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Computer-Guided Deep Brain Stimulation Programming for Parkinson's Disease

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Abstract

Objective—Pilot study to evaluate computer-guided deep brain stimulation (DBS) programming designed to optimize stimulation settings using objective motion sensor-based motor assessments.

Materials and Methods—Seven subjects (5 males; 54–71 years) with Parkinson's disease (PD) and recently implanted DBS systems participated in this pilot study. Within two months of lead implantation, the subject returned to the clinic to undergo computer-guided programming and parameter selection. A motion sensor was placed on the index finger of the more affected hand. Software guided a monopolar survey during which monopolar stimulation on each contact was iteratively increased followed by an automated assessment of tremor and bradykinesia. After completing assessments at each setting, a software algorithm determined stimulation settings designed to minimize symptom severities, side effects, and battery usage.

Results—Optimal DBS settings were chosen based on average severity of motor symptoms measured by the motion sensor. Settings chosen by the software algorithm identified a therapeutic window and improved tremor and bradykinesia by an average of 35.7% compared to baseline in the “off” state ($p < 0.01$).

Conclusions—Motion sensor-based computer-guided DBS programming identified stimulation parameters that significantly improved tremor and bradykinesia with minimal clinician

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involvement. Automated motion sensor-based mapping is worthy of further investigation and may one day serve to extend programming to populations without access to specialized DBS centers.

Keywords

Deep brain stimulation (DBS); programming strategies; Parkinson's disease; motion sensing; objective measures

Introduction

The clinical utility of deep brain stimulation (DBS) for the treatment of movement disorders such as Parkinson's disease (PD) is well established; however, large outcome disparity exists among recipients due to varied standards for postoperative management, particularly concerning DBS programming optimization (1–3). There are few expert DBS programmers compared to the number and geographic locations of individuals with PD, and even expert programmers have only a limited time with a patient to determine an optimal set of DBS parameters (namely, contact, polarity, frequency, pulse width, and amplitude) from thousands of possible combinations. No matter how well the lead is positioned during surgery, suboptimal programming can lessen efficacy, permit unnecessary side effects, and drain the implanted pulse generator (IPG) battery more quickly than necessary. Additionally, surgeries to correct an improperly positioned electrode are rare and the clinical outcome is strongly dependent on the programming (4). As the therapeutic mechanisms of DBS are largely unknown and the optimal stimulation location differs across patients (3), programming must be individualized to each patient's individual response.

Approaches to programming can vary greatly across institutions. Strict iterative procedures such as those suggested by Montgomery (3) and Volkmann et al. (5) are quite time consuming and often not followed. Additionally, programming sessions are typically limited to 1–3 hours since longer sessions result in patient fatigue (6,7). Multiple visits lead to additional travel costs and can be particularly difficult for those traveling from rural areas (8). Many patients have inadequate access to DBS programming resources, which are often at centers far from a patient's home (8). Additionally, there is a shortage of health care professionals highly trained in DBS programming possibly due to reluctance to participate in DBS management due to complexities in electrophysiology or burden of postoperative DBS management (3).

Depending on the institution, DBS programming may be performed by movement disorder neurologists, neurosurgeons, fellows, occupational and physical therapists, nurses, or nurse practitioners (7). During DBS programming sessions, the symptomatic benefits of DBS are typically evaluated by clinicians using clinical rating scales, most commonly the Unified Parkinson's Disease Rating Scale (UPDRS) (9). However, studies have shown that objective assessment using motion sensors provides improved reliability and resolution of motor responses to DBS compared to subjective scales (10,11). Additionally, motion sensor-based assessment during clinician-guided programming has been shown to identify DBS settings that improve symptoms significantly greater than settings chosen by clinicians, though typically at the expense of increased stimulation amplitude (12). The goal of this pilot study

was to evaluate the feasibility of computer-guided DBS programming using automated objective motion sensor-based motor assessments and algorithms for determining an optimal set of DBS programming parameters with minimal clinician involvement. This study represents the first of several necessary steps on the path towards fully automated DBS programming.

Methods

Seven adults (5 males; age 54-71 years; disease duration 6-17 years; Off UPDRS-III scores 39.0 ± 18.9) with PD and recently implanted bilateral subthalamic nucleus (STN) DBS systems (Medtronic Activa, lead 3387) were recruited. Any DBS recipient willing to return to the clinic to undergo the study protocol within three days of their initial post-operative programming was permitted to participate. This work was approved by the institutional review boards of the University of Cincinnati and Great Lakes NeuroTechnologies and completed in accordance with the Declaration of Helsinki. All participants provided signed informed consent prior to participation. Participants were asked to not take any PD medications the night before undergoing the study protocol and did not take any PD medications the day of the study until the protocol was complete. To reduce potential bias, a movement disorders fellow (EUM) not present during the initial post-operative programming served as the programming technician for the protocol. Before the start of data collection, the participant's IPG was turned off for at least 30 minutes to allow the after-effects of stimulation to wear off (13). A small wireless motion sensor (Kinesia™, Great Lakes NeuroTechnologies, Cleveland, OH) containing a triaxial accelerometer and gyroscope was then placed on the index finger of the participant's more affected hand. Prototype software developed in MATLAB (MathWorks Inc., Natick, MA) guided the fellow through the programming processes.

The fellow made changes to the participant's IPG settings as directed by the software (see below) and only intervened if side effects were observed. All IPG adjustments were applied to the DBS lead contralateral to the more affected hand. At each setting, tremor was evaluated with arms at rest whereas bradykinesia was evaluated during repetitive finger tapping. Motion data was transmitted from the Kinesia motion sensor to a computer in real-time as the motor tasks were performed for automated scoring. Clinically validated Kinesia algorithms processed the motion sensor data into 0-4 scores that have previously been shown to be highly correlated with expert clinician UPDRS ratings of resting tremor (14) and modified bradykinesia rating scale (MBRS) ratings of bradykinesia (15).

The mapping procedure (Figure 1) began with an assessment with the IPG turned off to determine a baseline, and then proceeded with an automated monopolar survey – the process of iteratively increasing monopolar stimulation on each contact followed by a motor assessment. The software instructed the fellow to set the IPG to constant-current mode, Contact 0 to be the cathode, and the IPG case to be the anode (monopolar stimulation). Based on recommendations for conducting a monopolar survey (3), pulse width and frequency were initially set to 90 μ s and 130 Hz. The software instructed the fellow to increase the current amplitude from zero in 0.3 mA steps. After the settings were implemented in the IPG, the fellow clicked a button in the software confirming that the IPG

was properly set. The software then instructed the participant to perform the tremor and finger tapping evaluations and calculated severity ratings. The fellow was blinded to the calculated severity ratings. The software continued to direct increases in stimulation amplitude until persistent side effects (e.g., dysarthria, paresthesia, blurred vision, muscle contractions) were noted by the clinician or subject or pulse amplitude approached safety limits. If pulse amplitude approached this maximum, the frequency would be increased in 30 Hz steps up to a maximum recommended by the manufacturer and if symptoms did not improve, pulse width would then be increased in 10 μ s steps to a maximum recommend by the manufacturer before proceeding to the next contact. If persistent side effects were noted, the software automatically stopped increasing stimulation and proceeded to the next contact. All symptom severities and side effects measured at each DBS setting were stored in the software to create an internal symptom-response map for determining an optimal set of programming parameters.

Once the symptom-response map was created, a parameter space search algorithm in the software navigated the map to determine an optimal set of settings (Figure 2). The algorithm identified a therapeutic window in which symptom severity improved but persistent side effects did not occur and then chose IPG settings that minimized the average severity of tremor and bradykinesia (Kinesia score). If symptoms were improved equally at multiple sets of settings, the software selected those with the lowest battery draw (i.e., amplitude, pulse width, and frequency). To minimize regulatory concerns, prior to leaving the clinic, the IPG was programmed to the settings previously specified by a nurse practitioner during routine post-operative programming.

Results

The automated programming algorithm (Figure 1) successfully guided programming for the seven study participants. In practice, the programming algorithm never reached the point where adjustments in frequency or pulse width were necessary. The programming time and DBS settings output by the parameter space search algorithm (Figure 2) for each subject are listed in Table 1.

The computer-guided mapping software created internal symptom response maps for each participant. Figure 3 shows a graphical representation of the symptom response map for Subject 7, the participant with the greatest improvement from baseline. For this participant, tremor and bradykinesia (speed, amplitude, and rhythm) all improved within a very clear therapeutic window.

Kinesia scores for all participants with DBS off and at the settings output by the parameter space search algorithm are listed in Table 1. Settings chosen by the parameter space search algorithm were able to improve tremor and bradykinesia by an average of 35.7% ($p < 0.01$, Wilcoxon signed-rank test).

Discussion

In this pilot study, automated motion sensor-based mapping software successfully guided DBS programming and identified stimulation parameters that significantly improved tremor

and bradykinesia without inducing immediate side effects. The average improvement in tremor and bradykinesia was similar to the improvement in UPDRS motor scores observed following STN DBS in two recent clinical trials (16,17). Clinician involvement in this study was limited to adjusting DBS settings as instructed by the software, identifying side effects, and ensuring safety. This suggests that computer-guided DBS programming using automated motion sensor-based mapping may one day be feasible and is worthy of further investigation. If successful, these techniques could extend expert programming strategies to populations who do not have access to specialized DBS centers. Technologies that could be used by a general practitioner or nurse at a local medical facility without years of experience in DBS programming could increase access to high-quality postoperative DBS management. Tools to simplify the programming process will be even more important as newer DBS systems greatly increase the parameter space with techniques such as current steering, multi-polar stimulation, temporal patterning, and multiple stimulation frequencies (18–23). Computational models that estimate the volume of tissue activated in the brain have been shown to improve patient outcomes and reduce programming time (24–28). However, every patient's clinical response to DBS is different (3,29). Consequently, DBS optimization will necessarily involve more than anatomical localization. Optimization using external motion sensor-based symptom assessment will likely complement techniques based on computational modeling as recent studies have recommended that quantitative measurement devices, such as the Kinesia motion sensor used in this study, should play an important role improving the efficacy of treatment optimization (30). For example, field location could provide initial constraints to avoid stimulating anatomical regions known to induce side effects, but then objective motion sensor-based symptom assessment could provide final parameters that optimize specific motor symptoms.

This pilot study does include several limitations. All study participants had received bilateral implants; however, to reduce programming time, the computer-guided protocol was only applied to the lead contralateral to the more affected hand while the ipsilateral lead remained turned off. Optimizing DBS bilaterally would likely further improve symptomatic benefits. Additionally, the mapping software used in this pilot study was designed to explore only monopolar settings. It is possible that more advanced shaping of the electric field could have further improved symptomatic benefits and is an area worthy of further investigation. Also, only tremor and bradykinesia were examined in this feasibility study. Though these are two of the symptoms most commonly optimized during DBS programming (3), including objective measurements of other symptoms such as rigidity could potentially improve outcomes, particularly for patients whose primary complaint is not tremor or bradykinesia. However, optimization of additional symptoms will likely come at the expense of increased programming time and, consequently, it will important to be judicious in determining which symptoms to optimize. Another limitation is related to the time it takes for changes in DBS settings to take effect. Some symptoms respond very quickly to DBS (e.g., tremor and rigidity), while others take much longer to fully respond (e.g., gait and bradykinesia) (13). The short times between changing the DBS settings and measuring the response in this study may have limited the impact of the settings changes; however, this limitation also applies to traditional programming sessions due to time constraints (3,7), and the Kinesia motion

sensor has been shown to have a greater sensitivity than clinician ratings for detecting small changes in DBS (11).

It is important to note that this pilot study showing motion sensor-based computer-guided programming can significantly improve tremor and bradykinesia represents the first of many steps that will be necessary to achieve automated motion sensor-based DBS programming. To investigate feasibility, we relied on a technician to adjust the IPG to each setting as instructed. Our future plans include integrating programming and assessment algorithms in software that communicates directly with the DBS hardware, which should greatly improve programming efficiency. A study is planned investigate how metrics such as UPDRS scores, battery usage, and programming time compare between the integrated system and experienced DBS programmers. Further studies will then investigate the longer-term benefits of automated motion sensor-based DBS programming.

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Figure 1. Automated programming algorithm

This block diagram illustrates the algorithm used to guide programming. PA, Pulse amplitude; F, frequency; PW, pulse width.

Figure 2. Parameter Space Search Algorithm

The software chose IPG settings that minimized average severity of all symptoms. If symptoms were ameliorated equally at multiple settings, the software selected the set of settings with the lowest stimulation amplitude, pulse width, and frequency.

Figure 3. Symptom Response Map

A) For Subject 7, motor symptoms severity scores based on the motion sensor-based assessments are plotted as a function of contact and stimulation amplitude. The color corresponds to symptom severity (0, normal; 4 most severe). The four columns for each contact correspond to tremor (t), finger tapping speed (s), finger tapping amplitude (a), and finger tapping rhythm (r). Settings with white triangles in the top left indicate the presence of persistent side effects. The black box indicates the optimal settings chosen by the algorithm and the brackets indicate a therapeutic window. **B)** Scores for the four motor symptoms shown in (A) are averaged and converted to percent change from baseline.

Table 1
Symptomatic Improvement Using Computer-Guided Programming

Subject	Programming Time (min)	Contact / Polarity	Amplitude	Kinesia Score Off	Kinesia Score On After Computer-Guided Programming	Percent Improvement
1	70	0-/C+	1.8 mA	0.5	0.4	14.5%
2	57	1-/C+	0.5 mA	0.9	0.5	47.9%
3	93	0-/C+	1.2 mA	1.8	1.5	13.7%
4	105	2-/C+	3.9 mA	2.8	2.0	29.6%
5	90	0-/C+	2.4 mA	0.9	0.7	23.4%
6	93	1-/C+	1.5 mA	1.5	0.9	38.1%
7	120	1-/C+	2.4 mA	2.8	0.5	82.7%
Average						35.7%

The parameter space search algorithm was able to identify settings that significantly improved motor symptoms by an average of 35.7% ($p < 0.01$, Wilcoxon signed-rank test). The pulse width and frequency for each subject were set to 90 μ s and 130Hz, respectively.