Unpleasant		Pleasant	
		Estimate (SE)	p-value	Estimate (SE)	p-value
Theta	OCD – PD Off	0.214 (0.149)	.367	0.828 (0.173)	<.0001
	OCD – PD On	0.212 (0.182)	.367	0.914 (0.210)	<.0001
	PD Off – PD On	-0.002 (0.158)	.990	0.086 (0.177)	.626
Alpha	OCD – PD Off	0.137 (0.138)	.717	0.475 (0.159)	.004
	OCD – PD On	0.033 (0.168)	.842	0.655 (0.193)	.002
	PD Off – PD On	-0.103 (0.145)	.717	0.18 (0.162)	.268
Low beta	OCD – PD Off	0.257 (0.107)	.048	-0.014 (0.123)	.909
	OCD – PD On	0.275 (0.130)	.052	0.156 (0.149)	.445
	PD Off – PD On	0.018 (0.113)	.871	0.170 (0.126)	.445
High beta	OCD – PD Off	0.127 (0.107)	.236	0.268 (0.124)	.046
	OCD – PD On	0.268 (0.131)	.124	0.342 (0.151)	.046
	PD Off – PD On	0.141 (0.114)	.236	0.073 (0.127)	.563
Gamma	OCD – PD Off	0.0666 (0.057)	.240	0.010 (0.065)	.873
	OCD – PD On	0.1704 (0.069)	.042	-0.049 (0.079)	.805
	PD Off – PD On	0.1038 (0.060)	.125	-0.059 (0.067)	.805

		Non-motor trials			
Frequency	Groups	Unpleasant		Pleasant	
		Estimate (SE)	p-value	Estimate (SE)	p-value
Theta	OCD – PD Off	-0.145 (0.14)	.452	0.509 (0.164)	.003
	OCD – PD On	-0.193(0.168)	.452	0.624 (0.196)	.003
	PD Off – PD On	-0.048 (0.142)	.733	0.115 (0.166)	.488
Alpha	OCD – PD Off	0.141 (0.129)	.273	0.468 (0.150)	.003
	OCD – PD On	-0.174 (0.155)	.273	0.777 (0.180)	<.0001
	PD Off – PD On	-0.315 (0.131)	.048	0.309 (0.152)	.042
Low beta	OCD – PD Off	0.171 (0.101)	.260	0.120 (0.117)	.456
	OCD – PD On	0.120 (0.122)	.474	0.168 (0.140)	.456
	PD Off – PD On	-0.051 (0.105)	.616	0.048 (0.118)	.682
High beta	OCD – PD Off	0.164 (0.101)	.156	0.081 (0.117)	.736
	OCD – PD On	0.277 (0.121)	.067	0.118 (0.141)	.736
	PD Off – PD On	0.113 (0.102)	.269	0.037 (0.119)	.757
Gamma	OCD – PD Off	-0.028 (0.053)	.601	0.099 (0.062)	.163
	OCD – PD On	0.097 (0.060)	.192	0.128 (0.074)	.163
	PD Off – PD On	0.122 (0.050)	.061	0.029 (0.063)	.645

		Passive trials			
Frequency	Groups	Unpleasant		Pleasant	
		Estimate (SE)	p-value	Estimate (SE)	p-value
Theta	OCD – PD Off	-0.366 (0.146)	.037	0.271 (0.164)	.147
	OCD – PD On	-0.282 (0.180)	.178	0.352 (0.186)	.147
	PD Off – PD On	0.085 (0.159)	.599	0.081 (0.165)	.622
Alpha	OCD – PD Off	-0.188 (0.135)	.372	0.096 (0.150)	.532
	OCD – PD On	-0.192 (0.166)	.372	0.190 (0.170)	.532
	PD Off – PD On	-0.004 (0.147)	.979	0.095 (0.151)	.532
Low beta	OCD – PD Off	0.152 (0.104)	.219	0.033 (0.116)	.777
	OCD – PD On	0.270 (0.129)	.109	-0.181 (0.132)	.255
	PD Off – PD On	0.118 (0.114)	.299	-0.214 (0.117)	.203
High beta	OCD – PD Off	0.180 (0.105)	.130	-0.049 (0.117)	.679
	OCD – PD On	0.224 (0.13)	.130	0.081 (0.133)	.679
	PD Off – PD On	0.043 (0.115)	.705	0.130 (0.118)	.679
Gamma	OCD – PD Off	0.112 (0.056)	.134	0.158 (0.062)	.032
	OCD – PD On	0.065 (0.069)	.445	0.132 (0.070)	.089
	PD Off – PD On	-0.046 (0.061)	.444	-0.025 (0.062)	.687

Table 4: Comparisons of mean activity at the time of the motor response between groups

Frequency	Groups	Motor trials			
		Unpleasant		Pleasant	
		Estimate (SE)	p-value	Estimate (SE)	p-value
Theta (3-8 Hz)	OCD – PD Off	0.575 (0.155)	.001	0.318 (0.186)	.131
	OCD – PD On	0.579 (0.191)	.004	-0.085 (0.229)	.711
	PD Off – PD On	0.004 (0.168)	.979	-0.403 (0.197)	.122
Alpha (8-12 Hz)	OCD – PD Off	0.174 (0.147)	.529	0.105 (0.172)	.542
	OCD – PD On	0.169 (0.182)	.529	-0.254 (0.211)	.344
	PD Off – PD On	-0.005 (0.160)	.975	-0.359 (0.182)	.145
Low beta (12-25 Hz)	OCD – PD Off	0.114 (0.116)	.386	-0.102 (0.134)	.652
	OCD – PD On	0.223 (0.143)	.356	0.074 (0.165)	.652
	PD Off – PD On	0.109 (0.126)	.386	0.177 (0.142)	.638
High beta (25-35 Hz)	OCD – PD Off	0.098 (0.111)	.773	0.221 (0.135)	.151
	OCD – PD On	0.039 (0.137)	.773	0.311 (0.166)	.151
	PD Off – PD On	-0.058 (0.120)	.773	0.090 (0.142)	.529
Gamma (40-80 Hz)	OCD – PD Off	-0.011 (0.058)	.843	0.045 (0.067)	.558
	OCD – PD On	-0.063 (0.071)	.565	0.087 (0.083)	.558
	PD Off – PD On	-0.075 (0.063)	.565	0.042 (0.071)	.558