Published in final edited form as:

Parkinsonism Relat Disord. 2015 April ; 21(4): 378–382. doi:10.1016/j.parkreldis.2015.01.018.

Motion Sensor Strategies for Automated Optimization of Deep Brain Stimulation in Parkinson's disease

Christopher L. Pulliam¹, Dustin A. Heldman¹, Tseganesh H. Orcutt², Thomas O. Mera¹, Joseph P. Giuffrida¹, and Jerrold L. Vitek²

¹Great Lakes NeuroTechnologies, Cleveland, Ohio, USA

²University of Minnesota, Minneapolis, Minnesota, USA

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.

© 2015 Published by Elsevier Ltd.

Corresponding Author: Christopher L Pulliam, PhD, Phone: (216) 361-5410, cpulliam@glneurotech.com.

The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH/NIA.

Full Financial Disclosures for the Previous 12 Months

CL Pulliam has received compensation from Great Lakes NeuroTechnologies for employment.

DA Heldman has received compensation from Great Lakes NeuroTechnologies for employment.

TH Orcutt has nothing to disclose.

TO Mera has received compensation from Great Lakes NeuroTechnologies for employment.

JP Giuffrida has received compensation from Great Lakes NeuroTechnologies for employment.

JL Vitek is a consultant for and has received honoraria from St. Jude Medical, Boston Scientific, Eli Lilly, Medtronic, NeuroNexus, and Great Lakes NeuroTechnologies. He is also on the speaker bureau for Medtronic and has research support from NIH/NINDS.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

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.

Keywords

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 patients¹⁻⁴. 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 patients⁵⁻⁷. 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.

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 constraints⁷. 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 nurses¹¹. Many patients have inadequate access to experienced DBS programmers due to physicians and patients relocating and implantations occurring at facilities far from patients' homes¹². 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 neurologists¹². Furthermore,

programming sessions must be limited to 1–3 hours 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 areas¹². 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.

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 practice¹⁴. 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 minutes 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 DBS⁹, 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.

Results

Tuning Map Visualization

Figure 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).

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 (Figure 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).

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 (Figure 3). While the programming strategy was not a significant factor overall ($p > 0.1$), for this 6 session subset the stimulation amplitude could have been decreased by an average of 50% relative to clinician settings while providing an improvement in total motor score of 31.5% from OFF versus a 24.8% decrease using clinician settings. Figure 4 summarizes statistical comparisons of the performance of the automated algorithms relative to the settings determined by the clinician.

Discussion

During DBS programming sessions, clinicians attempt to determine a set of programming parameters that balances the trade-off between minimizing symptom severities and side effects and maximizing battery life¹⁷. Given the number of variables that must be considered (e.g., multiple motor symptoms, side effects, stimulation parameters), this process can be a significant challenge, require multiple programming sessions, and may result in suboptimal therapeutic benefit. In the example shown in Figure 1, comparable therapeutic benefit could likely have been achieved while lowering the stimulation amplitude by 0.5 V. The emergence of rechargeable DBS platforms may relax the practical constraints imposed by battery life by reducing the frequency of replacement surgeries¹⁸ refocusing programmers' efforts towards maximizing motor benefit. An automated objective method that is able to maximize motor benefit while reducing programming time would be an important contribution to the field. The current method was able to accomplish this, as demonstrated by the fact that an additional reduction of 13 percentage points in symptom severity could have been accomplished using DBS settings selected by the algorithm when compared to those selected by the clinician (Figures 2 and 4). The enhanced benefit would have required larger stimulation amplitudes to achieve the greatest improvement in both tremor and bradykinesia. This is consistent with conceptual models of PD, since larger stimulation amplitudes would be required to modulate activity in anatomically segregated motor circuits which are implicated in the distinct clinical symptoms^{19,20}. When battery life is an important consideration, quantitative tools may also be able to identify settings that lower stimulation amplitude while providing additional therapeutic benefit relative to clinician settings for a significant subset of patients (Figure 3 and 4). It is worth noting that this study was performed at a highly experienced and well trained DBS programming clinic. One might expect the difference in motor outcomes between clinician and algorithm derived settings to be larger if we were to consider centers without this expertise. Thus, an automated motor assessment system may be able to improve access and outcomes to a degree even greater than that reported here.

Primary limitations of this study include reliance on upper extremity tremor and bradykinesia for quantification of therapeutic benefit, the small number of subjects, and lack

of long-term follow-up. The automated algorithms optimized stimulation settings considering only tremor and bradykinesia in the arm and hands. Other manifestations of the disease, such as rigidity and lower extremity motor symptoms, likely impact the selection of stimulation parameters and may partially explain differences between the clinician-determined and algorithm-determined stimulation settings. In future studies, these additional symptoms can be captured and integrated as additional inputs to the algorithm. The small sample size prevents the findings from being generalized to the broader patient population based on this study alone. In this study, programming outcomes were evaluated in a retrospective manner on data collected during standard DBS programming sessions. A prospective longitudinal study will be necessary to determine if the therapeutic benefit achieved using the parameters determined by automated algorithms provide a stable effect over time. An additional limitation of this study is that the protocol relied upon a monopolar review of the stimulation parameter space with fixed pulse width and frequency. While this is consistent with standard many programming practices, advanced algorithms have the potential to improve the time efficiency of these sessions by leveraging different search techniques and thus reduce the cost of post-operative DBS-management. This is an increasingly important factor as the parameter space expands to include new features such as temporal patterning, multi-polar stimulation, and current steering^{21–23}. Finally, an objective for future studies will be to combine therapeutic benefit and battery life optimization into a single algorithm that can properly weight both constraints at the same time. Still, the results presented herein support the value of automated objective assessment and DBS parameter selection algorithms in DBS programming, while additional sensing modalities could be integrated in the future to capture a more complete picture of the parkinsonian state or focus on selective motor signs based on individual patient preference.

Acknowledgments

This work was supported by grant number R44AG033520 from the National Institute on Aging.

References

1. Katayama Y, Kasai M, Oshima H, Fukaya C, Yamamoto T, Ogawa K, et al. Subthalamic nucleus stimulation for Parkinson disease: benefits observed in levodopa-intolerant patients. *J Neurosurg*. 2001 Aug; 95(2):213–21. Internet. cited 2014 Apr 24. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/11780890>. [PubMed: 11780890]
2. Deuschl G, Schade-Brittinger C, Krack P, Volkmann J, Schäfer H, Bötzel K, et al. A randomized trial of deep-brain stimulation for Parkinson's disease. *N Engl J Med*. 2006 Aug 31; 355(9):896–908. Internet. cited 2014 Mar 25. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/16943402>. [PubMed: 16943402]
3. Odekerken VJJ, van Laar T, Staal MJ, Mosch A, Hoffmann CFE, Nijssen PCG, et al. Subthalamic nucleus versus globus pallidus bilateral deep brain stimulation for advanced Parkinson's disease (NSTAPS study): a randomised controlled trial. *Lancet Neurol*. 2013 Jan; 12(1):37–44. Internet. cited 2014 May 2. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/23168021>. [PubMed: 23168021]
4. Williams NR, Foote KD, Okun MS. STN vs. GPi Deep Brain Stimulation: Translating the Rematch into Clinical Practice. *Mov Disord Clin Pract* (Hoboken, NJ). 2014 Apr 1; 1(1):24–35. Internet. cited 2014 May 7 Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24779023>.
5. Kluger BM, Foote KD, Jacobson CE, Okun MS. Lessons learned from a large single center cohort of patients referred for DBS management. *Parkinsonism Relat Disord*. 2011 May; 17(4):236–9.

Internet. cited 2014 Apr 24. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/20627660>. [PubMed: 20627660]

6. Moro E, Poon Y-YW, Lozano AM, Saint-Cyr JA, Lang AE. Subthalamic nucleus stimulation: improvements in outcome with reprogramming. *Arch Neurol*. 2006 Sep; 63(9):1266–72. Internet. cited 2014 Apr 24. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/16831958>. [PubMed: 16831958]
7. Montgomery, EB. *Deep Brain Stimulation Programming: Principles and Practice*. 1. Oxford University Press; USA: 2010.
8. Goetz CG, Tilley BC, Shaftman SR, Stebbins GT, Fahn S, Martinez-Martin P, et al. Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): scale presentation and clinimetric testing results. *Mov Disord*. 2008 Nov 15; 23(15): 2129–70. Internet. cited 2014 Mar 20. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/19025984>. [PubMed: 19025984]
9. Mera, T.; Vitek, JL.; Alberts, JL.; Giuffrida, JP. *J Neurosci Methods*. Vol. 198. Elsevier B.V; 2011 Jun 15. Kinematic optimization of deep brain stimulation across multiple motor symptoms in Parkinson's disease; p. 280–6. Internet. cited 2013 Nov 10. Available from: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3122330&tool=pmcentrez&rendertype=abstract>
10. Heldman DA, Espay AJ, LeWitt PA, Giuffrida JP. Clinician versus machine: Reliability and responsiveness of motor endpoints in Parkinson's disease. *Parkinsonism Relat Disord*. 2014 Mar 5; 20(6):590–5. Internet. cited 2014 Mar 24. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24661464>. [PubMed: 24661464]
11. Hunka K, Suchowersky O, Wood S, Derwent L, Kiss ZHT. Nursing time to program and assess deep brain stimulators in movement disorder patients. *J Neurosci Nurs*. 2005 Aug; 37(4):204–10. Internet. cited 2014 Apr 24. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/16206546>. [PubMed: 16206546]
12. Okun MS, Tagliati M, Pourfar M, Fernandez HH, Rodriguez RL, Alterman RL, et al. Management of referred deep brain stimulation failures: a retrospective analysis from 2 movement disorders centers. *Arch Neurol*. 2005; 62(8):1250–5. [PubMed: 15956104]
13. Kumar R. Methods for programming and patient management with deep brain stimulation of the globus pallidus for the treatment of advanced Parkinson's disease and dystonia. *Mov Disord*. 2002; 17(Suppl 3):S198–207. [PubMed: 11948777]
14. Montgomery, EB, JrMD. *Deep Brain Stimulation Programming: Principles and Practice* (Google eBook) [Internet]. Oxford University Press; 2010. cited 2014 Apr 24. Available from: <http://books.google.com/books?id=zBYLTrEsSIC&pgis=1>
15. Giuffrida JP, Riley DE, Maddux BN, Heldman DA. Clinically deployable Kinesia technology for automated tremor assessment. *Mov Disord*. 2009 Apr 15; 24(5):723–30. Internet. cited 2013 Nov 13. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/19133661>. [PubMed: 19133661]
16. Heldman DA, Giuffrida JP, Chen R, Payne M, Mazzella F, Duker AP, et al. The modified bradykinesia rating scale for Parkinson's disease: reliability and comparison with kinematic measures. *Mov Disord*. 2011 Aug 15; 26(10):1859–63. Internet. cited 2013 Nov 13. Available from: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3324112&tool=pmcentrez&rendertype=abstract>. [PubMed: 21538531]
17. Volkmann J, Moro E, Pahwa R. Basic algorithms for the programming of deep brain stimulation in Parkinson's disease. *Mov Disord*. 2006; 21(S14):S284–9. Internet. cited 2013 Jul 22. Available from: <http://onlinelibrary.wiley.com/doi/10.1002/mds.20961/abstract>. [PubMed: 16810675]
18. Waln, O.; Jimenez-Shahed, J. Rechargeable Deep Brain Stimulation Implantable Pulse Generators in Movement Disorders: Patient Satisfaction and Conversion Parameters. *Neuromodulation*. 2013 Sep 24. Internet. cited 2014 Apr 4; Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24112630>
19. Helmich RC, Hallett M, Deuschl G, Toni I, Bloem BR. Cerebral causes and consequences of parkinsonian resting tremor: a tale of two circuits? *Brain*. 2012 Nov 1; 135(Pt 11):3206–26. Internet. cited 2014 Jun 10. Available from: <http://brain.oxfordjournals.org/content/135/11/3206>. [PubMed: 22382359]
20. Helmich RC, Janssen MJR, Oyen WJG, Bloem BR, Toni I. Pallidal dysfunction drives a cerebellothalamic circuit into Parkinson tremor. *Ann Neurol*. 2011 Feb; 69(2):269–81. Internet.

cited 2014 Jun 17. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/21387372>. [PubMed: 21387372]

21. Hess CW, Vaillancourt DE, Okun MS. The temporal pattern of stimulation may be important to the mechanism of deep brain stimulation. *Exp Neurol*. 2013 Sep;247:296–302. Internet. cited 2014 Apr 24. Available from: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3742615&tool=pmcentrez&rendertype=abstract>. [PubMed: 23399890]
22. Hariz M. Deep brain stimulation: new techniques. *Parkinsonism Relat Disord*. 2014 Jan; 20(Suppl 1):S192–6. Internet. cited 2014 Apr 23. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24262179>. [PubMed: 24262179]
23. Barbe MT, Maarouf M, Alesch F, Timmermann L. Multiple source current steering - A novel deep brain stimulation concept for customized programming in a Parkinson's disease patient. *Parkinsonism Relat Disord*. 2014 Apr; 20(4):471–3. Internet. cited 2014 Apr 24. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24041939>. [PubMed: 24041939]

Highlights

- We use motion sensors to quantify DBS response during outpatient programming
- Post-hoc algorithms identify optimal settings for symptom benefit and battery life
- Automated search can identify settings that improve symptoms relative to clinician
- Automated search can obtain similar benefit as clinician with improved battery life

Figure 1.

Tuning maps based on Kinesia ratings of rest tremor, postural tremor, and bradykinesia for a single subject. The blue box indicates the final DBS settings the clinician selected. The white box indicates the presence of stimulation-induced side effects

Figure 2.

Automated selection of stimulation parameters to maximize therapeutic benefit. (A) Total motor score with stimulation off ("OFF"), on the final DBS settings selected by the clinician ("ON-Clinician"), and on settings selected by the search algorithm ("ON-Algorithm").

Figure 3. Automated selection of stimulation parameters to minimize stimulation voltage while maintaining therapeutic benefit achieved by clinician settings.

Figure 4. Summary of automated algorithms for selecting DBS settings. P-values are provided for paired t-test comparisons.