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Selection of Optimal Programming Contacts Based on Local Field Potential Recordings From Subthalamic Nucleus in Patients With Parkinson's Disease

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Abstract

BACKGROUND—In the United States, the most commonly used surgical treatment for patients with Parkinson's disease is the implantation of deep brain stimulation (DBS) electrodes within the subthalamic nucleus. However, DBS device programming remains difficult and is a possible source of decreased efficacy.

OBJECTIVE—We investigated the relationship between local field potential (LFP) activities in the subthalamic nucleus and the therapeutic response to programming.

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Disclosure

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METHODS—We recorded LFPs with macroelectrodes placed unilaterally for DBS in 4 PD patients, 3 weeks after implantation, before the start of long-term DBS. Power-frequency spectra were calculated for each of 7 possible electrode contacts or contact pairs, over multiple 5- to 10-minute quiet waking epochs and over 30-second epochs during hand movements. Subsequently, DBS devices were programmed, with testing to determine which electrode contacts or contact pairs demonstrated optimal therapeutic efficacy.

RESULTS—For each patient, the contact pair found to provide optimal efficacy was associated with the highest energy in the β (13–32 Hz) and γ (48–220 Hz) bands during postoperative LFP recordings at rest and during hand movements. Activities in other frequency bands did not show significant correlations between LFP power and optimal electrode contacts.

CONCLUSION—Postoperative subband analysis of LFP recordings in β and γ frequency ranges may be used to select optimal electrode contacts. These results indicate that LFP recordings from implanted DBS electrodes can provide important clues to guide the optimization of DBS therapy in individual patients.

Keywords

Deep brain stimulation; Local field potentials; Parkinson's disease; Programming; Subthalamic nucleus

Parkinson's disease (PD) affects more than 500,000 people in the United States, with an annual incidence of 50,000 new cases per year.¹ There is a sizable proportion of PD patients whose motor symptoms cannot be adequately controlled with medications. In these patients, deep brain stimulation (DBS) of the subthalamic nucleus (STN) has emerged as an effective neurosurgical treatment.

DBS therapy involves implanting quadripolar electrodes into specific targets in the brain and connecting the electrodes to an implanted pulse generator (IPG). The procedure is generally done in 2 stages, the first involving DBS electrode implantation and, at a later stage, IPG implantation followed by IPG programming to deliver constant stimulation at a particular voltage, rate, and pulse width. DBS programming for each patient includes the selection of appropriate electrode contacts, voltage, and pulse width to maximize efficacy and minimize side effects of stimulation. The programming process requires time-consuming assessments by experienced personnel of efficacy and side effects at each of 4 brain electrode contacts, individually and in various combinations. Improperly programmed DBS devices can be a source of inadequate symptom control.² Information that could identify in advance the optimal contacts for stimulation would expedite and increase the accuracy of the programming process.

The 4 electrode contacts, numbered 0 to 3 from most caudal to most rostral, are 1.5 mm in length, spaced 0.5 mm apart, and span a total distance of 7.5 mm (Medtronic model 3389; Medtronic Corp., Minneapolis, Minnesota). As the rostrocaudal extent of the STN is 4 to 5 mm, typically no more than 2 DBS electrode contacts are located within the STN.

In addition to delivering stimulation, DBS electrodes can also be used to record local field potentials (LFPs). LFPs are thought to represent aggregate activity from populations of

neurons, synapses, axons, and glia surrounding the electrode tip. LFP recordings have been used to glean information about neural rhythms involving the STN and surrounding structures.³ Recent data suggest that LFPs recorded from the STN can provide important clues about target localization^{4,5} and disease state in patients. Normal voluntary movements appear to be preceded by a decrease in the amplitude of β -band LFP oscillations and an increase in γ -band activity in the STN and other elements of the basal ganglia–thalamocortical circuitry.⁶ A pathological increase in the antikinetic β -band activity, as well as a decrease in the prokinetic γ -band activity, is thought to accompany parkinsonism.⁷

Most studies of LFP activity recorded from the STN of PD patients have been conducted in the immediate postoperative period. In this study, we chose to record LFP activity 3 weeks after electrode implantation, when the potentially confounding effect on neuronal activity posed by the focal cerebral edema induced by surgery can be expected to have abated. Thus, 48 hours of LFP recordings were obtained at the time when patients with implanted DBS electrodes returned to the hospital for surgery to connect their previously implanted DBS electrodes to the IPG.

Our goal was to test the hypothesis that LFP data recorded from DBS electrodes could be used to identify the optimal contact(s) for postoperative DBS programming. To this end, patients underwent postoperative DBS programming, and results were then compared with LFP data collected from each contact to check for correlations. In addition, we compared the results of the postoperative LFP recordings with LFP recordings made during the DBS electrode implantation procedure to examine the utility of intra-operative LFP recordings in guiding electrode contact selection for IPG programming.

METHODS

After approval by the University of Minnesota Institutional Review Board, 6 patients with idiopathic PD and typical parkinsonian symptoms, including tremor, akinesia, and rigidity, were recruited for participation in the study. Before surgery, all patients underwent formal neuropsychological evaluation and testing with the Unified Parkinson's Disease Rating Scale on and off dopamine replacement therapy.

Inclusion and Exclusion Criteria

Inclusion criteria for the study included the diagnosis of idiopathic PD, a positive response to medication, greater than 30% improvement on the motor portion of the Unified Parkinson's Disease Rating Scale (mUPDRS), brain magnetic resonance imaging (MRI) without significant abnormalities, and medical clearance for surgery. All study subjects provided written consent for participation.

Patients older than the age of 70 or younger than the age of 18, those at increased risk of infection (eg, comorbid diabetes or history of recurrent infections), and patients with significant cognitive deficits or untreated psychiatric disorders (eg, depression) detected on neuropsychological testing were excluded from this study.

Surgical Procedure

During the DBS electrode implantation surgery (stage I surgery; Figure 1), stereotactic MRI, microelectrode recording, and macrostimulation were used to guide the placement of quadripolar DBS electrodes (Model #3389; Medtronic Corp.) within the STN, according to standard surgical procedure.⁸ The DBS electrodes bear 4 cylindrical, platinum-iridium contacts (each contact is 1.5 mm wide and measures 1.27 mm in diameter, with a contact separation of 0.5 mm), numbered 0 to 3, from caudal to rostral (see Figure 1, Supplemental Digital Content 1, <http://links.lww.com/NEU/A314>). The intended coordinates for contact 0 were 12 mm lateral to midline, 3 mm posterior to the mid-commissural point, and 4 mm below the intercommissural plane.^{9,10} After placement, the DBS electrode was secured to the cranium, and the end of the electrode was coiled underneath the scalp. The scalp incision was then closed, and immediate postoperative MRI of the brain was performed in each patient, as described in the following.

Patients returned for stage II surgery 3 weeks later (Figure 1) to allow for interval resolution of the cerebral edema caused by stage I surgery and any resultant improvement in PD symptoms. At this time, the distal end of the DBS electrode was identified by palpation and brought out through a small incision in the scalp. The end of the electrode was attached to a sterile percutaneous extension cable, the distal end of which was brought out through a separate stab incision several centimeters away from the end of the electrode, and the incisions were closed. The extension cable was later used for LFP recordings (see the following).

Electrode Localization

Proper positioning of the DBS electrode contacts within the STN was verified based on the following data: (1) intraoperative microelectrode recordings that identified cells with firing characteristics consistent with STN neurons; (2) antiparkinsonian benefit and side effects of macrostimulation; (3) preoperative stereotactic T1- and T2-weighted images merged to postoperative MRI demonstrating the position of the DBS electrode within the borders of the STN; (4) the use of Framelink (Medtronic Corp.) software to analyze postoperative MRI (see Figure 1, Supplemental Digital Content 1, <http://links.lww.com/NEU/A314>), verifying that a line through the x, y, and z coordinates of the contacts 0 and 3 of the DBS electrode traversed the STN¹¹; and (5) evaluation of the efficacy of postprogramming stimulation on each patient's contralateral motor symptoms.

Postoperative MRI scans were loaded onto a StealthStation TREON System (Medtronic Corp., Sunnyvale, Colorado), and Framelink software was used to merge pre- and postoperative images and to determine the stereotactic coordinates of each DBS electrode location. Aspects of the localization procedure are demonstrated (see Figure 1, Supplemental Digital Content 1, <http://links.lww.com/NEU/A314>), and the results are shown (see Table 1, Supplemental Digital Content 1, <http://links.lww.com/NEU/A318>).

LFP Recording Procedure

LFP recordings were made in the operating room at the completion of DBS electrode testing and during an extended inpatient stay during which patients underwent 48 hours of

continuous LFP recording from the implanted DBS electrode with concurrent videotaping in the context of another study to be reported later. In addition to LFP data, electroencephalographic, electromyographic, and tremor accelerometry recordings were obtained with EMU40 (XLTEK-Natus, San Carlos, California) at a sampling rate of 1024 Hz. All channels were high-pass filtered at 0.1 Hz. The recording period included periods of sleep and wakefulness in each patient. mUPDRS examinations were performed and recorded by a study nurse before initiation of recordings, and simplified ratings were applied every 3 hours during recordings to document and quantify the severity of each patient's symptoms and signs. All patients underwent mUPDRS testing during 2 on periods and 2 off periods during the 48-hour monitoring sessions. On and off periods were defined by patients' subjective assessment of maximal dopaminergic medication effect or absence, respectively, in conjunction with mUPDRS examinations after each administration of antiparkinsonian medications. A schematic diagram summarizing the experimental paradigm is provided in Figure 1. mUPDRS testing included alternating hand supination/pronation and fist open/close movements, each lasting approximately 30 seconds. We report only the off period results in our patients.

Surgery for Connection of DBS Electrodes to the IPG

At the end of 48-hour recordings, each patient returned to the operating room for removal of the percutaneous extension cable, followed by implantation of a lead extension and the IPG (stage II surgery; Figure 1) and connection of these components to the existing DBS electrode, following standard procedure.

Programming of DBS Devices

DBS programming was carried out after IPG implantation (ie, on the day after completion of the 48-hour recordings (Figure 1)). Programming was performed independent of any knowledge about LFP spectral analysis. All subjects underwent programming in the off state, and clinical benefits and voltage thresholds for side effects were recorded for each electrode contact in monopolar and bipolar modes. At each contact setting, subjects were asked to provide subjective assessments of rigidity, bradykinesia, and tremor and whether side effects of stimulation were felt, and the rater performed mUPDRS assessments of patient symptoms. Subjects then received their regular morning dose of PD medication and were assessed 30 minutes later to verify the absence of side effects from the combination of stimulation and medications. Optimized programming settings for each subject were based on these data (Table 1). Data collected consisted of current amplitude, pulse width, frequency, and contact(s) of stimulation. Voltages required for maximal clinical benefit and voltage thresholds for stimulation-induced side effects were collected for each contact in monopolar and bipolar mode.

LFP Signal Processing

The recorded LFP data were exported to ASCII files from an XLTEK system to be imported and further analyzed in Matlab (Mathworks, Natick, Massachusetts). The LFP data from all contacts were low-pass filtered using an FIR filter with 220 Hz cutoff frequency, and then down-sampled to 512 Hz. For each subject, 5- to 10-minute LFP data segments, recorded during episodes of rest, were selected and used for spectral analysis. These segments were

identified from concurrent video recordings and immediately preceded segments during which patients performed alternating hand movement tasks, which were also used for spectral analysis. Power spectra of the monopolar and bipolar LFP signals were computed using a modified Welch periodogram. A 1024-point fast Fourier transform was computed for spectral analysis, using a 1-second Hamming window. This analysis window was shifted by 32 samples along the signal. The length of the analysis windows provided 1-Hz resolution in the constructed spectra. Raw LFP data of bipolar contacts and their spectra are illustrated in Figure 2, for a representative subject.

After computation of the power spectra in each 1-second time segment, the power in the θ - (3–7 Hz), α - (7–13 Hz), β - (13–32 Hz), and γ - (48–220 Hz) bands was computed and normalized using the following procedure. For each monopolar and bipolar derivation, an average energy level was computed by accumulating the energy of all frequency subbands and then averaging it across available contacts (3 for bipolar and 4 for monopolar). The energy in each subband was then divided by the average energy, converted to decibels (decibel scale), and used as a feature for statistical analysis. This provided a feature matrix representing the relative subband power changes during rest- and movement-related segments for each monopolar and bipolar contact.

Statistical Analysis

To examine the relationship between the clinically optimal contact and the distribution of normalized subband energies, we used the following technique. Repeated-measures analyses of variance were fit to the median of LFP power, within each subband (3–7, 7–13, 13–32, and 48–220 Hz), across the 7 possible contacts, and for each patient's resting and movement states. Power was predicted by an indicator for that contact deemed optimal for each patient by study staff and patient self-report, without knowledge of the LFP data. A second analysis adjusted the optimal/not optimal comparison for inherent differences observed across the contact positions (eg, contact E1 had consistently higher power compared with E3).

RESULTS

Patient Demographics

Six patients completed the LFP recording protocol as outlined in the Methods section. Patient demographics and clinical characteristics are listed in Table 2. There were 4 men and 2 women, with a mean age of 59.3 years (range 48–69 years). The mean duration of PD in these patients was 12.3 years,^{8–16} the mean levodopa equivalent daily dose (see calculation method in the footnote to Table 2) was 936.8 mg (range 271–2100), and the mean preoperative improvement in mUPDRS was 59.1% in the on versus off state.

Technical Problems and Complications/Adverse Events

Technical problems associated with the microelectrode recording in patient 6 resulted in performing multiple microelectrode passes through the STN. The microelectrode recording in this patient was ultimately unsuccessful, and the DBS electrode was placed based on the stereotactic MRI information, with location confirmed using macrostimulation. Subsequent postoperative MRI confirmed that the tip of the electrode was located within the STN.

Because of a persistent microlesion effect, this patient's DBS device has still not been activated.

In addition, patient 4 had a previously implanted contralateral DBS electrode that was not turned off during LFP recordings. As a consequence, the patient's data were not included here. The LFP recording data in this report are therefore based on studies in the remaining 4 patients.

There were no peri- or postoperative complications or adverse events in our study populations, and, in particular, no postoperative infections or adverse events related to LFP recording.

Electrode Localization

For each subject, postoperative MRI scans were merged with the preoperative MRI scans to obtain the lateral, anteroposterior, and vertical locations of the inferiormost (contact 0) and superiormost (contact 3) (see Table 1, Supplemental Digital Content 1, <http://links.lww.com/NEU/A318>) DBS contacts in stereotactic space (see the Methods section). The rostral and caudal borders of the STN are not easily identified on 1.5-T MRI, and there is sufficient artifact from the presence of the DBS electrode to obscure the determination of whether a particular contact lies within the STN or immediately outside the STN. However, microelectrode recording in 4 subjects (excluding patient 6 as mentioned previously) served to identify the rostral and caudal boundaries of, and trajectories through, the STN.

Relationship Between Maximal β - and γ -Band Activity and Optimal Contacts for Stimulation at Rest and During Hand Movement

Figure 2(B) displays spectral analysis of the LFP signals in patient 2 during the resting state, demonstrating a distinct peak in the β -band. Note that the bipolar derivation demonstrating peak β -band activity (E0E1; red line) corresponds to the electrode contact pair associated with optimal benefit (contacts 0 and 1), according to both the patient and the rater.

Table 1 shows the programming results for a different subject (patient 3), with the optimal programming settings highlighted in bold type. Ratings increase from 0 (asymptomatic) to 4 (severe) and are reported from patient's (subjective) and rater's (objective) perspective. Note that according to the experienced rater's assessment, no distinction could be found in efficacy between stimulation at contacts 0 and 1 versus contacts 1 and 2, nor could the patient's reported rating distinguish between these 2 contact pairs. However, the patient selected contact pair 0 and 1 for optimal programming because subjectively, this combination "felt best." Independently, maximal β and γ activity were found to be associated with this pair of contacts (Table 3; patient 3).

Figure 3 is a box-and-whisker plots of log-transformed normalized power in the β -band (13–32 Hz) derived from monopolar and bipolar recordings of electrode contact pairs (E0E1, E1E2, and E2E3) during the resting state. Box-and-whisker plots for the γ -band at rest and for the β - and γ -bands during hand movements are shown (see Figures 2–4, Supplemental Digital Content 2–4, <http://links.lww.com/NEU/A315>, <http://links.lww.com/NEU/A316>, <http://links.lww.com/NEU/A317>). Median values of the normalized power of β - and γ -

frequency bands in the resting and movement states are shown in Table 3. Note that, for the resting state, the optimal contacts for stimulation correspond to the contacts with significantly higher power in the β - and γ -bands. No such correlation existed across subjects for other bands in the LFP spectrum (data not shown). Interestingly, when subjects performed either of 2 hand movement tasks (hand supination/pronation or open/close), the relative power in the β - and γ -bands increased. The movement state showed a more significant correlation than the resting state with the optimal contact, within the γ -frequency band.

Significant differences in power were observed for the β -band between contacts deemed optimal for patient symptoms versus contacts that were not optimal, in both resting states ($P < .0001$) and during hand movement tasks (hand supination/pronation, $P < .0001$; hand open/close tasks, $P < .0001$). Similar results were seen for the γ -band ($P = .0053$ for resting; $P = .0006$ for hand supination/pronation; $P = .0013$ for hand open/close), but not for α - or θ -bands (all P values $> .05$). Adjustment for inherent contact differences gave similar results for optimal versus not optimal β -band ($P = .0003$ for resting, $P = .0065$ during hand supination/pronation, and $P = .0005$ for hand open/close), but no differences were observed after adjustment for the remaining subbands.

In 2 patients, the experienced programmer was unable to distinguish between 2 sets of bipolar contacts in terms of optimal benefit, but the patients provided feedback that resulted in selection of an electrode pair that was later found to correspond to the contacts with the greatest β -band activity in these individuals (Table 1).

To quantify the power changes in β - and γ -bands during movement and resting states, we computed the ratio of the power in β - and γ -bands during movement to the resting condition at the best contact position. Because the optimal benefit was obtained in bipolar contact derivations, these values were computed for bipolar case and then were converted to the decibel scale. The mean of the ratio estimated from all subjects in β - and γ -bands was -2.49 dB and 0.75 dB, respectively. The ratios indicated that the power at the optimal stimulation contact position decreased during the movements in the β -band but increased in the γ -band. This can be explained by the synchronization and desynchronization phenomenon in γ - and β -frequency bands, respectively.¹² We also calculated the ratio of the power at the optimal stimulation contacts to the mean of other possible contacts (Table 4). We found that for the β -band, the ratios were smaller in the movement than in the rest condition, whereas the reverse was true for the γ -band. These findings indicate that, in the γ -band, the optimal stimulation contact position is best predicted during the movement states, whereas the predictive power of the β -band activity is greatest at rest. The results also show that β -band oscillations provided overall more robust indicators of the optimal electrode contact position, regardless of behavioral state (rest or movement).

DISCUSSION

We recorded LFP activity from DBS electrodes implanted in the STN for the treatment of PD. This pilot study evaluated whether LFP spectral powers in the θ -, α -, β -, and γ -bands could be used to guide contact selection for postoperative IPG programming. Although these

results come from a small sample of patients, they are promising because they suggest that maximum β - and γ -band activity during rest, but not activity in other frequency bands, is recorded from the pair of electrode contacts that is associated with the greatest efficacy of stimulation. Additionally, maximal β - and γ -band activity was recorded from the contact pair associated with optimal programming during the movement state. Movement was associated with a decrease in the amplitude of overall β -band activity before normalization (see Methods section), consistent with what other investigators have reported.¹³

A tendency for neurons in the basal ganglia to oscillate and synchronize their activity has been documented both in animal models of PD and in patients with PD undergoing surgery for the implantation of DBS electrodes.¹⁴ Oscillations in the β -band are especially prominent in patients with PD in the off state.⁶ Although the origin of LFP β -band activity remains unclear,⁵ oscillations in this range have been noted to decrease in PD patients immediately before voluntary movements.⁶ β -Band activity is also suppressed after administration of levodopa in these patients.⁶ These observations have led to the hypothesis that β -band activity is antikinetic; that is, it suppresses movement-related activity. Additionally, Chen et al⁴ reported that β -band activity in intraoperatively recorded LFP signals can be used to guide DBS electrode placement, and Weinberg et al⁵ demonstrated that this activity is primarily located in the dorsal aspect of the STN.

Intraoperative LFP Data and Electrode Position Within the STN

Consistent with the reports of others,^{4,5} peak β - and, in our study, γ -band activity, during both rest and hand movements, were located within the boundaries of the STN, based on intra-operative microelectrode recording and postoperative image analysis. This finding raises the possibility that LFP recording might serve as a useful adjunct to microelectrode recording, by confirming the location of the STN. Whether LFP recordings could serve as an alternative to microelectrode recording for localizing the STN is less clear. It would be beneficial to compare microelectrode-derived boundaries of the STN with the power distribution of LFP signals. This sort of analysis may identify intraoperative LFP recordings as a mapping tool, offering the potential benefit that LFPs can be recorded through the same electrode that is ultimately implanted in the patient for stimulation and therefore do not carry the same risk of intracranial hemorrhage that has been attributed to microelectrode recording,¹⁵ although this increase in hemorrhage risk has not been universally found.¹⁶ The downside of LFP recordings, if obtained through the DBS electrode, is that the relative size of the DBS electrode would cause more damage than the much smaller microelectrode, if more than 1 electrode pass were required. LFP recordings may therefore be useful to identify the correct target depth, but less useful to adjust the anteroposterior or mediolateral coordinates of the stereotactic target.

LFP Data and Predicting the Choice of Optimal DBS Contact(s) for Programming

In the resting state, we noted that maximal β - and γ -band activity corresponded to the electrode pairs associated with optimal postoperative DBS programming results. Although there was a clear difference between the β -band energies of the best and other contact pairs, there was a lack of consistent β -band energy decrease on the neighboring individual STN contacts, recorded with monopolar derivations, demonstrating the much lower spatial

resolution of this recording modality. In practical terms, this indicates that bipolar LFP recordings are far superior to monopolar montages in identifying the most promising DBS contacts.

During hand movement tasks, maximal β - and γ -band activity was found in the contact pair to be associated with optimal programming. Activity in other frequency bands did not show this correspondence with optimal programming contacts. Interestingly, in the 2 patients for whom objective rating of bradykinesia, rigidity, and tremor during programming identified 2 contact pairs that seemed equivalent in terms of efficacy, each patient provided subjective feedback, resulting in the selection of 1 of these 2 pairs as most effective. The selected pair in each of these 2 cases corresponded to the pair associated with maximum β - and γ -band activity. This observation suggests that the use of maximum β - and γ -band activity to select the optimal contacts for programming can be a useful and sensitive adjunct to objective testing by experienced personnel.

We can only speculate as to why maximal β - and γ -band activity is associated with the DBS electrode contacts that prove optimal for programming. It is possible that maximal β - and γ -band activity simply serves to identify the STN, as opposed to surrounding structures, and have little to do with PD itself. Alternatively, it is possible that maximal β - and γ -band activity identifies the region of the STN most heavily affected by PD.

Should the relationship between maximal β - and γ -band activity and optimal contacts for DBS programming prove replicable in a larger number of patients, such postoperative recordings could be used to streamline the DBS programming process. Ideally, such signals would be recorded through modified IPGs featuring LFP recording capabilities,¹⁷ along with telemetric transmission of raw or processed data to help with the identification of contacts with high β - and γ -band activity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS

DBS	deep brain stimulation
IPG	implanted pulse generator
LFP	local field potential
mUPDRS	motor portion of the Unified Parkinson's Disease Rating Scale
PD	Parkinson's disease
STN	subthalamic nucleus

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FIGURE 1.

Overview of experimental design. All subjects underwent local field potential (LFP) recording 3 weeks after electrode implantation, followed by implantable pulse generator (IPG) implantation surgery. All patients underwent testing in the on and off medication states. DBS, deep brain stimulation.

FIGURE 2.

A, representative raw postoperative local field potential (LFP) data from a single subject. The vertical lines represent 1-second time intervals. Reconstruction of the location of contact E1 indicated that it was located within the borders of the subthalamic nucleus. Arrows indicate phase reversals between E0E1 and E1E2, suggesting that the oscillatory activity is locally generated. **B**, LFP spectra, from the same subject as in **A**, from 3 bipolar derivations (postoperative recordings), estimated over a 5-minute period during rest. The spectrum of each contact is normalized to the average energy of all contacts. Note that the bipolar derivation demonstrating peak β -band activity (E0E1; solid blue line) corresponds to the electrode contact pair associated with optimal benefit during programming (contact pair 0 and 1).

FIGURE 3.

Box-and-whisker plots of the normalized β -band (13–32 Hz) power in decibel scale estimated from 4 monopolar (E0, E1, E2, and E3) and 3 bipolar (E0E1, E1E2, and E2E3) derivations, all simultaneously recorded under resting conditions in the off medication state. In each case, the montage with the highest β -band activity corresponded to the clinically most efficacious contacts (E0E1 in patients 1 to 3, E1E2 in patient 5).

TABLE 1
Example of the Relationship Between the Results of Deep Brain Stimulation Programming (Patient 3)^a

Contacts/Voltage	Rigidity		Bradykinesia		Tremor		SE Voltage (0–8 V)
	Subjective	Objective	Subjective	Objective	Subjective	Objective	
Case+ and 0–/2.2 V	1	1	1	2	1	2	3.2 V, arm pulling
Case+ and 1–/2.5 V	1	1	1	2	0	0	2.5 V, head fullness
Case+ and 2–/2.5 V	0	1	0	1	0	0	3.5 V, head fullness
Case+ and 3–/2.5 V	1	1	1	1	1	1.5	2.5 V, head fullness
0– and 1+/3.0 V	0	0	0	1	0	0	4.5 V, difficulty with tasks
1– and 2+/2.0 V	0	0	0	1	0	0	5.2 V, head fullness
2– and 3+/2.0 V	1	1	1	2	0	0	4.0 V, head fullness

^aSE, side effect +, positive; –, negative. The optimal programming settings, based on rater's and patient's assessments, are shown in bold type. Ratings between 0 (asymptomatic) and 4 (severe) are reported both from the patient's (subjective) and rater's (objective) perspective. Voltages listed in the first column are those at which specified severity of rigidity, bradykinesia, or tremor was recorded. The last column lists the voltages at which the specified side effects were noted. Although results for contacts 0 and 1 are indistinguishable from those obtained at contacts 1 and 2 based on the rater's and patient's per-symptom assessment, the patient still selected contact pair 0 and 1 as optimal. See text for further explanation.

TABLE 2

Patient Demographics and Preoperative Characteristics^a

Patient	Sex/Age, y	PD Duration, y	mUPDRS Off Score	mUPDRS On Score	mUPDRS % Change	LEDD, ^b mg	STN
1	F/65	12	45	28	38	700	L
2	M/61	8	59	20.5	66	2100	L
3	M/56	13	51	14	73	875	L
5	M/57	13	54	37	32	750	L

^aPD, Parkinson's disease; mUPDRS, motor portion of the Unified Parkinson's Disease Rating Scale; LEDD, levodopa equivalent daily dose; STN, subthalamic nucleus; L, left.

^bThe LEDD was calculated according to the following formula: LEDD = levodopa/carbidopa regular + (levodopa/carbidopa controlled release [CR] × 0.75) + [levodopa/carbidopa regular + (levodopa/carbidopa CR × 0.75)] × 0.25 if on tolcapone + (pramipexole × 67.75) + (pergolide × 100) + (ropinirole × 16.67) + (bromocriptine × 10).¹⁸

TABLE 3

Median of the Normalized Power in the β - (13–32 Hz) and γ - (48–220 Hz) Bands Recorded With Monopolar Recording Methods From Contacts E0–E3 or Bipolar Recording Methods Using Contact Pairs E0E1, E1E2, or E2E3^a

State/Patient	E0	E1	E2	E3	E0E1	E1E2	E2E3
β -Band Resting State							
<i>Patient 1</i>	-5.18	-4.74	-5.33	-5.98	-1.08	-4.85	-3.69
<i>Patient 2</i>	-2.44	-1.89	-4.87	-8.82	1.00	-6.13	-6.28
<i>Patient 3</i>	-9.02	-8.23	-8.92	-9.02	-0.57	-5.48	-7.65
<i>Patient 5</i>	-5.95	-7.19	-7.34	-8.51	-5.65	-0.01	-6.89
γ -Band Resting State							
<i>Patient 1</i>	-19.10	-19.27	-20.66	-22.34	-8.77	-11.63	-10.91
<i>Patient 2</i>	-13.02	-13.08	-15.20	-17.06	-11.59	-13.09	-16.66
<i>Patient 3</i>	-10.08	-10.02	-10.21	-10.30	-7.18	-8.26	-10.76
<i>Patient 5</i>	-10.49	-10.52	-10.72	-12.15	-5.05	-4.60	-7.37
β -Band Movement							
<i>Patient 1</i>	-3.20	-3.16	-4.32	-5.65	-0.13	-2.85	-1.27
<i>Patient 2</i>	-2.78	-3.20	-6.71	-9.94	-1.02	-7.02	-7.74
<i>Patient 3</i>	-9.29	-8.76	-9.64	-9.92	-0.99	-6.44	-7.70
<i>Patient 5</i>	-10.45	-11.29	-11.01	-11.40	-10.14	-6.68	-9.15
γ -Band Movement							
<i>Patient 1</i>	-15.64	-15.64	-16.95	-18.56	-7.42	-10.55	-9.74
<i>Patient 2</i>	-13.76	-13.50	-16.07	-18.33	-11.14	-12.52	-16.22
<i>Patient 3</i>	-9.29	-9.17	-9.38	-9.50	-4.92	-6.39	-8.72
<i>Patient 5</i>	-16.59	-16.35	-16.53	-17.58	-13.74	-11.92	-14.43

^a All recordings were done in the off-medication state. Movement refers to alternating hand movements. The optimal contact pairs for stimulation highlighted in bold. Shown are the normalized subband power measurements, expressed in decibels. The optimal contacts for stimulation correspond to the contacts with significantly higher power in both β - and γ -bands in resting and movement conditions in the off-medication state. After normalization, the subband powers were converted to decibel scale. There was no such correlation noted across subjects for other bands within the local field potential spectrum (data not shown)

TABLE 4

Power Ratio of the Optimal Stimulation Contact Pair to the Mean of Other Possible Contact Pairs in β - and γ -Frequency Bands During Off-Medication States

Band	Resting	Movement
β (13–32 Hz)	11.2 dB	8.6 dB
γ (48–220 Hz)	4.5 dB	5.1 dB