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Motion sensor strategies for automated optimization of deep brain stimulation in Parkinson's disease

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ABSTRACT

Background: Deep brain stimulation (DBS) is a well-established treatment for Parkinson's disease (PD). Optimization of DBS settings can be a challenge due to the number of variables that must be considered, including presence of multiple motor signs, side effects, and battery life.
Methods: Nine PD subjects visited the clinic for programming at approximately 1, 2, and 4 months post-surgery. During each session, various stimulation settings were assessed and subjects performed motor tasks while wearing a motion sensor to quantify tremor and bradykinesia. At the end of each session, a clinician determined final stimulation settings using standard practices. Sensor-based ratings of motor symptom severities collected during programming were then used to develop two automated programming algorithms – one to optimize symptom benefit and another to optimize battery life. Therapeutic benefit was compared between the final clinician-determined DBS settings and those calculated by the automated algorithm.
Results: Settings determined using the symptom optimization algorithm would have reduced motor symptoms by an additional 13 percentage points when compared to clinician settings, typically at the expense of increased stimulation amplitude. By adding a battery life constraint, the algorithm would have been able to decrease stimulation amplitude by an average of 50% while maintaining the level of therapeutic benefit observed using clinician settings for a subset of programming sessions.
Conclusions: Objective assessment in DBS programming can identify settings that improve symptoms or obtain similar benefit as clinicians with improvement in battery life. Both options have the potential to improve post-operative patient outcomes.

1. Introduction

The clinical efficacy of deep brain stimulation (DBS) for the treatment of Parkinson's disease (PD) has been well established. Numerous studies have shown significant benefit of DBS delivered to the subthalamic nucleus (STN) and the globus pallidus internus (GPi) in PD patients [1–4]. However, there can be significant challenges to managing patients following implantation largely due to challenges associated with DBS programming optimization and medication management. These can lead to significant disparity in outcomes among DBS patients [5–7]. Challenges faced by DBS programmers in the outpatient setting include their level of experience, subjective rating scales, patient fatigue, and the growing number of DBS parameters to be optimized (contact, polarity, frequency, pulse width, and amplitude) within the time constraints of a programming session. Programmers would benefit significantly from an automated objective measure and tracking of the response of patients motor symptom response to specific settings both during a session and over multiple sessions as well as understanding how the symptom responses may change in the days after programming. Programming DBS patients can be a challenging procedure requiring experience and time. As such, providing programmers with new tools to help them optimize DBS setting selection to control PD symptoms, minimize side effects, and maximize battery life of the implanted pulse generator (IPG) should improve quality of life for patients and the clinical experience for both patients and programmers.

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For the vast majority of centers the symptomatic benefits of DBS are evaluated using clinical rating scales, most commonly the Unified Parkinson's Disease Rating Scale (UPDRS) [8]. Symptoms are rated on a 0–4 integer scale corresponding to normal, slight, mild, moderate, and severe. The motor section of the UPDRS contains 18 items; however, typically only a few symptoms that predominantly affect patients (e.g., tremor, bradykinesia, and rigidity) are rated during DBS programming sessions due to time constraints [7]. This assessment can be highly subjective and dependent on the observer's skill in evaluating these motor symptoms. Objective assessment using motion sensors can enhance resolution and improve reliability, and thus may provide a more accurate assessment of symptomatic responses to DBS [9,10].

Depending on the institution, DBS programming may be performed by movement disorder neurologists, neurosurgeons, fellows, occupational and physical therapists, or nurses [11]. Many patients have inadequate access to experienced DBS programmers due to physicians and patients relocating and implantations occurring at facilities far from patients' homes [12]. Additionally, there is a shortage of health care professionals highly trained in DBS programming. Retrospective studies found that DBS programming sessions take more than twice as long as typical evaluations by movement disorder neurologists [12]. Furthermore, programming sessions must be limited to 1–3 h since longer sessions result in patient fatigue [11,13]. Multiple visits for DBS programming lead to additional travel costs and can be particularly difficult for those traveling from rural areas [12]. Optimizing DBS settings quickly and in a way that minimizes costs and patient travel burden are important factors for DBS follow-up care. The goal of this study was to determine if automated objective assessment of the effect of DBS on PD motor signs would lead to different settings from those chosen by the clinician without this tool and whether DBS settings determined through automated objective assessments could improve the therapeutic benefit and/or extend battery life compared to clinician settings.

2. Methods

This work was approved by the institutional review boards of the University of Minnesota and Great Lakes NeuroTechnologies and completed in accordance with the Declaration of Helsinki. All subjects provided signed informed consent prior to participation. Nine subjects (6 male, 3 female; age 64–76 years) meeting criteria for idiopathic PD with average tremor and/or bradykinesia UPDRS scores greater than or equal to 2 when off medication (6 targeting STN, 3 targeting GPI) were recruited at the University of Minnesota Department of Neurology prior to or just after DBS implant surgery to undergo several programming sessions over a time course of four months. Subjects visited the clinic for programming sessions at approximately 1, 2, and 4 months post-surgery, withholding antiparkinsonian medication overnight prior to each visit. A total of 16 programming sessions were completed due to partial data collection for some subjects. During each session, subjects wore a motion sensor (Kinesia, Great Lakes NeuroTechnologies Inc., Cleveland, OH) containing three orthogonal accelerometers and three orthogonal gyroscopes on the most distal portion of the first finger of the more affected hand.

During each programming session, a clinician performed a monopolar unilateral DBS review according to standard practice [14]. Stimulation settings were assessed at various monopolar settings. Subjects performed four standardized motor tasks from the UPDRS (tremor at rest, postural tremor, finger taps, and rapid alternating movements) using the contralateral limb following each change in stimulation. The clinician recorded UPDRS severity scores for each task using a touchscreen tablet computer, which also saved the kinematic data from the finger-worn motion sensor to disk. To start the monopolar review the subject was first assessed with DBS off. Following the off assessment the voltage was increased along contact 0-/case+ according to standard practice (typically 0.5 V increments with approximately 1–2 min between the stimulation adjustment and symptom measurement) and the subject repeated the four motor tasks. Pulse width and frequency were fixed throughout the session. Once voltage had been increased such that persistent stimulation side effects were present or symptoms were no longer improving based on clinical judgment, the clinician turned stimulation off and repeated the voltage increment process along contacts 1-/case+, 2-/case+, and 3-/case+. Upon completion of the programming session, the clinician programmed the final DBS settings on which the subjects were discharged using standard practices.

To objectively determine the optimal set of programming parameters after the monopolar reviews were completed, tuning maps, or visualizations of motor response to DBS [9], were created using scores based upon previously validated algorithms that utilize kinematic data recorded on the motion sensor to provide objective measures of tremor and bradykinesia that are highly correlated with standard clinical outcome measures [15,16]. The algorithms provide separate severity scores for tremor at rest and postural tremor. Speed, amplitude, and rhythm are scored separately for both the finger tapping and rapid alternating movement tasks, resulting in a total of eight motor symptom severity scores. Contact number was plotted on the x-axis, while stimulation amplitude was plotted on the y-axis. For each stimulation/contact combination, a color-coded symptom severity rating was plotted. Symptom severity is coded from continuously green (non-existent, or a score of 0) to red (most severe, or a score of 4). Two algorithms were developed to determine the stimulation contact and voltage combinations that would have optimized motor symptoms based on the objective symptom severity scores. First, an algorithm was developed to maximize therapeutic benefit by identifying the contact and amplitude at which the therapeutic benefit was maximized. Total Kinesia motor score, or the sum of the eight symptom severity scores, was utilized as a measure of therapeutic benefit and the algorithm searched for the settings with the lowest total Kinesia motor score. Since stimulation amplitude is a significant determinant of battery life, a second, independent algorithm was developed to minimize voltage while maintaining the therapeutic benefit achieved by the clinician settings. That is, this algorithm determined the lowest stimulation amplitude that resulted in a total Kinesia motor score that was less than or equal to that observed on the clinician settings. The relative effectiveness of the optimal settings determined by the clinician and those determined by each algorithm were compared in terms of their therapeutic benefit (i.e., reduction in motor symptom severity) and stimulation amplitude using an analysis of variance with post-hoc multiple comparisons.

3. Results

3.1. Tuning map visualization

Fig. 1 shows tuning maps from a single programming session for all four motor tasks. As various DBS settings were evaluated, this subject had marked improvements in tremor severity, with more subtle changes in bradykinesia. The white box indicates the presence of stimulation-induced side effects, while the blue box indicates the final DBS setting selected by the clinician (i.e., Contact 2, 2.0 V).

3.2. Automated optimization of therapeutic benefit

DBS using settings determined by the clinician had a therapeutic effect (i.e., decreased the total Kinesia motor score) when compared to OFF in 15 out of 16 programming sessions (Fig. 2). The algorithm tuned for minimizing symptom severity identified settings which would have increased therapeutic benefit relative to the clinician settings in 14 out of 16 programming sessions. Both tremor ($n = 10$) and bradykinesia ($n = 13$) would have improved across the large majority of these sessions. On average, the clinician settings yielded a 31.7% decrease in total motor score from OFF ($p < 0.01$), while the algorithm settings would have reduced symptoms by 45.1% from OFF ($p < 0.01$). The additional 13 percentage point reduction achieved by the algorithm settings ($p < 0.05$), however, most often came at the expense of an increase in stimulation amplitude with an average increase of 64.1% compared to clinician settings ($p > 0.01$, Fig 2B).

3.3. Automated optimization of battery life

When the algorithm for optimizing battery life was applied, the therapeutic benefit could have been maintained or improved at lower stimulation voltages for 6 out of 16 programming sessions (Fig. 3). While the programming strategy was not a significant