Basal ganglia dysfunction in OCD: subthalamic neuronal activity correlates with symptoms severity and predicts high-frequency stimulation efficacy

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Introduction

Obsessive–compulsive disorder (OCD) is a common disabling disease, but its neural substrate remains poorly understood. A large set of imaging and neurophysiological data obtained in OCD patients have suggested, however, a dysfunction of the ventromedial corticosubcortical loop.1–9 In the light of these results, deep brain stimulation (DBS) of the caudate nucleus and adjacent structures has been proposed for the treatment of severe and refractory OCD patients.10–15 Recently, the subthalamic nucleus (STN) has appeared as another potential target for DBS following serendipitous results from Parkinson’s disease (PD) patients16–18 and its role in associative and limbic information processing in human and non-human primates.19–21 Data obtained in rats and human also suggest that the STN is implicated in the ability to stop or inhibit an already initiated response, highlighting its potential role in impulse control disorders.22,23 We have recently confirmed the efficacy of stimulation applied in the medial part of the STN in OCD patients with a multicentre clinical trial.24 The usefulness of STN stimulation has also been investigated in rats and monkeys with induced compulsive-like behaviour.25–28 The fact that modulation of the STN neuronal activity by DBS improves OCD symptoms suggests that this basal ganglia structure may be dysfunctional in human patients.

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One way to understand the potential role of the basal ganglia system and its dysfunction in OCD symptoms is to investigate subcortical structures electrophysiologically. Neuronal recordings of the striatum have already been reported in three OCD patients where an increased and more irregular pattern was found during observations. As the STN is the main target for DBS in patients with Parkinson’s disease (PD), a large set of electrophysiological data have been reported in patients and non-human primate models of PD, and consistently show increased neuronal activity, occurrence of bursts, synchrony and oscillations. In such patients, an electrophysiological analysis has allowed, at least in part, to understand how STN dysfunction is linked to the motor symptoms and how these electrophysiological characteristics are related to the clinical outcome of STN stimulation. In OCD patients, the target was defined in part, to understand how STN dysfunction is linked to the clinical outcome of STN stimulation. This study aimed to further explore the relationship between STN neuronal activity and OCD symptoms. Subthalamic electrophysiological recordings were obtained in OCD patients during surgery for DBS and analysed in relation to both OCD severity and STN stimulation outcome. Subthalamic neuronal activity recorded in PD patients operated under the same conditions was used for comparison. Previous studies led us to hypothesise that (1) subthalamic neuronal activity would be differentially affected in OCD compared with PD patients, especially in the ventromedial (associative–limbic) subdivision; and (2) the neuronal activity characteristics would be linked to clinical severity or response to STN stimulation of OCD symptoms.

Materials and methods

Participants. A total of 12 patients with severe and refractory OCD and 12 patients with severe form of PD were included in this study. Patients with OCD were operated for bilateral high-frequency STN stimulation in a therapeutic trial (ClinicalTrials.gov number, NCT00169377) (see Supplementary Material and Table S1). All patients gave informed written consent and the protocol was approved by the local ethics committee. Patients with PD were operated for bilateral STN stimulation as routinely performed in our centre (see Supplementary Material). None of the patients showed contraindication to surgical procedure, dementia or abnormal brain imaging.

Neurosurgical procedure. The surgery was performed as described previously. Briefly, the implantation of bilateral stimulating electrodes (Medtronic, model 3389, Minneapolis, MN, USA) was performed the same day using both preoperative anatomical and perioperative electrophysiological targeting. Subthalamic nuclei were preoperatively targeted by means of stereotactic magnetic resonance imaging, with additional ventriculography in some OCD patients (depending on the local protocol). In OCD patients, the target was defined 2 mm anterior and 1 mm medial to the PD target at the boundary of STN associative and limbic subdivisions.

Micro-electrode recordings. Perioperative electrophysiological recordings were performed in awake patients, at rest (see Supplementary Material). Drug treatment was discontinued the evening before surgery in all patients. Extracellular single-unit neuronal activity was recorded simultaneously from 3 to 5 leads, used to identify and localise the STN for 2 min at rest, each 200–500 μm within the STN.

Off-line analysis. Neuronal recordings were exported offline as text files to a PowerLab system (ADI instruments; Phymep, Paris, France) and analysed using the Spike 2 software suite (Version 5; Cambridge Electronic Device, Cambridge, UK). Spikes were discriminated from noise and the mean firing rate, mean interspike interval (ISI) and coefficient of variation were calculated for each neuron (see Supplementary Material). The mean bursting index (S), burst frequency, duration, intraburst frequency and interval interburst were calculated for each neuron. Analysis of oscillatory activity was performed by frequency band using a Matlab program (see Supplementary Material). The mean bursting index (S), burst frequency, duration, intraburst frequency and interval interburst were calculated for each neuron. Imaging. The location of each recorded neuron within the functional subdivisions, that is, motor, associative and limbic, of the STN was determined by using a three-dimensional deformable histological atlas adjusted to the individual brain geometry of each patient (see Supplementary Material).

STN stimulation in OCD patients. A 3-month STN stimulation period was tested in the 12 OCD patients. At the end of the on-stimulation period, the Yale–Brown Obsessive–Compulsive Scale (Y-BOCS) score was decreased by 22% (see Supplementary Material).

Statistical analysis. Results for continuous variables are reported as mean ± s.d. To compare neuronal activity between OCD and PD cells, we used mixed models (analysis of variance with random effect) with a random effect for patients and two fixed factors for the group (OCD vs PD) as the between-subject factor and neuronal recording localisation (sensorimotor, associative, limbic) as the within-STN factor, and the interaction between these two fixed factors. When significant effects were found, pairs of means were compared using a Tukey–Kramer correction. For categorical data, generalised linear models with a logistic link function were used with similar effects as for the linear mixed model used for continuous data. As changes in STN neuronal activity have been reported, we examined the differences in STN neuronal activity between OCD patients with (n = 4 subjects, 48 cells) and without (n = 4 subjects, 50 cells) neuroleptic treatment, and between left and right sides, using the Student’s t-test for continuous variables and the Fisher’s exact test for categorical variables.
obessions and compulsions (Y-BOCS global and obsession and compulsion subscores), the improvement in OCD symptoms induced by STN stimulation and the STN neuronal activity characteristics were also evaluated using the non-parametric Spearman’s correlation test. For these purposes, the mean discharge frequency, ISI, coefficient of variation, $S$ index, burst frequency and duration, intraburst frequency and interval interburst, the proportion of STN neurons displaying oscillatory activities, power and peak in each band frequency were calculated for each subject. The postoperative percentage improvement in OCD symptoms was calculated for each patient, as follows: (score before the on-stimulation period – score at the end of the 3-month STN stimulation period) $\times 100$/score before the on-stimulation period) (see Supplementary Material).

Statistical analyses were performed with the SAS 9.2 software (SAS Institute, Cary, NC, USA). The level of significance for all statistical tests was fixed at $P<0.05$. No Bonferroni correction was applied.

**Results**

In all, 138 cells were isolated and recorded from the STN of the 12 OCD patients and 173 cells from the STN of the 12 PD patients. The average recording duration was $59.6 \pm 39.4$ s and the average number of spikes $1417 \pm 1191$.

**Discharge frequency and pattern.** The mean STN firing rate in OCD patients (STN-OCD) was significantly lower, with a higher mean ISI, compared with STN neurons of PD patients (STN-PD; Table 1). The distribution of the three types of discharge pattern in STN neurons did not differ between OCD and PD patients ($P=0.14$), with a predominant burst-like firing pattern (Table 1). The mean bursting index, burst duration and interval interburst were significantly higher and the mean burst frequency and intraburst frequency significantly lower in STN-OCD neurons compared with STN-PD neurons (Table 1).

**Oscillatory activity.** Over the entire bandwidth analysed, the proportion of neurons displaying oscillatory activity was lower in STN-OCD compared with STN-PD (46 vs 68%; Figure 1). In both groups, about half of the oscillatory neurons showed peaks in more than one frequency band (Figure 1). The distribution of oscillatory activity was similar in the two groups of patients, but for the presence of more $\theta$ activity in STN-OCD neurons and in the $\beta$-low band in STN-PD neurons (Figure 1A; $P<0.02$). The mean frequency in the $\beta$-low band was significantly lower in STN-OCD compared with STN-PD neurons (Table 1).

**Influence of the neuroleptic treatment.** No significant difference in neuronal activity was found between STN neurons ($n=48$ cells) recorded in OCD patients undergoing neuroleptic treatment compared with those without ($n=50$ cells) (see Supplementary Material).

**Localisation of STN neuronal activity in OCD and PD patients.** A total of 81 right and 57 left STN neurons and 123 right and 50 left STN neurons were recorded in OCD and PD patients, respectively.

STN-OCD neurons were located more anteriorly than STN-PD neurons, with no difference in mean laterality or depth (Table S2 and Supplementary Material). The majority of recorded neurons were located in the associative STN in both groups (Figure 2a).

**Neuronal activity as a function of laterality and position within the STN.** No significant differences in neuronal activity were found between right and left STN neurons in OCD patients (not shown). However, the mean bursting index, number of spikes per burst and burst duration were significantly lower in the second ($n=36$ cells) vs the first ($n=102$ cells) STN operated ($P<0.04$, not shown). In PD patients, compared with the first-side STN neurons (right STN, $n=123$ cells), second-side STN neurons (left STN, $n=50$ cells) exhibited less burst-type and more regular patterns (burst-type: 72 vs 54%; regular: 5 vs 14%, $P<0.04$) and lower mean power in $\beta$ band oscillation ($P<0.02$, not shown).

The mean discharge frequency of STN-OCD neurons was significantly lower compared with STN-PD neurons in all subdivisions of the STN (Figure 2b; $P<0.05$), with no

| Table 1 Discharge frequency, pattern and oscillatory activity of subthalamic neurons in 12 OCD and 12 PD patients |
|-----------------------------------------------|-----------------------------------------------|
| **OCD patients** ($n=138$ cells) | **PD patients** ($n=173$ cells) |
| **Discharge frequency (Hz)** | $22.4 \pm 13.7^*$  | $31.6 \pm 13.5$ |
| **Mean ISI (ms)** | $71.8 \pm 63.5^*$  | $40.1 \pm 26.3$ |
| **Coefficient of variation** | $1.3 \pm 0.4$  | $1.2 \pm 0.3$ |
| **Pattern of discharge: proportion of (%)** | | |
| Regular | $13\%$ | $8\%$ |
| Irregular | $18\%$ | $24\%$ |
| Burst-type | $69\%$ | $67\%$ |
| **Burst (S) index** | $9.8 \pm 4.0^*$  | $8.3 \pm 3.1$ |
| **Burst frequency (Hz)** | $0.33 \pm 0.26$  | $0.41 \pm 0.28$ |
| **Burst duration (ms)** | $823.5 \pm 665.0^*$  | $340.3 \pm 246.1$ |
| **Intraburst frequency (Hz)** | $53.7 \pm 52.6^*$  | $74.4 \pm 34.7$ |
| **Intraburst interval (s)** | $5.2 \pm 7.0^*$  | $2.9 \pm 2.6$ |

Abbreviations: ISI, interspike interval; OCD, obsessive–compulsive disorder; PD, Parkinson’s disease.

Results are expressed as mean $\pm$ s.d.

* $P<0.05$ when compared with PD patients.

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interaction between the subjects (OCD vs PD) and the neuronal recording locations (motor vs associative vs limbic) (Figure 2b; \( P = 0.098 \)). A significant interaction between subjects and localisation was found for the mean ISI (interaction: \( P < 0.03 \)). The mean ISI of the STN-OCD neurons located in the motor part was significantly higher compared with the mean ISI of the STN-OCD neurons located in the associative and limbic parts in OCD patients and with all subdivisions for STN-PD neurons (\( P < 0.005 \), not shown).

No significant interaction between subjects and location was found either for the pattern of discharge or for the bursting index (not shown). However, the mean bursting index of STN-OCD neurons was significantly higher in the motor and associative parts compared with STN-PD neurons recorded in the same STN territories (Figure 2c; \( P < 0.008 \) and \( P < 0.005 \) for the motor and associative parts, respectively). No significant interaction between subjects and location was found for the burst characteristics (burst frequency, duration of burst, intraburst frequency—not shown). However, the mean burst duration of STN-OCD neurons was significantly greater (not shown, \( P < 0.03 \)) and the mean intraburst frequency significantly lower in the motor part compared with STN-PD neurons recorded in the same STN territory (Figure 2d; \( P < 0.01 \)). A significant interaction between subjects and location was found for the interburst interval (interaction: \( P < 0.007 \)), which was higher in the motor part of the STN compared with the other subdivisions in OCD patients (not shown).

Over the whole frequency range, STN-OCD neurons showed more oscillation in the limbic part, whereas STN-PD neurons showed more oscillation in the motor part (Figure 1b; \( P < 0.04 \)). The frequency analysis showed more oscillation for STN-PN neurons in the \( \delta \) and \( \alpha \) bands in the motor compared with either the associative or limbic parts of the STN (interaction: \( P = 0.03 \); Figure 1b). STN-OCD neurons showed more oscillation in the \( \alpha \) band in the limbic compared with other STN subdivisions (interaction: \( P < 0.001 \); Figure 1b). No significant interaction between subjects and location was found for the presence of \( \beta \)-low, \( \beta \)-high or \( \gamma \) oscillatory activity (Figure 1b).

Subthalamic neuronal activity as a function of obsessions and compulsions. No significant relationship was found between the preoperative severity of OCD symptoms and mean discharge frequency, bursting index and burst frequency of STN-OCD neurons (Table 2). Obsessions and compulsions severity were significantly correlated with burst duration and mean intraburst frequency and interburst interval (Table 2).

No significant relationship was found between OCD severity (Y-BOCS, obsession and compulsion subscores) and the mean proportion, peak frequency and power in the \( \theta \), \( \beta \)-low, \( \beta \)-high and \( \gamma \) band frequencies. The Y-BOCS global and obsession subscores were correlated with the mean peak frequency in the \( \delta \) band. OCD severity was also significantly correlated with mean power in the \( \delta \) frequency band and with the mean proportion of STN neurons with \( \alpha \) oscillations and the mean \( \beta \) band peak frequency.

In summary, the more severe the obsessions, the lower the burst duration and interburst interval, and the higher the mean discharge and intraburst frequencies, peak and power in the \( \delta \) band frequency. The more severe the compulsions, the higher the intraburst frequency and the proportion of STN neurons with \( \alpha \) oscillations with lower peak frequency.

STN neuronal activity as a function of the STN stimulation efficacy. The improvement in Y-BOCS global and obsession subscores with STN stimulation was significantly correlated with the mean discharge frequency (\( r = 0.86, P < 0.01 \); Figure 3a), burst frequency (\( r = 0.69, P = 0.04 \); Figure 3b), intraburst frequency (\( r = 0.76, P < 0.02 \); Figure 3c) and the mean interburst interval (\( r = -0.96, P < 0.004 \); Figure 3d) of STN neurons. The improvement in compulsion subscores with STN stimulation was significantly correlated with the mean discharge frequency (\( r = 0.78, P < 0.02 \); Figure 3a) and the mean interburst interval (\( r = -0.81, P < 0.02 \)). No significant correlation was found between the improvement in OCD symptoms (Y-BOCS global, obsession and compulsion subscores) and the
presence and characteristics (peak frequency and power) of STN oscillatory activities (not shown).

Discussion

This study reports for the first time the relationship between spontaneous subthalamic neuronal activity and symptom severity in OCD patients and their response to STN stimulation. We found that the mean firing rate of subthalamic neurons was significantly lower in OCD patients than in PD patients, with a predominantly burst-type activity, less frequent but longer bursts, and a predominant oscillatory activity in the δ band (Table 1 and Figures 1–3). In patients with the most severe OCD, STN neurons exhibited bursts with higher intraburst frequency and more oscillations in the low-frequency bands. In OCD patients with best postoperative clinical outcome with STN stimulation, STN neurons displayed higher mean discharge, burst and intraburst frequencies, but lower mean interburst interval. Neuronal activity differences observed between OCD and PD patients could result from the fact that neurons recorded in both groups were not similarly localised within the STN (Figure 2 and Supplementary Table S2). The fact that, to our knowledge, no data in the literature have shown that STN neurons are morphologically and physiologically different in different subregions of the STN,48 except for the presence of more passive movement-responsive neurons in the dorsolateral part of the STN (motor subregion),30,32 does not favour this hypothesis, however.

The mean firing rate of STN-OCD neurons was close to that reported in normal monkeys,49 essential tremor,34 dystonic50 and OCD patients.38 No significant relationship was found between firing rate and OCD severity. In our PD patients, the higher mean firing rate of STN neurons was similar to that reported previously,31,32,34 and thought to result from the disinhibition of the subthalamic activity secondary to the degeneration of nigral dopaminergic neurons.30,51 These data suggest that in OCD patients symptoms are not related to an increase or decrease in the STN neuronal discharge. Conversely, the firing patterns were similarly distributed between OCD and PD patients, with a predominant burst-type activity (Table 1). In PD patients, the increase in burst-type activity is thought to result from the degeneration of nigral dopaminergic neurons30,52,53 and resolves with dopaminergic treatment.54 In OCD patients, the increase in the burst-type activity, also reported previously,38 could be related to the
intake of neuroleptic treatment resulting in a dopaminergic receptors blockade, as previously reported in animal studies. However, the fact that the proportion of bursting STN neurons was similar in the four OCD patients who received neuroleptic treatment in the days before surgery compared with the four OCD patients without neuroleptic treatment (64 vs 74%) fails to support this hypothesis, as discussed previously. Compared with STN-PD neurons, STN-OCD neurons have a higher bursting index with longer but less frequent bursts (Table 1), and OCD severity was significantly related to some burst characteristics (Table 2). Moreover, OCD improvements with STN stimulation were dependent on frequent bursts (Table 1), and OCD severity was significantly related to some burst characteristics (Table 2).}

|                      | Y-BOCS  | Obsessions | Compulsions |
|----------------------|---------|------------|-------------|
| Mean discharge frequency | 0.46    | 0.54       | 0.31        |
| **Burst discharges**  |         |            |             |
| Mean burst (S) index  | −0.32   | −0.40      | −0.32       |
| Mean burst frequency  | 0.02    | 0.14       | −0.03       |
| Mean burst duration   | −0.46   | −0.60*     | −0.40       |
| Mean intraburst frequency | 0.68* | 0.78*      | 0.60*        |
| Mean interburst interval | −0.55 | −0.65*     | −0.58*       |
| δ band (1–4 Hz)       |         |            |             |
| Mean proportion of neurons | 0.11    | −0.13       | 0.37         |
| Mean peak frequency   | 0.79*   | 0.81*       | −0.08        |
| Mean power peak frequency | 0.38   | 0.61*      | −0.02        |
| θ band (4–8 Hz)       |         |            |             |
| Mean proportion of neurons | −0.48  | −0.50       | −0.05        |
| Mean peak frequency   | −0.07   | 0.01       | −0.11        |
| Mean power peak frequency | 0.17   | 0.10       | 0.38         |
| α band (8–12 Hz)      |         |            |             |
| Mean proportion of neurons | −0.45  | −0.45       | 0.73*        |
| Mean peak frequency   | −0.12   | 0.06       | −0.62*        |
| Mean power peak frequency | −0.26  | 0.02       | −0.65*        |
| β-low band (12–20Hz)  |         |            |             |
| Mean proportion of neurons | −0.56  | −0.04       | −0.02        |
| Mean peak frequency   | −0.02   | 0.01       | 0.01         |
| Mean power peak frequency | −0.26  | 0.34       | −0.07        |
| β-high band (20–35Hz) |         |            |             |
| Mean proportion of neurons | −0.50  | −0.30       | 0.12         |
| Mean peak frequency   | −0.04   | −0.10      | −0.27        |
| Mean power peak frequency | 0.40   | 0.27       | 0.20         |
| γ band (> 35Hz)       |         |            |             |
| Mean proportion of neurons | −0.22  | 0.03       | −0.49        |
| Mean peak frequency   | −0.32   | 0.11       | −0.01        |
| Mean power peak frequency | −0.32  | −0.34      | −0.40        |

**Abbreviations:** OCD, obsessive–compulsive disorder; Y-BOCS, Yale–Brown Obsessive–Compulsive Scale.

**Values are correlation coefficients (non-parametric Spearman's regression).**

**Entries shown in bold *P < 0.05 after univariate analysis.**

Table 2: Relationship between severity of obsessions and compulsions and subthalamic neuronal activity in OCD patients

The table shows the correlation coefficients between OCD severity and subthalamic neuronal activity in four OCD patients who underwent STN stimulation. The activity was measured in different frequency bands: δ (1–4 Hz), θ (4–8 Hz), α (8–12 Hz), β (12–20 Hz), and γ (20–35 Hz). The table includes the mean proportion of neurons, mean peak frequency, and mean power peak frequency for each frequency band. The correlations are highlighted in bold for significance levels *P < 0.05 after univariate analysis.
stimulation may be related to changes in these cortical regions, as recently reported in the same group of patients. In our OCD patients, about half of the STN neurons displayed oscillatory activity (Figure 1). Conversely, in other non-parkinsonian patients, such as those suffering from essential tremor or dystonia, only 18 and 6.5% of STN neurons show oscillatory activity in the 3–30 Hz band frequency, respectively. This observation suggests that oscillatory activity is augmented in the STN of OCD patients. A simple explanation could be that the high proportion of oscillations observed in STN-OCD neurons is related to neuroleptic treatment; however, the fact that oscillations tended to be less frequent in STN neurons of OCD patients undergoing neuroleptic treatment (42%) compared with STN neurons of OCD patients without (74%) fails to support this hypothesis. In PD patients, STN oscillation predominated in the STN motor part, as reported previously. In the δ and α band frequencies, oscillations appear to be related to tremor, and in the β band to movement inhibition and akinesia and predictive of STN stimulation outcome. In OCD patients, δ and α frequency band oscillation, which predominated in the STN associative and limbic parts, was significantly related to OCD symptom severity (Table 2). Our results are in line with reports obtained with EEG techniques in such patients who show an increase in low-frequency (δ, θ and α) oscillation, in resting state activity, at both cortical (in frontal and frontotemporal regions) and subcortical (in the thalamus and the striatum) levels, and related to symptom severity. Lastly, whereas β band STN oscillatory activity has been identified as a marker of akinesia in PD patients, about 35% of STN neurons exhibited β band oscillations in OCD patients (Figure 1). This result is in line with the report of a relationship between the severity of symptoms and β band power in frontal cortical regions in untreated OCD patients. An increase in the β power frequency has also been identified as one of the bioelectrical markers in various anxious states, and the question remains as to whether oscillations in the β band activity observed in the STN of OCD patients could be related to anxiety. Finally, the increase in low frequencies observed in the STN in our OCD patients, predominantly in the limbic portion, is consistent with changes reported at the limbic cortical level and support the hypothesis of an involvement of cortico-subcortical functional connections in this disorder.

Significant relationships between STN neuronal activities, which resembled parkinsonian STN neuronal activity (higher firing rate, burst and intraburst frequencies, and lower interburst interval), and STN stimulation efficacy were found in our OCD patients. This could mean that the main dysfunction in OCD patients improved by STN stimulation is one of the nigrostriatal dopaminergic system. However, this hypothesis seems unlikely as these neuronal activities were not identified as being predictive of the STN stimulation efficacy in PD patients. This result would rather suggest that OCD patients with a more disturbed STN neuronal activity are better candidates for this surgical treatment. The electrophysiological effects of high-frequency STN stimulation are not fully understood; however, a decrease in neuronal

Figure 3 Improvement in obsessions and compulsions with subthalamic nucleus stimulation as a function of subthalamic neuronal activity in obsessive–compulsive disorder patients. The graphs represent the relationship between the improvement in the Yale–Brown Obsessive–Compulsive Scale (Y-BOCS) global (green circles), obsession (blue crosses) and compulsion (red squares) subscores and the mean (a) discharge frequency, (b) burst frequency, (c) intraburst frequency and (d) interburst interval.
activity in the STN with retrograde and anterograde activations of input (cortex and GPe) and output (GPI and SNr) structures has been reported in patients and animal models of PD. Finally, the therapeutic effect of high-frequency stimulation of the STN is thought to result from complex changes in the neuronal activity of the entire cortico-basal ganglia circuitry, leading to a disruption of the pathological neuronal activity.

In conclusion, STN neurons in OCD patients display increased bursting activity with a high proportion of oscillatory activity, in relation to symptom severity and response to STN stimulation. In line with the accepted role of the STN in decision making and action sequencing, one might expect that dysfunction of this subcortical region could result in the setting of an inappropriate (increase or decrease) decision threshold in the context of reinforcement and decision conflicts. Consequently, an increase in this threshold could result, at least in part, in an inability to make a decision or a difficulty in terminating an action sequence, thereby resulting in obsessions and compulsions. Lastly, the fact that some STN neuronal activity characteristics are predictive of the STN stimulation-induced improvement suggests that some patients may be considered as good candidates for this treatment regarding the predominant involvement of the STN in the occurrence of their symptoms. This hypothesis will be explored in future studies.

Conflict of interest

The authors declare no conflict of interest.

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Author contributions

Dr Welter had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Appendix

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