European Journal of Neuroscience

WILEY

EJN European Journal of Neuroscience FENS

SPECIAL ISSUE ARTICLE OPEN ACCESS

Basal Ganglia and Related Disorders: From Cellular and Circuit Dysfunctions to Therapy

Subthalamic Activity Is Associated With Proactive Inhibition in Parkinson's Disease Patients

Luna Damiani[1] | Marion Albares[1] | Pauline Laviron[2] | Jean-Eudes Le Douget[2] | Philippe Boulinguez[3,4,5,6] | Carine Karachi[1,7] | Marie-Laure Welter[1,2,8] | Jérôme Munuera[1] | Brian Lau[1]

[1]Sorbonne Université, Institut du Cerveau-Paris Brain Institute-ICM, Inserm, CNRS, APHP, Paris, France | [2]PANAM Core Facility, Institut du Cerveau-Paris Brain Institute-ICM, Paris, France | [3]Université de Lyon, Lyon, France | [4]Université Lyon 1, Villeurbanne, France | [5]Inserm, U1028, Lyon Neuroscience Research Center, Lyon, France | [6]CNRS, UMR 5292, Lyon Neuroscience Research Center, Lyon, France | [7]Neurosurgery Department, Hôpital Pitié-Salpêtrière, Paris, France | [8]Neurophysiology Department, CHU Rouen, Rouen University, Rouen, France

Correspondence: Brian Lau (brian.lau@icm-institute.org)

Received: 30 September 2024 | **Revised:** 7 February 2025 | **Accepted:** 25 February 2025

Associate Editor: Yoland Smith

Funding: This research was supported by grants from the Agence Nationale de la Recherche (ANR-16-CE37-0007) to B.L., P.B., and M.-L.W. and from the national programme 'Investissements d'avenir' ANR-10-IAIHU-0006. M.A. received financial support from the Fondation France Parkinson and Fondation pour la Recherche Médicale.

Keywords: basal ganglia | dopamine | electrophysiology | executive function | motor control

ABSTRACT

The subthalamic nucleus (STN) is a key element of the indirect pathway of the basal ganglia (BG) and an effective target for improving motor symptoms in Parkinson's disease (PD) using deep brain stimulation (DBS). While dopamine neuron loss in PD results in a net shift towards increased inhibitory output from the BG, the precise mechanisms by which STN contributes to diminished movement remain unclear due to the complexity and multiplicity of processes underlying response inhibition. We used a modified Go/NoGo task varying uncertainty about Go or NoGo responses to determine how changes in response inhibition are related to STN local field potentials measured in 19 PD patients operated for STN-DBS. When engaged in the task, low-frequency band (LFB, 2–7 Hz; including the theta band, 4–7 Hz) power was significantly increased by dopamine treatment. LFB power significantly increased when there was uncertainty about the requirement of executing or withholding a response compared to when a response was certain. Increases in LFB power in individual trials were also significantly associated with faster reaction times. By contrast, beta band (12–30 Hz) power exhibited an inverted profile: It was significantly decreased by dopamine treatment, increased by response certainty and associated with slower reaction times. Our results suggest that STN low-frequency activity during voluntary behaviour may complement and enhance information obtained from the beta band and should be considered as a possible biomarker for the regulation of inhibition in uncertain contexts.

Abbreviations: BG, basal ganglia; DBS, deep brain stimulation; dmPFC, dorsomedial prefrontal cortex; DOPA, dopamine medication; GAMM, generalized additive mixed model; ICD, impulse-control disorder; LFB, low-frequency band; LFP, local field potential; LMM, linear mixed model; PD, Parkinson's disease; RT, reaction time; SMA, supplementary motor area; STN, subthalamic nucleus; UPDRS, Unified Parkinson's Disease Rating Scale.

Luna Damiani and Marion Albares are cofirst authors. Marie-Laure Welter, Jérôme Munuera and Brian Lau are colast authors.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

© 2025 The Author(s). *European Journal of Neuroscience* published by Federation of European Neuroscience Societies and John Wiley & Sons Ltd.

1 | Introduction

Efficient actions require both the activation of desired behaviours and the inhibition of undesired ones. Response inhibition can occur in several ways: (1) reactive and selective, where a specific action is inhibited in response to a particular stimulus (Ridderinkhof 2002); (2) proactive and selective, where we prepare and anticipate stopping a specific action (Jaffard et al. 2008; Aron 2011); (3) reactive and unselective, where all actions are inhibited when faced with conflicting or difficult choices (Frank et al. 2007; Cavanagh et al. 2011; Criaud et al. 2021); and (4) proactive and unselective, where all actions are inhibited in advance of the selection of one to perform (Boulinguez et al. 2008). Proactive unselective inhibitory control has recently been identified as a key component of executive function, specifically in complex and uncertain contexts, as it adaptively prevents erroneous responses (Wardak et al. 2012). Proactive and unselective inhibition may constitute a 'default mode' of the executive brain (Criaud et al. 2012), encompassing preparing for possible Stop or NoGo stimuli and enhancing reactive inhibitory success (van den Wildenberg et al. 2022).

The neural bases supporting proactive inhibitory control remain unclear (Criaud et al. 2017). Evidence in healthy individuals suggests that proactive inhibition during uncertainty involves the frontoparietal network including the dorsal medial prefrontal cortex (dmPFC) and the presupplementary motor area (preSMA) and the basal ganglia (BG) (Jaffard et al. 2008; Aron 2011; Criaud et al. 2012; Albares et al. 2014). Dysregulation in these pathways could thus lead to abnormal inhibition, with either excessive inhibition leading to delayed motor initiation, or excessive disinhibition with impulsivity (Berardelli et al. 2001; Obeso et al. 2011, 2014; Rodriguez-Oroz et al. 2011). Parkinson's disease (PD) exemplifies these opposing behaviours that remain, from a theoretical point of view, largely obscure (Spay et al. 2018; Meyer et al. 2019). On the one hand, PD patients exhibit slower reaction times (RTs) and movement initiation failure that contribute to akinesia, which can be partly attributed to impaired control of proactive inhibition over movement triggering mechanisms (Criaud et al. 2016). Patients may show difficulty switching from a proactive mode of movement inhibition to a reactive automatic mode of sensorimotor processing. On the other hand, various forms of cognitive and motor impulsivity can be observed in PD (Ballanger et al. 2009; Rodriguez-Oroz et al. 2011; Leroi et al. 2013). The fact that they are usually induced by dopaminergic medication or deep brain stimulation (DBS) of the subthalamic nucleus (STN; Frank 2006; Evans et al. 2009) raises questions about (i) the dysfunctional cortico-BG circuits and neurotransmitters systems supporting the symptoms (Favre et al. 2013; Albares et al. 2014; Spay et al. 2018; Criaud et al. 2022) and (ii) the mechanistic interweaving of motor and nonmotor dysfunctions.

While the STN is implicated in reactive inhibition, decision making, action selection or movement initiation (Frank 2006; Kojovic et al. 2016; Marmor et al. 2020), the role played by the STN in the encoding of proactive control remains unclear since executive (or cognitive) function impairments can, like motor control dysfunctions, disturb movement execution (Favre et al. 2013; Herz et al. 2024). STN neurophysiological activity could be at this junction between motor and nonmotor symptoms. Indeed, changes in STN beta band power correlates with motor improvement (Doyle et al. 2005; West et al. 2016; Mathiopoulou et al. 2024), while increases in theta and alpha band power, by contrast, are associated with decision making (Zénon et al. 2016), conflict resolution (Fumagalli et al. 2011; Zavala, Tan, Ashkan, et al. 2016), selective reactive response inhibition and risk aversion (Brittain et al. 2012; Voon et al. 2024). Yet, theta band power in the STN also correlates with motor aspects, such as performance in grip tasks (Anzak et al. 2012; Tan et al. 2013). The STN is therefore a good candidate for the integration of both cognitive and motor aspects of movement performance.

In this study, we explored the role of the STN in inhibitory processes in PD patients during a modified Go/NoGo task allowing us to disentangle 'proactive' from 'reactive' inhibition by varying response uncertainty. While patients performed the task, we recorded STN local field potentials (LFPs), aiming to distinguish motor from executive neural mechanisms and the neurobehavioural effect of manipulating patients' antiparkinsonian medication.

2 | Methods

2.1 | Participants

We recruited 19 PD patients (17 men, median age 56 years; Table 1) scheduled to receive STN-DBS at the Pitié-Salpêtrière Hospital (Inserm promotion, RBM #C11-40, N°IDRCB 2012-A00225-38). The inclusion criteria were (1) diagnosis of PD based on the UK Parkinson's Disease Society Brain Bank criteria; (2) age between 18 and 70 years; (3) validation of the indication of STN-DBS according to the local neurosurgical and neurological staff, including high responsiveness of motor disability to levodopa treatment, existence of levodopa-related motor complications, no ongoing psychiatric disorders or dementia (Mini-Mental Status score greater than 24) and no contraindication to surgical intervention for DBS implantation; (4) voluntary consent to participate in the study; and (5) had social insurance.

This study was performed in accordance with the declaration of Helsinki and good clinical practice guidelines. The local ethics committee approved the study (CPP Paris VI, Project #20-12), and participants signed written informed consent to participate. This study was registered on a clinical trial website (ClinicalTrials.gov: NCT01682668).

2.2 | Experimental Protocol and Data Acquisition

2.2.1 | Surgical Procedure and Subthalamic LFP Recordings

Two stimulating electrodes (Model 3389, Medtronic), one in each hemisphere, were implanted in the same surgical procedure as previously reported (Welter et al. 2014). The STN was directly targeted using 3D T2 Flair-weighted images on preoperative 1.5-T MRI and was additionally indirectly targeted using a BG atlas (Bardinet et al. 2009). The electrodes were connected to externalized cables to allow LFP recordings performed in the 1–4 days following surgery, before implantation of the neurostimulator.

TABLE 1 | Demographic and clinical characteristics of the PD patients.

Patient	Sex	Age (years)	Disease duration (years)	UPDRS III		LEDD (mg/day)	UPPS	Hand used	Side most affected
				DOPA^{ON}	DOPA^{OFF}				
1	M	60	8	9	33	1000	36[a]	R	R
2	M	51	9	4	27	1260	—[a]	R	L
3	M	29	13	0	13	1050	31[a]	R	L
4	F	67	12	4	30	1000	35	R	L
5	M	61	8	4	21	350	53	L	R
6	F	55	11	2	30	1400	49[a]	L	R
7	M	56	8	4	41	900	42	R	L
8	M	65	13	7	39	1000	41	R	R
9	M	56	6	4	28	1200	22[a]	R	L
10	M	64	14	19	42	1745	28	R	L
11	M	54	14	3	45	862.5	43[a]	R	L
12	M	68	15	12	35	525	35.5	R	L
13	M	56	8	11	52	887.5	31	R	L
14	M	51	10	11	37	725	36[a]	R	R
15	M	66	15	7	44	350	45	R	L
16	M	52	13	15	49	300	39[a]	L	L/R
17	M	38	8	3	38	1075	38	L/R	L
18	M	63	9	22	46	825	38[a]	R	L
19	M	69	14	16	35	950	—	R	—

Abbreviations: LEDD, levodopa equivalent daily dosage; UPDRS, Unified Parkinson's Disease Rating Scale.
[a]Reported history of ICD.

LFPs were derived from adjacent contact pairs using three bipolar recording montages (0–1, 1–2 and 2–3) for each electrode (1.27 mm large, 1.5 mm high, separated by 0.5 mm; Contact 0 being the most ventral and Contact 3 the most dorsal), yielding six bipolar LFP recordings per patient. The signals were amplified, filtered (band-pass filter: 0.05–500 Hz; notch filter: 50 Hz) and sampled at 2048 Hz (Porti 32, TMS International, Enschede, the Netherlands), referenced to a shoulder site and grounded on the collarbone.

2.2.2 | Experimental Task

Patients performed a modified Go/NoGo task (Albares et al. 2014; Albares, Lio, and Boulinguez 2015). They performed blocks of trials where they pressed a button as fast as possible (Go) or refrained from pressing it (NoGo) in response to a visual instruction (Figure 1A). Patients were seated in front of a computer monitor, and each trial began with a blank screen. Patients used a hammer grip to hold a small cylinder that allowed resting the thumb on a mechanical button wired to a momentary switch. Patients were instructed to press and release the button with their thumb whenever instructed (Go trials). They used the hand they were most comfortable with to complete the task (Table 1). A centrally located plus sign (cue) indicating the block condition appeared after a delay of 0.8–1.2 s, replaced by the instruction stimulus (Go or NoGo), presented after a pseudorandom delay between 1 and 2 s. The task consisted of two distinct blocks of trials: (1) the Go-certain condition, with only Go trials that started with a green plus sign (cue, presented for 100 ms) followed by a filled green circle (instruction, presented for 100 ms). (2) The Go-uncertain condition, with a mixture of Go and NoGo trials that started with a red plus sign (cue, presented for 100 ms) followed by the instruction stimulus with either a filled green circle for Go signals or a green cross for NoGo signals. The patient either executed a button press within 1.5 s following instruction (Go) or withheld response for at least 1.5 s following instruction (NoGo) for a trial to be considered correct.

The experiment started with a block of 10 Go-certain trials, followed by a block of 40 Go-uncertain trials, in equal proportion of Go and NoGo trials presented in a pseudorandomized order (with no more than three consecutive identical trials) and then another block of 10 Go-certain trials (Figure 1A). This sequence of three blocks was repeated two to three times in both DOPA^{OFF} and DOPA^{ON} conditions.

Patients were familiarized with the task and performed at least one run before STN-DBS surgery and were reminded of the task

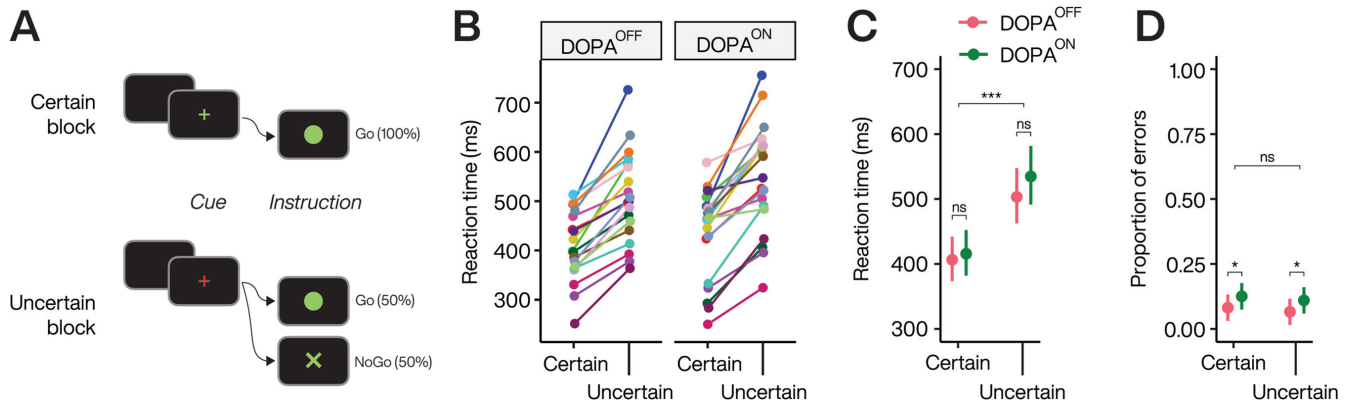

FIGURE 1 | Task design and behavioural results. Patients showed faster RTs in the certain rather than the uncertain condition, with no significant effect of DOPA condition on RTs. (A) Go/NoGo task. Trials were presented in distinct blocks. In the Go-certain block, a Go instruction was presented on every trial, while there was equal chance of Go or NoGo trials in the Go-uncertain block. (B) Effects of block and levodopa on reaction time. Average RTs for individual patients split by dopamine status and block type. Colours represent individuals. (C) Estimated RTs from LMM. Error bars represent 95% confidence intervals. (D) Estimated proportion of errors from GLMM. Error bars represent 95% confidence intervals. $^{*}p < 0.05$, $^{***}p < 0.001$, $^{ns}p > 0.05$.

postsurgery with a small number of practice trials before STN-LFP recordings. They were assessed both without (DOPA^{OFF}, after a 12-h interruption of antiparkinsonian medication) and with (DOPA^{ON}, after the administration of a suprathreshold dose of levodopa, corresponding to the usual morning levodopa dosage + 50 mg) dopamine medication.

2.2.3 | Clinical Assessment

Parkinsonian motor disability was assessed using the Unified Parkinson's Disease Rating Scale (UPDRS) Part III during a preoperative levodopa challenge. History of impulse-control disorders (ICDs) was assessed preoperatively using the Ardouin Scale Part IV (Ardouin et al. 2009). The level of impulsivity at the time of LFP recordings was assessed using the UPPS Impulsive Behavior Scale (Whiteside and Lynam 2001), administered before patients performed the Go/NoGo task.

2.3 | Data Analysis

2.3.1 | Behavioural Measures

Task performance was assessed by examining RTs, corresponding to the delay between the instruction onset (Go signal) and the button press (movement). Any trial where the patient did not respond to a 'Go' stimulus within the alloted time, responded to a 'NoGo' stimulus or pressed the button before the instruction stimulus was shown was considered an error trial and was not included for LFP analyses.

2.3.2 | Signal Processing

We first estimated spectral power in each frequency band as a function of time using a multitaper estimation algorithm implemented in the Chronux library (Version 2.11, http://chronux.org). For each bipolar LFP recording, we transformed signals to the time–frequency domain using a multitaper estimation algorithm (Percival and Walden 1993) implemented in the Chronux library (http://chronux.org). We calculated power between 0 and 40 Hz using three orthogonal tapers with a time bandwidth product of 2, using 500-ms windows stepped by 50-ms steps. Time–frequency maps were computed for LFP recordings in individual trials and visualized by averaging spectral power for selected epochs of interest (Figure S1).

2.4 | Statistical Analysis

We used linear mixed models (LMMs) to model RTs based on Go-condition (certain or uncertain), DOPA condition (DOPA^{OFF} and DOPA^{ON}) and disease severity (as reflected by the UPDRS Part III score). RTs were log-transformed prior to fitting LMMs, and results were back transformed for visualization. DOPA condition, Go-condition and their interactions were included as fixed effects. Where possible, maximal random effects with patient as the grouping factor were used (i.e., variables treated as fixed effects were also included as random effects). Significance testing was performed using likelihood ratio tests as implemented in the afex package in R, and estimated marginal means were calculated using the emmeans package in R.

To characterize the LFP power changes across task factors, we fitted generalized additive mixed models (GAMMs) to epoch-averaged spectra, that is, baseline (−750 to −250 ms before cue appearance), cue presentation (150 ms before cue appearance to 350 ms after cue appearance), instruction presentation (150 ms before instruction appearance to 350 ms after instruction appearance) and movement (move, button press to 500 ms after) epochs. Data were modelled at the single trial level, where for each patient, individual trial data were derived by averaging together the epoch-averaged spectra for all recording sites (i.e., averaged over all bipolar channels for both hemispheres). We used penalized smoothing to include smooth terms that accounted for potentially nonlinear associations between, for example, RT or disease severity with spectral power in different frequency bands. These nonlinear smooths were modelled as fixed effects, and we included random intercepts with patients as the grouping factor. Significance of

model parameters was obtained using approximate Wald tests as implemented in the mgcv package in R, and estimated marginal means and associated confidence intervals were calculated using the emmeans package in R. When presenting specific contrasts between task factors as a function of frequency, the contrast was considered significant at frequencies where the confidence interval did not include 0 ($\alpha = 0.05$). We also highlighted frequencies that were significant when controlling for the false discovery rate (Benjamini and Hochberg 1995).

3 | Results

3.1 | Effects of Uncertainty, Dopamine and Disease Severity on Task Performance

We investigate patients' RTs during the task under different levels of uncertainty and dopaminergic medications. Figure 1B illustrates the average RTs for individual patients. Patients showed significantly faster RTs in the Go-certain trials compared to the Go-uncertain trials (430 < 542 ms, $p < 0.001$, Figure 1C). RTs were not significantly different between DOPA^{OFF} and DOPA^{ON} conditions ($p = 0.15$) nor was there a significant interaction between the uncertainty and DOPA conditions ($p = 0.25$).

We also observed a significant association between increased disease motor severity (UPDRS Part III) and slower RTs ($p = 0.014$, Figure 2). The effect of Go-condition remained significant ($p < 0.001$), and the effects of the DOPA condition remained non-significant ($p = 0.572$), with no interaction between disease severity and either DOPA ($p = 0.899$) or uncertainty condition ($p = 0.873$).

3.2 | Error Rates and Impulsivity

On average, patients performed the task correctly for over 90% of trials (i.e., 9.37% errors). Error rates were not significantly associated with certainty context but were significantly increased in the DOPA^{ON} compared to the DOPA^{OFF} condition (Figure 1D). We then split errors into three categories: omissions, where the patient did not press the button on a Go trial (59.7% of all errors); commissions, where the patient pressed the button on a NoGo trial (20.4% of all errors); and false alarms, where the patient pressed the button before the instruction was given (19.9% of all errors).

Nine patients had a previous history of ICDs (Table 1). However, we found no significant relationship between the level of impulsivity (UPPS scores) during the experiment and performance (RTs) nor with 'impulsive' errors (commissions and false alarms combined—see Figure S2).

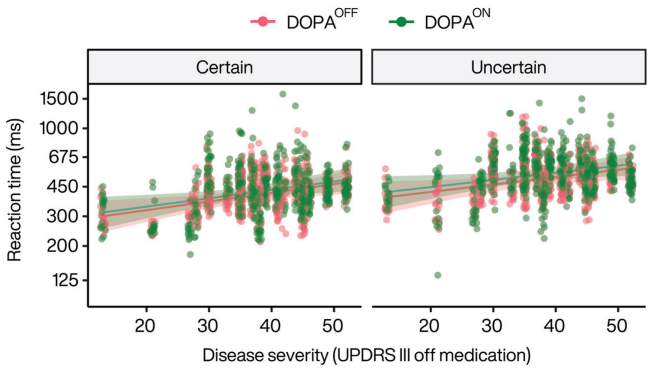

FIGURE 2 | Increased disease severity (UPDRS III) is associated with slower RTs ($p = 0.014$). Reaction times for each patient are plotted under both levodopa states for both block types (points represent RTs from individual trials, with transparency to visualize density). Each patient has one measure of disease severity (UPDRS III measured off levodopa prior to DBS surgery) and data points are jittered horizontally slightly to aid visualization. Lines with shading represent estimated trends with 95% CI for each condition from an LMM. The ordinate is logarithmically scaled.

3.3 | Subthalamic Neuronal Activity Is Modulated by Uncertainty and Dopamine State

We observed modulations in low-frequency band (LFB, including the theta band, 4–7 Hz) and beta band power due to dopamine treatment (Figure 3A). During the instruction epoch, dopamine treatment significantly increased LFB power while significantly decreased beta band power (Figure 3B; see Figure S3 for all epochs). In addition, a significant increase in LFB power was observed in Go-uncertain blocks compared to Go-certain blocks during the instruction epoch (Figure 3C,D). Conversely, we found increased beta band power in the Go-certain blocks compared to the Go-uncertain blocks (Figure 3C,D), although this difference was smaller during the instruction epoch (see Figure S4 for all epochs).

In addition, LFB power was not significantly different between Go and NoGo trials within the Go-uncertain condition. However, there was a broad reduction in beta band power in Go trials compared to NoGo trials (Figure 3E,F), which started at the instruction epoch (see also Figure S5 for all epochs).

3.4 | Subthalamic Neuronal Activity Correlates With Motor Performance and Disease Severity

We next examined the trial-by-trial relationship between STN activity and RTs, after subtracting off the block-averaged RT for each patient. We found that spectral power in both the LFB and beta bands was significantly associated with RT. Specifically, trials where LFB power was increased were significantly associated with faster RTs (Figure 4A,B). By contrast, trials where beta band power was increased were significantly associated with slower RTs (Figure 4A,B). Examining associations between patients suggested that more severely affected patients (higher UPDRS III score) exhibited higher average LFB power compared to less severely affected patients, while maintaining the association between LFB power and RTs (Figure 4C,D; see Figure S6 for each patient).

Lastly, we investigated how disease severity and dopaminergic medication influenced STN activity during the task. We found that higher STN theta band power was significantly positively associated with higher UPDRS III scores measured off levodopa treatment ($p < 0.05$, Figure 5A) but not with UPDRS III scores measured on levodopa treatment ($p > 0.05$,

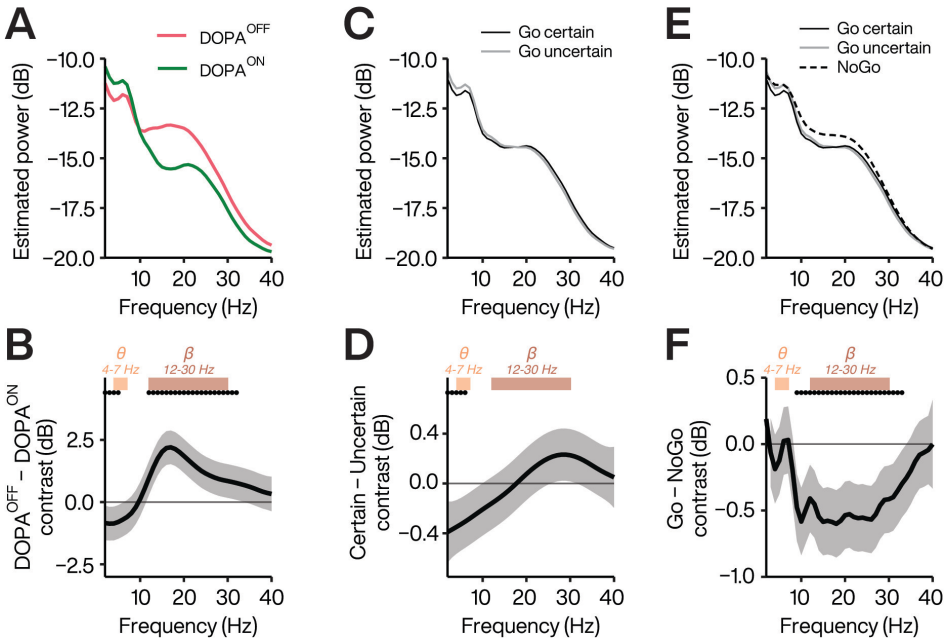

FIGURE 3 | LFP spectral power is modulated by levodopa treatment and task conditions. Theta power was increased, and beta power was decreased in the DOPA^{ON} compared to the DOPA^{OFF} condition. Theta power was also higher in the Go-uncertain condition than in the Go-certain condition, and beta power was higher during NoGo trials compared to Go trials. (A) Effects of levodopa treatment estimated from GAMM model fit to spectral power during instruction epoch. (B) Contrast between DOPA^{ON} and DOPA^{OFF}. The shaded region represents the 95% CI. The orange and red bars at the top of the plot highlight the theta and beta bands, respectively. The contrast is significant at frequencies where the confidence interval does not include 0 ($\alpha = 0.05$). The points at the top of the plot indicate frequencies that are significant when controlling for the false discovery rate (Benjamini and Hochberg 1995). (C) Effects of block type estimated from GAMM model fit to spectral power during instruction epoch. (D) Contrast between certain and uncertain blocks for Go trials averaging over DOPA^{ON} and DOPA^{OFF} conditions. Conventions as in (B). (E) Effects of instruction type estimated from GAMM model fit to spectral power during instruction epoch. (F) Contrast between Go and NoGo trials averaging over DOPA^{ON} and DOPA^{OFF} conditions. Conventions as in (B).

Figure 5B). We also examined whether this association depended on the location of the recording sites by dividing recordings sites into those in the posterior-sensorimotor part of the STN and those in the central-associative part based on divisions inferred from external globus pallidus afferents to the STN (Karachi et al. 2005; Bardinet et al. 2009). The association between theta band power and disease severity was significantly weaker in the posterior-sensorimotor STN area (see Figure S7). Finally, we examined the effect of dopaminergic medication at varying levels of disease severity across a broader frequency range (Figure 6A). While the reduction in beta band power due to dopaminergic medication was present across the disease severities represented in our cohort, LFB power was more strongly increased in the DOPA^{ON} condition in the most severe patients (Figure 6B).

4 | Discussion

We used a behavioural task eliciting proactive inhibition to study how STN activity was related to response inhibition in PD patients. We found that response uncertainty and disease severity were both associated with slower RTs. Low-frequency STN activity increased with uncertainty and motor disability but was paradoxically higher for faster motor responses within each uncertainty condition. By contrast, beta band activity increased with certainty but was paradoxically higher for slower motor responses within each uncertainty condition. These elements suggest that LFB and beta band power influence motor success in a context dependent way.

4.1 | LFB (Including Theta) Power Reflects Cognitive Control of Action

We observed significantly slower RTs during Go-uncertain trials, confirming that uncertainty modulates proactive inhibition in PD patients (Criaud et al. 2016). Dopamine medication did not affect this process. Whereas dopamine medication may affect movement times at specific levels of disease severity (Mirabella et al. 2023), we observed no influence of dopaminergic medication on proactive inhibition process in our patients, as previously reported (Favre et al. 2013). By contrast, STN-DBS has been shown to restore proactive inhibition (Favre et al. 2013; Albares, Lio, and Boulinguez 2015), an effect that is counteracted by noradrenergic agents (Albares, Thobois, et al. 2015). These findings suggest that proactive inhibition is primarily dependent on the nigrostriatal dopaminergic system but may be controlled by the STN. In our study, increased low-frequency activity in uncertain contexts was significantly correlated with faster RTs, consistent with higher LFB power facilitating quicker release of proactive inhibition. Increased low-frequency activity in uncertain contexts was also observed during NoGo trials, suggesting that this activity reflects the cognitive processes required to select appropriate responses regardless of whether the aim is to initiate or

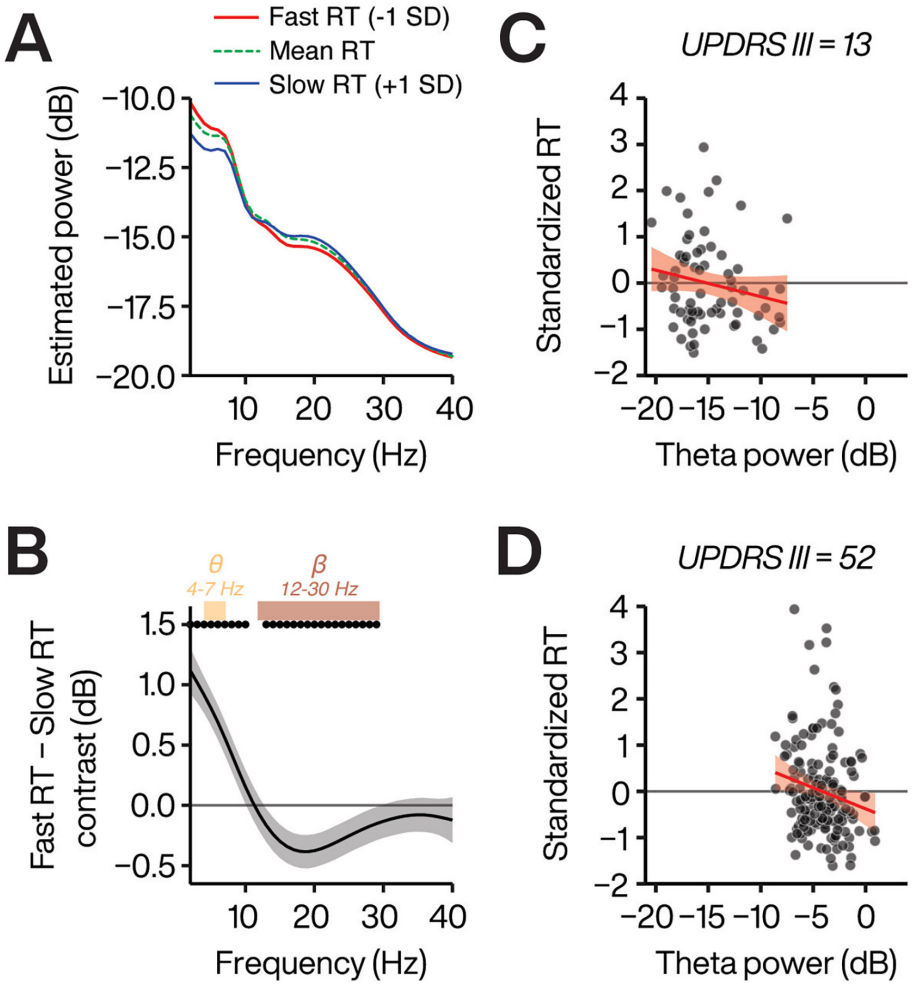

FIGURE 4 | Faster RTs were associated with increased theta power and decreased beta power. (A) RT association estimated from GAMM model fit to spectral power during instruction epoch. (B) Contrast between fast (1 SD faster than the mean) and slow (1 SD slower than the mean) RTs. Shaded region represents the 95% CI. The theta power band is highlighted in orange, the beta power band is highlighted in brown. Results are significant where the confidence interval does not include 0 ($\alpha = 0.05$). The points at the top of the plot indicate frequencies that are significant when controlling for the false discovery rate (Benjamini and Hochberg 1995). (C) Relationship between RT and theta power (averaged between 4 and 7 Hz) during the instruction epoch on individual Go trials for the least severe patient. Each point represents a trial, and the line illustrates a simple linear regression with 95% CI ($p = 0.133$, $R = 0.180$). (D) Same as (C) for the most severe patient ($p = 0.0214$, $R = 0.192$).

inhibit movement. Theta band power is predominant in this frequency range and may reflect cognitive engagement and resource allocation necessary for successfully performing the Go/NoGo task (Zénon et al. 2016; Avvaru et al. 2021).

The association between theta activity and the severity of motor disability further supports this hypothesis. More severely affected patients tend to lose motor automaticity and rely on more cognitive control of action (Redgrave et al. 2010; Wu et al. 2015). This suggests that, as the disease progresses, cognitive control may need to be increased, which could be reflected in increased theta band power in the STN. This mechanism seems to facilitate better responses in situations which require more cognitive control (such as uncertain situations) and thus act as a compensation mechanism for the degradation of automaticity with PD progression.

How LFB power modulation is integrated into networks of inhibition is not fully understood. At the cortical level, theta band modulations have been reported in the dorsal medial and prefrontal cortex of healthy individuals during uncertain tasks or visual attention tasks, where higher theta activity is associated with faster responses (Delorme et al. 2007; Albares et al. 2014). In PD patients, STN theta band modulations have been linked to conflict situations, where increased theta power corresponds to slower RTs (Cavanagh et al. 2011; Zénon et al. 2016; Singh 2018). Increased theta band in the STN has also been linked to more successful conflict control (Bowersock et al. 2025) and is modulated by dopamine, both at rest and in association to movement (West et al. 2016; Lofredi et al. 2018). In addition, cortico-STN coherence has been identified in the theta band (Zavala et al. 2014; Zavala, Tan, Ashkan, et al. 2016; Zavala, Tan, Little, et al. 2016). Notably, increased theta band cortico-STN coherence is associated with a shorter latency between motor intention and motor execution in simple movement tasks (Köhler et al. 2024), which may involve the hyperdirect pathway between cortical sensorimotor areas and the STN (Temiz et al. 2020). Altogether, these findings suggest that LFB activity may enhance movement by

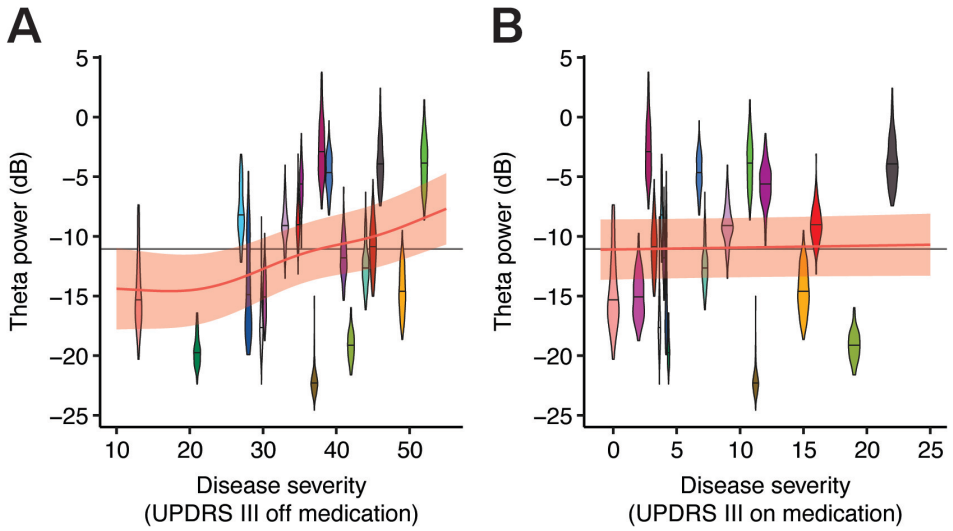

FIGURE 5 | Theta band power is associated with disease severity. (A) Relationship between theta power (averaged between 4 and 7 Hz) and disease severity (UPDRS III assessed off levodopa treatment) during the instruction epoch. The data are represented as violin plots illustrating the distribution of theta power across trials, with colours indicating individual patients, and the horizontal bar indicating median theta power. The red line represents the GAMM model fit to theta power during instruction epoch. The shaded region represents the 95% CI. The horizontal grey line represents the mean theta power across all patients. (B) Relationship between theta power (averaged between 4 and 7 Hz) and disease severity (UPDRS III assessed on levodopa treatment) during the instruction epoch. Conventions as in (B).

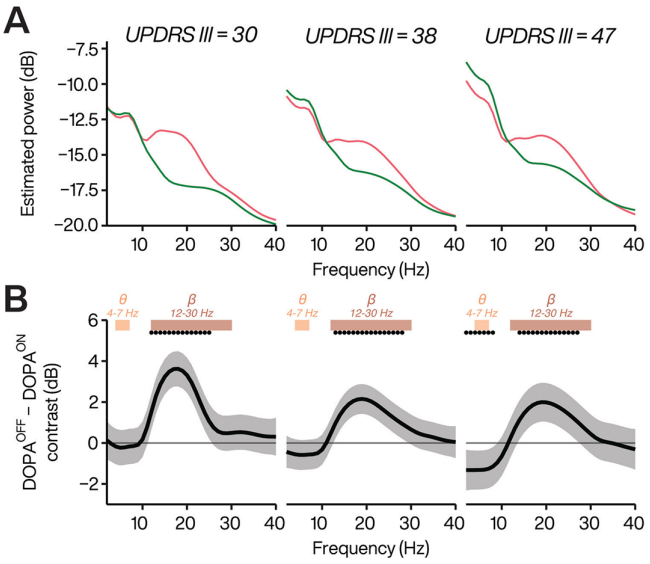

FIGURE 6 | Levodopa-induced changes in spectral power vary with disease severity. The DOPA^{ON} state decreased beta band power more in patients with lower disease severity and increased theta power more in patients with higher disease severity. (A) Estimated spectral power from a GAMM model fit to data from the instruction epoch. The column panels correspond to the 25th, median and 75th percentile of the distribution of UPDRS III scores measured off levodopa treatment. (B) Contrasts between DOPA^{OFF} and DOPA^{ON} conditions corresponding to panels in (A). Shaded region represents the 95% CI. The orange and red bars at the top of the plot highlight the theta and beta bands, respectively. The contrast is significant at frequencies where the confidence interval does not include 0 ($\alpha = 0.05$). The points at the top of the plot indicate frequencies that are significant when controlling for the false discovery rate (Benjamini and Hochberg 1995).

engaging cognitive control and that this might be mediated through cortical inputs via the prefrontal hyperdirect cortico-STN pathway.

4.2 | Relationship of Beta Band Power to Inhibitory Processes and Movement Performance

In our experiment, beta band modulation was mainly influenced by dopaminergic treatment. A significant decrease in low-beta band activity (centred around 18 Hz) was observed in the DOPA^{ON} condition compared to DOPA^{OFF}, consistent with previous reports of reduced beta activity correlating with motor improvement in PD patients (Kühn et al. 2004). In our study, beta power was higher during trials with slower RTs, consistent with elevated beta activity being associated with bradykinesia (Kühn et al. 2004; Little et al. 2012). Moreover, the reduction in beta power following dopaminergic treatment was more pronounced in patients with less severe motor disability. This suggests that, in less severe patients, beta power modulation may be sufficient for optimal task performance, and these patients may rely less on cognitive control linked with theta band changes.

We observed weaker modulation of beta power by uncertainty during movement initiation, suggesting that beta power may not be associated with cognitive control in the same way as theta power. However, beta power was higher in NoGo trials compared to Go trials. This aligns with findings that STN beta power decreases during movement compared to rest (Kühn et al. 2006, 2008; Little and Brown 2014; Mathiopoulou et al. 2024) and with the idea that although it is less directly correlated with cognitive control, it is more directly correlated with movement initiation than theta band power.

4.3 | The Trade-Off Between LFB and Beta Band Power Is Associated With Motor Success

We have shown that LFB power and beta band power are inversely correlated with RTs in our task. It may be interesting to further study how the relationship between LFB and beta band power influences motor performance (Zavala et al. 2018). We speculate that the trade-off between these two frequency bands, in addition to the absolute level of beta band power, is modulated in the context of proactive versus reactive inhibition. Asch et al. (2020) showed that the correlation between the beta and the theta bands is itself a biomarker of tremor symptom in PD. Our results suggest that this relationship merits further investigation in the context of response inhibition (Choi et al. 2024).

Beyond absolute levels of beta and LFB power, changes in each band relative to the other therefore seem to be an indicator of overall inhibition context (proactive or reactive). For example, if LFB power is indicative of cognitive load, it seems relevant that it would be higher in conditions of higher proactive inhibition such as in the uncertain context. Moreover, we also observed that in conditions that require less cognitive engagement (or executive control) and more automaticity (i.e., certain context with only Go trials), LFB power is lower and beta band modulation becomes predominant. Thus, if LFB and beta frequency interact, the reduced LFB power (and associated decrease cognitive load) may explain why beta band power is higher in the certain compared to the uncertain context, despite the increased probability of movement which is typically associated with a decrease in beta power (Little and Brown 2014). A similar mechanism may be at play in the relationship between dopaminergic medication and disease severity. At higher severities, we observed decreased beta band modulation and increased LFB modulation by dopaminergic medication. This suggests that as disease severity increases and patients lose automaticity (reviewed by Wu et al. 2015), executing successful movements imposes more cognitive load (akin to the uncertain compared to the certain context in our task). Overall, it seems that levels of LFB power and beta band power may evolve in opposition to one another, mediated by the context of the task; and the relationship between the two bands should be further considered as a biomarker for successful inhibition.

4.4 | Adaptive DBS Outlook

LFB power, and the interplay between this band and the beta band, may be useful biomarkers for use in adaptive DBS paradigms. In adaptive DBS (reviewed by Guidetti et al. 2021), stimulation can be turned on and off based on the presence or absence of specific biomarkers; the stimulation parameters can be modified based on electrophysiological activity levels; or parameters can be modified based on the 'state' of the patient (the activity that they are performing, time of day, etc.). Protocols are still largely exploratory and are most often based on alpha, beta or gamma band modulation (Isaias et al. 2024; Oehrn et al. 2024; Stanslaski et al. 2024). They have shown improvement in energy consumption for the stimulators and marginal improvement over specific movement-related symptoms (Little et al. 2013; Rosa et al. 2015, 2017; Arlotti et al. 2018). This method could potentially be the way to more effective DBS treatment strategies, provided that the appropriate biomarkers be used to adapt stimulation. Our findings suggest that it may be worthwhile to study LFB power further as a potential biomarker of successful movement, according to which stimulation parameters could be adjusted in real time.

4.5 | Limitations

This study has some limitations. Due to the relatively small number of patients, the between-patient effects of relating spectral power to disease severity would need to be validated in a larger cohort. For the same reason, and because some patients did not present bipolar montages in both STN subregions (sensorimotor and associative), spatial mapping within the STN was limited, and it would be of interest to test the association of severity, theta band power and STN subregion in a larger patient cohort. In addition, the contexts that we studied were organized by block; varying uncertainty context on a trial-by-trial basis would allow examining specific modulations of neuronal activity during switches between different levels of uncertainty. Lastly, as the blocks were always presented in the same order due to clinical constraints, there could be an effect of block that could be excluded by randomizing block order.

5 | Conclusion

Our findings highlight the complex interplay between LFB and beta band modulation within the STN in the release of proactive inhibition, particularly in uncertainty-related contexts. We observed that more severely affected PD patients rely more heavily on cognitive control, which was reflected in increased LFB activity. These results suggest that LFB power could serve as a valuable biomarker of internal cognitive states during motor tasks, particularly for adaptive DBS in more advanced PD cases.

Author Contributions

Luna Damiani: data curation, formal analysis, investigation, visualization, writing – original draft, writing – review and editing. **Marion Albares:** conceptualization, data curation, formal analysis, investigation, methodology, software, validation, visualization, writing – original draft. **Pauline Laviron:** investigation, software, visualization. **Jean-Eudes Le Douget:** software, visualization. **Philippe Boulinguez:** conceptualization, funding acquisition, methodology, writing – original draft, writing – review and editing. **Carine Karachi:** conceptualization, investigation, methodology, supervision, validation, writing – review and editing. **Marie-Laure Welter:** conceptualization, funding acquisition, investigation, methodology, supervision, validation, visualization, writing – original draft, writing – review and editing. **Jérôme Munuera:** methodology, supervision, visualization, writing – original draft, writing – review and editing. **Brian Lau:** conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, software, supervision, validation, visualization, writing – original draft, writing – review and editing.

Acknowledgements

The authors want to thank the patients who participated with dedication to this research programme, Anais Hervé for her help in clinical trial organization and the nurses of the Clinical Investigation Center of the Paris Brain Institute.

Conflicts of Interest

L. Damiani, M. Albares, P. Laviron, J.-E. Le Douget, P. Boulinguez, C. Karachi, J. Munuera, M.-L. Welter and B. Lau declare no competing financial interests directly linked to this study. M.-L. Welter reports personal fees from BIAL for scientific consulting and travel grants from Pfizer. C. Karachi reports personal fees from Boston Scientific and Medtronic for meetings and conferences.

Data Availability Statement

All relevant data are within the article. Requests for anonymized data should be sent to B. Lau at the Paris Brain Institute, 75013 Paris, France.

Peer Review

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/ejn.70055.

References

Albares, M., G. Lio, and P. Boulinguez. 2015. "Tracking Markers of Response Inhibition in Electroencephalographic Data: Why Should We and How Can We Go Beyond the N2 Component?" *Reviews in the Neurosciences* 26, no. 4: 461–478. https://doi.org/10.1515/revneuro-2014–0078.

Albares, M., G. Lio, M. Criaud, J. L. Anton, M. Desmurget, and P. Boulinguez. 2014. "The Dorsal Medial Frontal Cortex Mediates Automatic Motor Inhibition in Uncertain Contexts: Evidence From Combined fMRI and EEG Studies: Automatic Motor Inhibition." *Human Brain Mapping* 35, no. 11: 5517–5531. https://doi.org/10.1002/hbm.22567.

Albares, M., S. Thobois, E. Favre, et al. 2015. "Interaction of Noradrenergic Pharmacological Manipulation and Subthalamic Stimulation on Movement Initiation Control in Parkinson's Disease." *Brain Stimulation* 8, no. 1: 27–35. https://doi.org/10.1016/j.brs.2014.09.002.

Anzak, A., H. Tan, A. Pogosyan, et al. 2012. "Subthalamic Nucleus Activity Optimizes Maximal Effort Motor Responses in Parkinson's Disease." *Brain* 135, no. 9: 2766–2778. https://doi.org/10.1093/brain/aws183.

Ardouin, C., I. Chéreau, P. M. Llorca, et al. 2009. "Évaluation des Troubles Comportementaux Hyper- et Hypodopaminergiques Dans la Maladie de Parkinson." *Revue Neurologique* 165, no. 11: 845–856. https://doi.org/10.1016/j.neurol.2009.06.003.

Arlotti, M., S. Marceglia, G. Foffani, et al. 2018. "Eight-Hours Adaptive Deep Brain Stimulation in Patients With Parkinson Disease." *Neurology* 90, no. 11: e971–e976. https://doi.org/10.1212/WNL.0000000000005121.

Aron, A. R. 2011. "From Reactive to Proactive and Selective Control: Developing a Richer Model for Stopping Inappropriate Responses." *Biological Psychiatry* 69, no. 12: e55–e68. https://doi.org/10.1016/j.biopsych.2010.07.024.

Asch, N., Y. Herschman, R. Maoz, et al. 2020. "Independently Together: Subthalamic Theta and Beta Opposite Roles in Predicting Parkinson's Tremor." *Brain Communications* 2, no. 2: fcaa074. https://doi.org/10.1093/braincomms/fcaa074.

Avvaru, S., N. R. Provenza, A. S. Widge, et al. 2021. "Spectral Features Based Decoding of Task Engagement: The Role of Theta and High Gamma Bands in Cognitive Control." In *2021 43rd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC)*, 6062–6065. IEEE. https://doi.org/10.1109/EMBC46164.2021.9630923.

Ballanger, B., T. van Eimeren, E. Moro, et al. 2009. "Stimulation of the Subthalamic Nucleus and Impulsivity: Release Your Horses." *Annals of Neurology* 66, no. 6: 817–824. https://doi.org/10.1002/ana.21795.

Bardinet, E., M. Bhattacharjee, D. Dormont, 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." *Journal of Neurosurgery* 110, no. 2: 208–219. https://doi.org/10.3171/2008.3.17469.

Benjamini, Y., and Y. Hochberg. 1995. "Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing." *Journal of the Royal Statistical Society: Series B: Methodological* 57, no. 1: 289–300. https://doi.org/10.1111/j.2517–6161.1995.tb02031.x.

Berardelli, A., J. C. Rothwell, P. D. Thompson, and M. Hallett. 2001. "Pathophysiology of Bradykinesia in Parkinson's Disease." *Brain* 124, no. 11: 2131–2146. https://doi.org/10.1093/brain/124.11.2131.

Boulinguez, P., M. Jaffard, L. Granjon, and A. Benraiss. 2008. "Warning Signals Induce Automatic EMG Activations and Proactive Volitional Inhibition: Evidence From Analysis of Error Distribution in Simple RT." *Journal of Neurophysiology* 99, no. 3: 1572–1578. https://doi.org/10.1152/jn.01198.2007.

Bowersock, J. L., S. A. Wylie, A. Alhourani, et al. 2025. "Theta and Beta Power in the Subthalamic Nucleus Respond to Conflict Across Subregion and Hemisphere." *Brain Communications* 7, no. 1: fcaf021. https://doi.org/10.1093/braincomms/fcaf021/7958713.

Brittain, J.-S., K. E. Watkins, R. A. Joundi, et al. 2012. "A Role for the Subthalamic Nucleus in Response Inhibition During Conflict." *Journal of Neuroscience* 32, no. 39: 13396–13401. https://doi.org/10.1523/JNEUROSCI.2259–12.2012.

Cavanagh, J. F., T. V. Wiecki, M. X. Cohen, et al. 2011. "Subthalamic Nucleus Stimulation Reverses Mediofrontal Influence Over Decision Threshold." *Nature Neuroscience* 14, no. 11: 1462–1467. https://doi.org/10.1038/nn.2925.

Choi, J. W., M. Malekmohammadi, S. Niketeghad, et al. 2024. "Prefrontal-Subthalamic Theta Signaling Mediates Delayed Responses During Conflict Processing." *Progress in Neurobiology* 236: 102613. https://doi.org/10.1016/j.pneurobio.2024.102613.

Criaud, M., J. L. Anton, B. Nazarian, et al. 2021. "The Human Basal Ganglia Mediate the Interplay Between Reactive and Proactive Control of Response Through Both Motor Inhibition and Sensory Modulation." *Brain Sciences* 11, no. 5: 560. https://doi.org/10.3390/brainsci11050560.

Criaud, M., C. Laurencin, A. Poisson, et al. 2022. "Noradrenaline and Movement Initiation Disorders in Parkinson's Disease: A Pharmacological Functional MRI Study With Clonidine." *Cells* 11, no. 17: 2640. https://doi.org/10.3390/cells11172640.

Criaud, M., M. Longcamp, J. L. Anton, et al. 2017. "Testing the Physiological Plausibility of Conflicting Psychological Models of Response Inhibition: A Forward Inference fMRI Study." *Behavioural Brain Research* 333: 192–202. https://doi.org/10.1016/j.bbr.2017.06.030.

Criaud, M., A. Poisson, S. Thobois, et al. 2016. "Slowness in Movement Initiation Is Associated With Proactive Inhibitory Network Dysfunction in Parkinson's Disease." *Journal of Parkinson's Disease* 6, no. 2: 433–440. https://doi.org/10.3233/JPD-150750.

Criaud, M., C. Wardak, S. Ben Hamed, B. Ballanger, and P. Boulinguez. 2012. "Proactive Inhibitory Control of Response as the Default State of Executive Control." *Frontiers in Psychology* 3: 59. https://doi.org/10.3389/fpsyg.2012.00059.

Delorme, A., M. Westerfield, and S. Makeig. 2007. "Medial Prefrontal Theta Bursts Precede Rapid Motor Responses During Visual Selective Attention." *Journal of Neuroscience: The Official Journal of the Society for Neuroscience* 27: 11949–11959. https://doi.org/10.1523/JNEUROSCI.3477–07.2007.

Doyle, L. M. F., A. A. Kühn, M. Hariz, A. Kupsch, G. H. Schneider, and P. Brown. 2005. "Levodopa-Induced Modulation of Subthalamic Beta Oscillations During Self-Paced Movements in Patients With Parkinson's Disease." *European Journal of Neuroscience* 21, no. 5: 1403–1412. https://doi.org/10.1111/j.1460–9568.2005.03969.x.

Evans, A. H., A. P. Strafella, D. Weintraub, and M. Stacy. 2009. "Impulsive and Compulsive Behaviors in Parkinson's Disease." *Movement Disorders* 24, no. 11: 1561–1570. https://doi.org/10.1002/mds.22505.

Favre, E., B. Ballanger, S. Thobois, E. Broussolle, and P. Boulinguez. 2013. "Deep Brain Stimulation of the Subthalamic Nucleus, but Not Dopaminergic Medication, Improves Proactive Inhibitory Control of Movement Initiation in Parkinson's Disease." *Neurotherapeutics* 10, no. 1: 154–167. https://doi.org/10.1007/s13311-012-0166-1.

Frank, M. J. 2006. "Hold Your Horses: A Dynamic Computational Role for the Subthalamic Nucleus in Decision Making." *Neural Networks* 19, no. 8: 1120–1136. https://doi.org/10.1016/j.neunet.2006.03.006.

Frank, M. J., J. Samanta, A. A. Moustafa, and S. J. Sherman. 2007. "Hold Your Horses: Impulsivity, Deep Brain Stimulation, and Medication in Parkinsonism." *Science* 318, no. 5854: 1309–1312. https://doi.org/10.1126/science.1146157.

Fumagalli, M., G. Giannicola, M. Rosa, et al. 2011. "Conflict-Dependent Dynamic of Subthalamic Nucleus Oscillations During Moral Decisions." *Social Neuroscience* 6, no. 3: 243–256. https://doi.org/10.1080/17470919.2010.515148.

Guidetti, M., S. Marceglia, A. Loh, et al. 2021. "Clinical Perspectives of Adaptive Deep Brain Stimulation." *Brain Stimulation* 14, no. 5: 1238–1247. https://doi.org/10.1016/j.brs.2021.07.063.

Herz, D. M., M. J. Frank, H. Tan, and S. Groppa. 2024. "Subthalamic Control of Impulsive Actions: Insights From Deep Brain Stimulation in Parkinson's Disease." *Brain* 147, no. 11: 3651–3664. https://doi.org/10.1093/brain/awae184.

Isaias, I. U., L. Caffi, L. Borellini, et al. 2024. "Case Report: Improvement of Gait With Adaptive Deep Brain Stimulation in a Patient With Parkinson's Disease." *Frontiers in Bioengineering and Biotechnology* 12: 1428189. https://doi.org/10.3389/fbioe.2024.1428189.

Jaffard, M., M. Longcamp, J. L. Velay, et al. 2008. "Proactive Inhibitory Control of Movement Assessed by Event-Related fMRI." *NeuroImage* 42, no. 3: 1196–1206. https://doi.org/10.1016/j.neuroimage.2008.05.041.

Karachi, C., J. Yelnik, D. Tandé, L. Tremblay, E. C. Hirsch, and C. François. 2005. "The Pallidosubthalamic Projection: An Anatomical Substrate for Nonmotor Functions of the Subthalamic Nucleus in Primates." *Movement Disorders: Official Journal of the Movement Disorder Society* 20, no. 2: 172–180. https://doi.org/10.1002/mds.20302.

Köhler, R. M., T. S. Binns, T. Merk, et al. 2024. "Dopamine and Deep Brain Stimulation Accelerate the Neural Dynamics of Volitional Action in Parkinson's Disease." *Brain* 147, no. 10: 3358–3369. https://doi.org/10.1093/brain/awae219.

Kojovic, M., A. Higgins, and M. Jahanshahi. 2016. "In Parkinson's Disease STN Stimulation Enhances Responsiveness of Movement Initiation Speed to High Reward Value." *Neuropsychologia* 89: 273–280. https://doi.org/10.1016/j.neuropsychologia.2016.06.033.

Kühn, A. A., L. Doyle, A. Pogosyan, et al. 2006. "Modulation of Beta Oscillations in the Subthalamic Area During Motor Imagery in Parkinson's Disease." *Brain* 129, no. 3: 695–706. https://doi.org/10.1093/brain/awh715.

Kühn, A. A., F. Kempf, C. Brücke, et al. 2008. "High-Frequency Stimulation of the Subthalamic Nucleus Suppresses Oscillatory Beta Activity in Patients With Parkinson's Disease in Parallel With Improvement in Motor Performance." *Journal of Neuroscience: The Official Journal of the Society for Neuroscience* 28, no. 24: 6165–6173. https://doi.org/10.1523/JNEUROSCI.0282–08.2008.

Kühn, A. A., D. Williams, A. Kupsch, et al. 2004. "Event-Related Beta Desynchronization in Human Subthalamic Nucleus Correlates With Motor Performance." *Brain: A Journal of Neurology* 127, no. Pt 4: 735–746. https://doi.org/10.1093/brain/awh106.

Leroi, I., M. Barraclough, S. McKie, et al. 2013. "Dopaminergic Influences on Executive Function and Impulsive Behaviour in Impulse Control Disorders in Parkinson's Disease." *Journal of Neuropsychology* 7, no. 2: 306–325. https://doi.org/10.1111/jnp.12026.

Little, S., and P. Brown. 2014. "The Functional Role of Beta Oscillations in Parkinson's Disease." *Parkinsonism & Related Disorders* 20: S44–S48. https://doi.org/10.1016/S1353-8020(13)70013–0.

Little, S., A. Pogosyan, A. A. Kuhn, and P. Brown. 2012. "Beta Band Stability Over Time Correlates With Parkinsonian Rigidity and Bradykinesia." *Experimental Neurology* 236, no. 2: 383–388. https://doi.org/10.1016/j.expneurol.2012.04.024.

Little, S., A. Pogosyan, S. Neal, et al. 2013. "Adaptive Deep Brain Stimulation in Advanced Parkinson Disease." *Annals of Neurology* 74, no. 3: 449–457. https://doi.org/10.1002/ana.23951.

Lofredi, R., W. J. Neumann, A. Bock, et al. 2018. "Dopamine-Dependent Scaling of Subthalamic Gamma Bursts With Movement Velocity in Patients With Parkinson's Disease." *eLife* 7: e31895. https://doi.org/10.7554/eLife.31895.

Marmor, O., P. Rappel, D. Valsky, et al. 2020. "Movement Context Modulates Neuronal Activity in Motor and Limbic-Associative Domains of the Human Parkinsonian Subthalamic Nucleus." *Neurobiology of Disease* 136: 104716. https://doi.org/10.1016/j.nbd.2019.104716.

Mathiopoulou, V., R. Lofredi, L. K. Feldmann, et al. 2024. "Modulation of Subthalamic Beta Oscillations by Movement, Dopamine, and Deep Brain Stimulation in Parkinson's Disease." *npj Parkinson's Disease* 10, no. 1: 1–7. https://doi.org/10.1038/s41531-024-00693-3.

Meyer, G. M., C. Spay, C. Laurencin, B. Ballanger, G. Sescousse, and P. Boulinguez. 2019. "Functional Imaging Studies of Impulse Control Disorders in Parkinson's Disease Need a Stronger Neurocognitive Footing." *Neuroscience and Biobehavioral Reviews* 98: 164–176. https://doi.org/10.1016/j.neubiorev.2019.01.008.

Mirabella, G., A. Pilotto, A. Rizzardi, et al. 2023. "Effects of Dopaminergic Treatment on Inhibitory Control Differ Across Hoehn and Yahr Stages of Parkinson's Disease." *Brain Communications* 6, no. 1: fcad350. https://doi.org/10.1093/braincomms/fcad350.

Obeso, I., L. Wilkinson, E. Casabona, et al. 2011. "Deficits in Inhibitory Control and Conflict Resolution on Cognitive and Motor Tasks in Parkinson's Disease." *Experimental Brain Research* 212, no. 3: 371–384. https://doi.org/10.1007/s00221-011-2736-6.

Obeso, I., L. Wilkinson, E. Casabona, et al. 2014. "The Subthalamic Nucleus and Inhibitory Control: Impact of Subthalamotomy in Parkinson's Disease." *Brain* 137, no. 5: 1470–1480. https://doi.org/10.1093/brain/awu058.

Oehrn, C. R., S. Cernera, L. H. Hammer, et al. 2024. "Chronic Adaptive Deep Brain Stimulation Versus Conventional Stimulation in Parkinson's Disease: A Blinded Randomized Feasibility Trial." *Nature Medicine* 30, no. 11: 3345–3356. https://doi.org/10.1038/s41591-024-03196-z.

Percival, D. B., and A. T. Walden. 1993. *Spectral Analysis for Physical Applications*. Cambridge University Press.

Redgrave, P., M. Rodriguez, Y. Smith, et al. 2010. "Goal-Directed and Habitual Control in the Basal Ganglia: Implications for Parkinson's Disease." *Nature Reviews Neuroscience* 11, no. 11: 760–772. https://doi.org/10.1038/nrn2915.

Ridderinkhof, R. K. 2002. "Micro- and Macro-Adjustments of Task Set: Activation and Suppression in Conflict Tasks." *Psychological Research* 66, no. 4: 312–323. https://doi.org/10.1007/s00426-002-0104-7.

Rodriguez-Oroz, M. C., J. López-Azcárate, D. Garcia-Garcia, et al. 2011. "Involvement of the Subthalamic Nucleus in Impulse Control Disorders Associated With Parkinson's Disease." *Brain* 134, no. 1: 36–49. https://doi.org/10.1093/brain/awq301.

Rosa, M., M. Arlotti, G. Ardolino, et al. 2015. "Adaptive Deep Brain Stimulation in a Freely Moving Parkinsonian Patient." *Movement Disorders* 30, no. 7: 1003–1005. https://doi.org/10.1002/mds.26241.

Rosa, M., M. Arlotti, S. Marceglia, et al. 2017. "Adaptive Deep Brain Stimulation Controls Levodopa-Induced Side Effects in Parkinsonian Patients." *Movement Disorders* 32, no. 4: 628–629. https://doi.org/10.1002/mds.26953.

Singh, A. 2018. "Oscillatory Activity in the Cortico-Basal Ganglia-Thalamic Neural Circuits in Parkinson's Disease." *European Journal of Neuroscience* 48, no. 8: 2869–2878. https://doi.org/10.1111/ejn.13853.

Spay, C., G. Meyer, M. L. Welter, B. Lau, P. Boulinguez, and B. Ballanger. 2018. "Functional Imaging Correlates of Akinesia in Parkinson's Disease: Still Open Issues." *NeuroImage: Clinical* 21: 101644. https://doi.org/10.1016/j.nicl.2018.101644.

Stanslaski, S., R. L. S. Summers, L. Tonder, et al. 2024. "Sensing Data and Methodology From the Adaptive DBS Algorithm for Personalized Therapy in Parkinson's Disease (ADAPT-PD) Clinical Trial." *npj Parkinson's Disease* 10, no. 1: 1–11. https://doi.org/10.1038/s41531-024-00772-5.

Tan, H., A. Pogosyan, A. Anzak, et al. 2013. "Frequency Specific Activity in Subthalamic Nucleus Correlates With Hand Bradykinesia in Parkinson's Disease." *Experimental Neurology* 240: 122–129. https://doi.org/10.1016/j.expneurol.2012.11.011.

Temiz, G., S. B. Sébille, C. Francois, E. Bardinet, and C. Karachi. 2020. "The Anatomo-Functional Organization of the Hyperdirect Cortical Pathway to the Subthalamic Area Using in Vivo Structural Connectivity Imaging in Humans." *Brain Structure and Function* 225, no. 2: 551–565. https://doi.org/10.1007/s00429-019-02012-6.

van den Wildenberg, W. P. M., K. R. Ridderinkhof, and S. A. Wylie. 2022. "Towards Conceptual Clarification of Proactive Inhibitory Control: A Review." *Brain Sciences* 12, no. 12: 1638. https://doi.org/10.3390/brainsci12121638.

Voon, V., L. Manssuer, Y. J. Zhao, et al. 2024. "Modeling Impulsivity and Risk Aversion in the Subthalamic Nucleus With Deep Brain Stimulation." *Nature Mental Health* 2, no. 9: 1084–1095. https://doi.org/10.1038/s44220-024-00289-z.

Wardak, C., S. Ramanoël, O. Guipponi, P. Boulinguez, and S. B. Ben Hamed. 2012. "Proactive Inhibitory Control Varies With Task Context." *European Journal of Neuroscience* 36, no. 11: 3568–3579. https://doi.org/10.1111/j.1460–9568.2012.08264.x.

Welter, M.-L., M. Schüpbach, V. Czernecki, et al. 2014. "Optimal Target Localization for Subthalamic Stimulation in Patients With Parkinson Disease." *Neurology* 82, no. 15: 1352–1361. https://doi.org/10.1212/WNL.0000000000000315.

West, T., S. Farmer, L. Berthouze, et al. 2016. "The Parkinsonian Subthalamic Network: Measures of Power, Linear, and Non-Linear Synchronization and Their Relationship to L-DOPA Treatment and OFF State Motor Severity." *Frontiers in Human Neuroscience* 10: 517. https://doi.org/10.3389/fnhum.2016.00517.

Whiteside, S. P., and D. R. Lynam. 2001. "The Five Factor Model and Impulsivity: Using a Structural Model of Personality to Understand Impulsivity." *Personality and Individual Differences* 30, no. 4: 669–689. https://doi.org/10.1016/S0191-8869(00)00064–7.

Wu, T., M. Hallett, and P. Chan. 2015. "Motor Automaticity in Parkinson's Disease." *Neurobiology of Disease* 82: 226–234. https://doi.org/10.1016/j.nbd.2015.06.014.

Zavala, B., A. Jang, M. Trotta, C. I. Lungu, P. Brown, and K. A. Zaghloul. 2018. "Cognitive Control Involves Theta Power Within Trials and Beta Power Across Trials in the Prefrontal-Subthalamic Network." *Brain* 141, no. 12: 3361–3376. https://doi.org/10.1093/brain/awy266.

Zavala, B., H. Tan, K. Ashkan, et al. 2016. "Human Subthalamic Nucleus–Medial Frontal Cortex Theta Phase Coherence Is Involved in Conflict and Error Related Cortical Monitoring." *NeuroImage* 137: 178–187. https://doi.org/10.1016/j.neuroimage.2016.05.031.

Zavala, B., H. Tan, S. Little, et al. 2016. "Decisions Made With Less Evidence Involve Higher Levels of Corticosubthalamic Nucleus Theta Band Synchrony." *Journal of Cognitive Neuroscience* 28, no. 6: 811–825. https://doi.org/10.1162/jocn_a_00934.

Zavala, B. A., H. Tan, S. Little, et al. 2014. "Midline Frontal Cortex Low-Frequency Activity Drives Subthalamic Nucleus Oscillations During Conflict." *Journal of Neuroscience* 34, no. 21: 7322–7333. https://doi.org/10.1523/JNEUROSCI.1169–14.2014.

Zénon, A., Y. Duclos, R. Carron, et al. 2016. "The Human Subthalamic Nucleus Encodes the Subjective Value of Reward and the Cost of Effort During Decision-Making." *Brain* 139, no. 6: 1830–1843. https://doi.org/10.1093/brain/aww075.

Supporting Information

Additional supporting information can be found online in the Supporting Information section.