Published in final edited form as:

Neurologist. 2011 September ; 17(5): 263–268. doi:10.1097/NRL.0b013e31822d1069.

DBS Candidates That Fall Short on a Levodopa Challenge Test:

Alternative and Important Indications

Takashi Morishita, MD, PhD^{*}, Maryam Rahman, MD, MS^{*}, Kelly D. Foote, MD^{*}, Kyle M. Fargen, MD, MPH^{*}, Charles E. Jacobson IV, BS[†], Hubert H. Fernandez, MD[‡], Ramon L. Rodriguez, MD[†], Irene A. Malaty, MD[†], Dawn Bowers, PhD[§], Christopher J. Hass, PhD^{||}, Yoichi Katayama, MD, PhD^{¶, #}, Takamitsu Yamamoto, MD, PhD^{¶, #}, and Michael S. Okun, MD^{*, †}

^{*}Department of Neurosurgery, College of Medicine/Shands Hospital, McKnight Brain Institute, Gainesville, FL

[†]Department of Neurology, McKnight Brain Institute, Gainesville, FL

[§]Department of Clinical and Health Psychology, College of Medicine, McKnight Brain Institute, Gainesville, FL

^{||}Department of Applied Physiology and Kinesiology, University of Florida, Movement Disorders Center, Gainesville, FL

[¶]Department of Neurological Surgery, Nihon University School of Medicine, Tokyo, Japan

[#]Department of Advanced Medical Science, Division of Applied System Neuroscience, Nihon University School of Medicine, Tokyo, Japan

[‡]Center for Neurological Restoration, Cleveland Clinic, Cleveland, OH

Abstract

Introduction—Candidacy for deep brain stimulation (DBS) in Parkinson disease (PD) is typically assessed by the preoperative motor response to levodopa along with an interdisciplinary evaluation. However, recent cases treated at our institution have achieved good outcomes with DBS despite a sub-30% improvement in motor scores. The aim of this study was to examine the outcomes of DBS in a subset of patients who failed to reach the 30% motor improvement threshold.

Methods—A review of all DBS patients treated at the University of Florida Movement Disorders Center between 2002 and 2009 was performed utilizing a DBS database. All patients with sub-30% improvement in Unified Parkinson Disease Rating Scale Part III after dopaminergic medication administration were included.

Copyright © 2011 by Lippincott Williams & Wilkins

Reprints: Takashi Morishita, MD, PhD, Department of Neurosurgery, McKnight Brain Institute, 100 S Newell Dr, Room L2-100, Gainesville, FL 32610. takashi.morishita@neurosurgery.ufl.edu.

T.M., M.R., K.M.F., C.E.J., H.H.F., R.L.R., I.A.M., D.B., C.J.H., Y.K., T.Y. declare no conflict of interest. K.D.F. receives or has received research grants from the Michael J. Fox Foundation, the National Parkinson Foundation, the Parkinson Alliance and the National Institutes of Health. K.D.F. is a speaker for the Medtronic Focus on DBS course with honoraria donated to the University of Florida Foundation. K.D.F. also administers the Medtronic DBS fellowship. Dr Foote is a founder of the COMPRESS software used for DBS screening. M.S.O. receives or has received research grants from the Michael J. Fox Foundation, the National Parkinson Foundation, the Parkinson Alliance and the National Institutes of Health. M.S.O. is a paid consultant for the National Parkinson Foundation serving as the medical director and as the web-based ask the doctor patient consultant. M.S.O. is a speaker for the Medtronic Focus on DBS course with honoraria donated to the University of Florida Foundation. M.S.O. also administers the Medtronic DBS fellowship. M.S.O. is a founder of the COMPRESS software used for DBS screening.

Results—Nine patients were identified; DBS was performed for severe dyskinesia ($n = 5$), “on/off motor” fluctuations ($n = 1$) and medication-refractory tremor ($n = 3$). The target symptoms were improved in all patients. Postoperatively, scores on the Unified Parkinson Disease Rating Scale Part II and III and subscores on Parkinson disease questionnaire-39 improved ($P < 0.05$).

Conclusions—Although motor response to levodopa remains the primary selection criteria for DBS candidacy in Parkinson disease, patients who do not meet the 30% threshold and have disabling symptoms may still benefit from DBS. Select patients with severe dyskinesia, “on/off” motor fluctuations, and/or medication-refractory tremor may experience significant benefits from DBS and should be considered on a case by case basis through an interdisciplinary team evaluation.

Keywords

deep brain stimulation; Parkinson disease; levodopa challenge test; dyskinesia; on-off motor fluctuations; tremor; quality of life

Deep brain stimulation (DBS) is commonly employed for the treatment of medication-refractory symptoms in Parkinson disease (PD). Recent studies have revealed the efficacy of DBS for both subthalamic nucleus (STN) and globus pallidus interna (GPi) targets in well-selected patients.^{1–7} Institutions with expertise in DBS commonly employ neurocognitive and psychiatric testing along with a levodopa/ dopaminergic challenge test to screen potential candidates. In the latter, potential DBS candidates report to their neurologist’s office 12 hours off their dopaminergic medications, and are then evaluated with the Unified Parkinson Disease Rating Scale (UPDRS) in the “off” state. Afterwards, they are challenged with a supratherapeutic dose of dopaminergic medication and reevaluated at their best “on” state. Optimal surgical candidates typically demonstrate at least a 30% improvement in the motor portion (Part III) of the UPDRS,^{4,8–12} as levodopa response has been considered to be one of the strongest indicators of a positive outcome in DBS for PD.^{8,9,12} There may, however, be patients who do not achieve a 30% improvement with levodopa or dopaminergic medications but have alternative and potentially responsive indications for DBS (dyskinesia, “on/off” motor fluctuation, and medication-refractory tremor).¹² The aim of this study was to examine alternative indications and the surgical outcomes of a tailored unilateral DBS approach for a cohort of PD patients with a sub-30% improvement on a levodopa/dopaminergic challenge test.

METHODS

Study Design

A database query of the University of Florida Movement Disorders Center DBS database (approved by the Institutional Review Board) containing all patients treated by DBS at our institution from July 2002 to March 2009, was performed. Inclusion criteria included all patients treated with DBS for a primary diagnosis of PD who demonstrated a UPDRS Part III sub-30% improvement on levodopa/dopaminergic challenge testing. After patients were identified, retrospective chart reviews were performed and history, performance scores, operative information, and other information were obtained for each patient.

A levodopa/dopaminergic challenge test was performed on all potential DBS candidates, and definitive diagnosis of PD was confirmed by a movement disorders fellowship trained specialist at our institution. Patients reported to the clinic after being “off” levodopa/ dopaminergic therapy for a minimum of 12 hours. A supratherapeutic dose of their usual PD medications (1.5 times the dose) was then administered. The UPDRS Part III was collected in the “off” and then “on” medication states and the percentage improvement noted. Patients

with dose failures, 45 minutes after ingesting dopaminergics received an additional dose of carbidopa/levodopa 25/100 mg, in an attempt to document the best “on” response. Patients with a sub-30% improvement, but with disabling dyskinesia, “on/off” motor fluctuations, or medication-refractory tremor resulting in subjective impairment in quality of life (QOL) were further considered for DBS by our interdisciplinary DBS team (neurologist, neurosurgeon, neuropsychologist, psychiatrist). In addition, previous history of successful lesional surgery (eg, pallidotomy) was also considered as an indication for DBS despite a sub-30% response. Excluded were patients with a sub-30% improvement on a levodopa/dopaminergic challenge test without disabling tremor, dyskinesia, and/or on-off fluctuations. We did not specifically track those excluded.

Performance Testing

UPDRS Part III (motor) scores were obtained preoperatively in both “on” and “off” dopaminergic states and then repeated at 4 months, 1 year, and last follow-up in an “off medication/on DBS” state. In addition, the UPDRS Part II (activities of daily living), Part IV (motor fluctuations and dyskinesia), and dyskinesia rating scale contralateral to the side of DBS implantation were documented (range 0 to 5 with 5 being the worst).¹³ Parkinson disease questionnaire (PDQ-39) QOL scores were also assessed at baseline and at 6 months and last follow-up. The PDQ-39 is a validated measure of QOL in PD¹⁴ and the scale has 8 subscores (mobility, activities of daily living, emotional, stigma, social, cognition, community, and discomfort). Scores range from 0 to 100 with 100 representing the worst possible function. The Patient Global Impression Scale (PGIS) and the Clinician Global Impression Scale (CGIS) scores (1—very much improved; 2—much improved; 3—minimally improved; 4—no change; 5—minimally worse; 6—much worse; 7—very much worse) were also obtained 6 months after DBS. Annual cognitive evaluations [ie, Mini Mental Status Examination (MMSE) and dementia rating scale (DRS)] were also performed.

Surgical Procedure

A high-resolution, volumetric brain magnetic resonance imaging (MRI) was obtained 1 day before surgery followed by a stereotactic head computed tomography (CT) the morning of surgery. CT and MRI image fusion was then performed to map out the neuronal brain structures in coordinate space by software developed at our institution. The brain target point was selected utilizing a combination of direct and indirect targeting. For this series although STN was a target of choice in patients without cognitive issues, GPi was selected when patients had severe “on/off” fluctuations/dyskinesia and testing revealed mild cognitive impairment (dementia rating scale score <130). The anterior commissure, the posterior commissure, and a midline plane were identified to anchor the coordinate system. Multiple-pass microelectrode mapping was employed followed by intraoperative test stimulation to verify lead placement. Moreover, a postoperative CT scan was performed and fused to the MRI to assess lead location. An implantable pulse generator (IPG) was placed approximately 4 weeks after the procedure and DBS programming/medication adjustment was performed by protocol once a month for the first 6 months and then every 3 to 6 months.

Statistical Analysis

Comparisons were made between preoperative and postoperative UPDRS Part III scores in “off” medication states, levodopa equivalent dose, UPDRS Part II, and PDQ-39 values. The Wilcoxon signed rank tests were calculated to assess statistical significance. Statistical analyses were performed utilizing PASW statistics 16.0 (SPSS, Chicago, IL). For patients in the dyskinesia subgroup, the UPDRS Part IV item 32 (duration of dyskinesia) and the preoperative and postoperative dyskinesia rating scale scores¹³ were included for comparison. For the medication-refractory tremor subgroup, the UPDRS Part II item 16

(tremor) and Part III item 20 (resting tremor) were compared preoperatively and postoperatively.

RESULTS

Clinical Outcomes

The database search revealed 153 PD DBS patients of which 9 (8 men and 1 woman) with average age of 64.2 met inclusion criteria and had a sub-30% improvement on levodopa/dopaminergic challenge testing. These patients were followed up for at least for 6 months and for an average of 2.5 years. Staged bilateral GPi DBS was performed on the 2 patients with severe dyskinesia who also had mild cognitive impairment (DRS < 130). STN DBS was performed on the remaining patients for dyskinesia (n = 3), “on/off” motor fluctuations (n = 1) and medication-refractory tremor (n = 3). Of 9 patients, 7 patients had staged bilateral DBS. In addition, 2 patients were revealed to have a previous history of pallidotomy, and these patients had unilateral DBS (contralateral to the pallidotomy). The patient characteristics are summarized in Table 1.

DBS surgery led to a significant improvement in the UPDRS Part III scores at 4 months and 1 year (16% and 12.5% changes, respectively; $P < 0.05$) (Table 2). When followed to last clinical follow-up, statistical significance for change in motor overall motor score was lost, however, target symptoms remained improved. Furthermore, significant improvements ($P < 0.05$) were observed in the UPDRS Part II and PDQ-39 subscores (ie, activities of daily living, emotional, and stigma) with medium to large effect sizes (Table 3). Interestingly, the cognition subscore of the PDQ-39 improved in patients who underwent GPi DBS (cases 1 and 2), and no significant deteriorations were observed in MMSE and DRS scores 1 year after the first surgery. Overall improvements were demonstrated by the PGIS and CGIS scores; 5 patients had “very much improved” (score of 1) on both scales, whereas the other 4 had “much improved” (score of 2) on both scales (Table 4). Conversely, the statistical analyses failed to detect a significant change in preoperative and postoperative levodopa equivalent dose dosages at 1 year and the last follow-up (P -value > 0.05).

In the dyskinesia subgroup, duration of dyskinesia in waking time decreased in all 5 patients, as did scores on the dyskinesia rating scale (Table 4). The motor fluctuation patient (case 6) preoperatively complained of “off” periods during 50% of a day, however, these periods had completely resolved at 6 months after STN DBS. In the medication-refractory tremor patients, improvements were seen in both items 16 and 20 (Table 4).

Complications

Transient mental status change on postoperative day #1 was noted in 2 patients who underwent STN DBS (cases 5 and 7). A transient IPG seroma was encountered in a single patient (case 7). An intracerebral hemorrhage around the STN (12 mm³) resulted in a transient hemiparesis in 1 patient (case 9) that had resolved when the patient returned for the IPG implantation 4 weeks later.

DISCUSSION

The levodopa/dopaminergic challenge test is frequently utilized as the primary first-line screening method to select appropriate DBS candidates with PD.^{8–10,12} The test has proven particularly useful for excluding parkinsonian syndromes (syndromes deemed not to meet the criteria for idiopathic PD, but may have prominent parkinsonian features), for defining levodopa unresponsive symptoms (eg, gait, balance, speech), and for predicting surgical outcomes.¹⁵ The ability to exclude parkinsonian syndromes has been a particularly important use of the test and a recent study revealed that 5 of 41 referred patients with DBS

failure had misdiagnosis due to lack of appropriate challenge testing.¹⁵ Most authorities have promoted that >30% improvement after dopaminergic administration (UPDRS-III testing) may identify the optimal candidates for DBS and those who should move on to a complete interdisciplinary evaluation. Our data however, revealed that at least 3 scenarios exist where alternative indications for DBS might be useful: severe dyskinesia, “on/off” motor fluctuations, and medication-refractory tremor.^{3,5,6,16} Anecdotally, many expert centers have observed similar positive results to those reported here (author personal communications with National Parkinson Foundation and other Centers of Excellence for DBS therapy).

There are several important issues that emerge upon closer inspection of the levodopa/dopaminergic challenge test when utilized for screening potential DBS candidates. First, some patients may not tolerate clinically effective doses of levodopa due to complications such as nausea, sedation, and/or dyskinesia, and thus it may be difficult to glean clean data from a levodopa/dopaminergic challenge test.^{17,18} In some cases, severe dyskinesias can impair the performance on select items of the UPDRS such as finger tapping, hand movement, and rapid alternating movements, giving the impression of minimal improvements in these items as highlighted in case 7. In these patients, select examples of successful improvement of symptoms as a result of DBS have been previously reported.^{17,18} In addition, delayed gastric emptying may profoundly impact the measured response of a levodopa/dopaminergic challenge test,¹⁹ and some authors advocate apomorphine as a reasonable alternative in this scenario.¹¹ Further, another scenario that must be considered is a history of successful lesioning therapy (pallidotomy, thalamotomy, subthalamotomy) that may reduce the measured responsiveness of levodopa and other dopaminergics and ultimately reset the UPDRS off score to a lower (better) baseline. This particular scenario is highlighted in 2 of our reported cases (5 and 9), where previous pallidotomy may have contributed to the sub-30% responsiveness to levodopa/ dopaminergic challenge testing. Moreover, clinicians should be aware that a UPDRS “on/off” test does not reveal the extent or severity of “on/off” motor fluctuations which ultimately require careful history taking and/or formal documentation by a diary.^{20–22} Finally, the threshold values for the levodopa/dopaminergic challenge test have not been standardized for DBS; values vary in the literature from 25% to 50% in published surgical series.^{4,8,9,11,23,24} Clinicians should be aware that higher threshold levels on levodopa/dopaminergic challenge testing may lead to excluding potentially reasonable DBS candidates, especially those with dyskinesias, fluctuations, and tremor.

In our series, significant improvements were evidenced in the UPDRS Part II (activity of daily living) and in the PDQ-39 QOL subscores despite only subtle improvement in total motor scores, highlighting the importance of not overvaluing UPDRS motor scores. These findings further support the argument that DBS teams should remain vigilant for potential candidates that may not meet the 30% motoric improvement criteria. A recent meta-analysis of STN DBS outcomes revealed 52% improvement in the UPDRS Part III motor section after surgery.⁴ The UPDRS motor scores improved by only 16% and 12.5% at 4-month follow-up, respectively, in our series. These improvements may on the surface seem disappointing; however, these improvements failed to measure changes important for an individual patient, as the target symptoms were successfully addressed in each case (Table 4) and the improvement contributed to enhanced activity of daily living and QOL scores. The low motor improvement seen in several of our cases is in direct support of the notion that DBS has its effects on levodopa responsive motor symptoms, but that UPDRS III may not tell the whole story. PGIS and CGIS scores also support the observed improvements in our cohort.

Dyskinesia and “on/off” motor fluctuations represent most of the motor complications encountered with long-term levodopa therapy; however, these issues are potentially amenable to DBS therapy. Levodopa dosage and DBS unresponsive PD features (eg, gait, balance, speech) have been demonstrated in recent studies to progress over time, whereas improvements in dyskinesia and “on/off” motor fluctuations seem to persist up to 5 years after STN DBS.^{5,25} Further, a meta-analysis of available studies in the literature revealed 69.1% and 68.2% reduction in dyskinesia and daily off periods after DBS.⁴ Thus, those patients with a chief complaint of severe dyskinesia or “on/off” motor fluctuations may have the potential to experience symptomatic improvement from DBS and this improvement may translate into improved activities of daily living, QOL, and global outcome scores. This improvement may be evident even when significant improvement in UPDRS motor scores is absent.

The issue of preexisting cognitive dysfunction has led many groups to shy away from DBS implantation primarily because of fear of worsening deficits.²⁶ Typically DRS scores of 130 or above are considered to be the minimal cut-off for DBS surgery.⁸ Some groups have also alternatively used a MMSE score >24 as a selection criteria to exclude frank dementia.⁶ Interestingly, in our series, 2 patients had temporary mental status change after STN DBS, whereas the 2 patients with preexisting mild cognitive impairment seemed to tolerate the GPi target without worsening of the cognitive status. Although clearly more data are needed, recent studies have revealed the possibility that the incidence of cognitive adverse events may be lower with GPi DBS when compared with STN DBS.^{1,7,27,28} GPi DBS has been shown to be a powerful direct suppressor of dyskinesia and also is effective against “on/off” motor fluctuations.^{1,3,27} In this small series, we utilized the GPi option for preexisting cognitive dysfunction. It should be noted, however, that we did not attempt STN DBS, and thus we cannot comment on the superiority of one approach over another.

DBS has been recommended for advanced PD patients by the Core Assessment Program for Surgical Interventional Therapies in Parkinson’s Disease. This committee also recommended selecting patients with at least a 5-year disease duration.⁸ However, in our cohort 2 patients had disabling tremor despite relatively short disease durations (cases 7 and 8) and both benefitted from STN DBS. STN DBS may thus be a reasonable treatment option for medication-refractory tremor in earlier stage PD. Although ventral intermediate thalamic nucleus (Vim) is also a viable target for medically-refractory tremor, Vim DBS does not as effectively address other cardinal symptoms of PD or address the development of lower extremity tremor.²⁹ Fraix et al²⁹ reported favorable results when utilizing bilateral or contralateral STN DBS after thalamic surgery for tremor dominant PD patients. The relative roles of STN, GPi, and thalamic DBS in medication-refractory tremor have not been carefully analyzed in randomized controlled trials and currently most groups are choosing the STN as the target unless cognitive dysfunction is present. Further study is needed in this area.

The data from our cohort demonstrates benefit in well-selected PD patients with a preoperative sub-30% UPDRS motor change if the diagnosis of PD is a reasonable certainty. We would and therefore do argue that DBS indications should be tailored to the individual patient, and that the indications for surgery should be given strong weight in an interdisciplinary evaluation for selection of appropriate patients. Patients with severe dyskinesia, “on/off” fluctuations, and/or medication-refractory tremor may thus be reasonable DBS candidates even if they fail a classic levodopa/dopaminergic challenge test. Although this case series suffers from biases introduced by its retrospective and unblinded nature and the limited number of observations, we feel the data tell an important story. Further studies should be pursued to confirm these findings. In the meantime, we would encourage groups to employ an interdisciplinary screening process for DBS indications that

tailors decisions to the individual patient, even if the results of a levodopa/dopaminergic challenge test fall short of widely accepted criteria.

Acknowledgments

This study was supported by the National Parkinson Foundation Center of Excellence, the McKnight Brain Institute, UF and Shands, and NIH/ NINDS K23 NS044997.

References

1. Anderson VC, Burchiel KJ, Hogarth P, et al. Pallidal versus subthalamic nucleus deep brain stimulation in Parkinson disease. *Arch Neurol*. 2005; 62:554–560. [PubMed: 15824252]
2. Deuschl G, Schade-Brittinger C, Krack P, et al. A randomized trial of deep-brain stimulation for Parkinson's disease. *N Engl J Med*. 2006; 355:896–908. [PubMed: 16943402]
3. Group TD-BSfPDS. Deep-brain stimulation of the subthalamic nucleus or the pars interna of the globus pallidus in Parkinson's disease. *N Engl J Med*. 2001; 345:956–963. [PubMed: 11575287]
4. Kleiner-Fisman G, Herzog J, Fisman DN, et al. Subthalamic nucleus deep brain stimulation: summary and meta-analysis of outcomes. *Mov Disord*. 2006; 21:S290–S304. [PubMed: 16892449]
5. Krack P, Batir A, Van Blercom N, et al. Five-year follow-up of bilateral stimulation of the subthalamic nucleus in advanced Parkinson's disease. *N Engl J Med*. 2003; 349:1925–1934. [PubMed: 14614167]
6. Limousin P, Krack P, Pollak P, et al. Electrical stimulation of the subthalamic nucleus in advanced Parkinson's disease. *N Engl J Med*. 1998; 339:1105–1111. [PubMed: 9770557]
7. Okun MS, Fernandez HH, Wu SS, et al. Cognition and mood in Parkinson's disease in subthalamic nucleus versus globus pallidus interna deep brain stimulation: the COMPARE trial. *Ann Neurol*. 2009; 65:586–595. [PubMed: 19288469]
8. Defer GL, Widner H, Marie RM, et al. Core assessment program for surgical interventional therapies in Parkinson's disease (CAPSIT-PD). *Mov Disord*. 1999; 14:572–584. [PubMed: 10435493]
9. Lang AE, Houeto JL, Krack P, et al. Deep brain stimulation: preoperative issues. *Mov Disord*. 2006; 21:S171–S196. [PubMed: 16810718]
10. Lopiano L, Rizzone M, Bergamasco B, et al. Deep brain stimulation of the subthalamic nucleus in PD: an analysis of the exclusion causes. *J Neurol Sci*. 2002; 195:167–170. [PubMed: 11897249]
11. Pinter MM, Alesch F, Murg M, et al. Apomorphine test: a predictor for motor responsiveness to deep brain stimulation of the subthalamic nucleus. *J Neurol*. 1999; 246:907–913. [PubMed: 10552237]
12. Rodriguez RL, Fernandez HH, Haq I, et al. Pearls in patient selection for deep brain stimulation. *Neurologist*. 2007; 13:253–260. [PubMed: 17848865]
13. Langston JW, Widner H, Goetz CG, et al. Core assessment program for intracerebral transplantations (CAPIT). *Mov Disord*. 1992; 7:2–13. [PubMed: 1557062]
14. Peto V, Jenkinson C, Fitzpatrick R, et al. The development and validation of a short measure of functioning and well being for individuals with Parkinson's disease. *Qual Life Res*. 1995; 4:241–248. [PubMed: 7613534]
15. Okun MS, Tagliati M, Pourfar M, et al. Management of referred deep brain stimulation failures: a retrospective analysis from 2 movement disorders centers. *Arch Neurol*. 2005; 62:1250–1255. [PubMed: 15956104]
16. Krack P, Pollak P, Limousin P, et al. From off-period dystonia to peak-dose chorea: the clinical spectrum of varying subthalamic nucleus activity. *Brain*. 1999; 122:1133–1146. [PubMed: 10356065]
17. Katayama Y, Kasai M, Oshima H, et al. Subthalamic nucleus stimulation for Parkinson disease: benefits observed in levodopa-intolerant patients. *J Neurosurg*. 2001; 95:213–221. [PubMed: 11780890]
18. Lyons KE, Davis JT, Pahwa R. Subthalamic nucleus stimulation in Parkinson's disease patients intolerant to levodopa. *Stereotact Funct Neurosurg*. 2007; 85:169–174. [PubMed: 17259749]

19. Melamed E, Bitton V, Zelig O. Episodic unresponsiveness to single doses of L-dopa in parkinsonian fluctuators. *Neurology*. 1986; 36:100–103. [PubMed: 3941762]
20. Hauser RA, Deckers F, Leher P. Parkinson's disease home diary: further validation and implications for clinical trials. *Mov Disord*. 2004; 19:1409–1413. [PubMed: 15390057]
21. Hauser RA, Friedlander J, Zesiewicz TA, et al. A home diary to assess functional status in patients with Parkinson's disease with motor fluctuations and dyskinesia. *Clin Neuropharmacol*. 2000; 23:75–81. [PubMed: 10803796]
22. Hauser RA, Russ H, Haeger DA, et al. Patient evaluation of a home diary to assess duration and severity of dyskinesia in Parkinson disease. *Clin Neuropharmacol*. 2006; 29:322–330. [PubMed: 17095895]
23. Vingerhoets FJ, Villemure JG, Temperli P, et al. Subthalamic DBS replaces levodopa in Parkinson's disease: two-year follow-up. *Neurology*. 2002; 58:396–401. [PubMed: 11839838]
24. Welter ML, Houeto JL, Tezenas du Montcel S, et al. Clinical predictive factors of subthalamic stimulation in Parkinson's disease. *Brain*. 2002; 125:575–583. [PubMed: 11872614]
25. Schupbach WM, Chastan N, Welter ML, et al. Stimulation of the subthalamic nucleus in Parkinson's disease: a 5 year follow up. *J Neurol Neurosurg Psychiatry*. 2005; 76:1640–1644. [PubMed: 16291886]
26. Okun MS, Rodriguez RL, Mikos A, et al. Deep brain stimulation and the role of the neuropsychologist. *Clin Neuropsychol*. 2007; 21:162–189. [PubMed: 17366283]
27. Moro E, Lozano AM, Pollak P, et al. Long-term results of a multicenter study on subthalamic and pallidal stimulation in Parkinson's disease. *Mov Disord*. 2010
28. Okun MS, Green J, Saben R, et al. Mood changes with deep brain stimulation of STN and GPi: results of a pilot study. *J Neurol Neurosurg Psychiatry*. 2003; 74:1584–1586. [PubMed: 14617726]
29. Fraix V, Pollak P, Moro E, et al. Subthalamic nucleus stimulation in tremor dominant parkinsonian patients with previous thalamic surgery. *J Neurol Neurosurg Psychiatry*. 2005; 76:246–248. [PubMed: 15654041]

TABLE 1

Preoperative Patient Demographics

Case	Age	Gender	Duration (y)	F/U (y)	Handedness	Target	DBS Side	MMSE	DRS	LED (mg)	H&Y	Preoperative UPDRS motor scores		
												Off Med	On Med	% Change
Dyskinesia patients														
1	65	Male	17	1	Right	GPI	Bilateral	25	120	1200	3	35	27	-22.9
2	68	Male	19	3	Right	GPI	Bilateral	26	121	684.5	3	48	42	-12.5
3	48	Female	7	5	Right	STN	Bilateral	29	N/A *	500	2.5	49	35	-28.6
4	71	Male	8	2.5	Left	STN	Bilateral	30	138	1133.4	2	41	32	-22.0
5 ‡	66	Male	16	0.5	Right	STN	Right	28	135	987.5	3	51	40	-21.6
Motor fluctuation patients														
6	67	Male	11	0.5	Right	STN	Right	29	134	1100	3	37	28	-24.3
Medication-refractory tremor patients														
7	59	Male	4	1.5	Right	STN	Bilateral	29	138	301.5	1.5	11	16	45.5
8	64	Male	5	3.5	Right	STN	Bilateral	30	132	600	2	25	20	-20.0
9 ‡	70	Male	13	5.5	Right	STN	Right	30	138	350	3	41	33	-19.5
Mean (SD)	64.2 (7.03)		11.1 (5.46)	2.5 (0.6)				28.4 (1.81)	132 (7.43)	761.9 (349.6)	2.56 (0.58)	37.6 (12.8)	30.3 (8.6)	-14.0 (22.7)

* Unable to do, due to a language barrier as Spanish was her first language.

† Previous history of a contralateral pallidotomy.

DBS indicates deep brain stimulation; DRS, dementia rating scale; F/U, follow-up; GPI, globus pallidus interna; H&Y, modified Hoehn and Yahr staging; LED, levodopa equivalent dose; MMSE, Mini Mental Status Examination; N/A, not available; SD, standard deviation; STN, subthalamic nucleus; UPDRS, Unified Parkinson's Disease Rating Scale.

TABLE 2

UPDRS Part III (Motor) Scores and LED

Case	UPDRS Total Motor Scores							
	Preoperative		4 mo		1 y		Last F/U	
	Off medication	Off medication/On stim	Off medication/On stim	Off medication/On stim	Off medication/On stim	Off medication/On stim	LED	
1	35	26	30	30	30	1200	816.7	816.7
2	48	54	49	49	63	684.5	25.1	33.5
3	49	38	45	45	7	500	683.4	1000
4	41	21	37	37	41	1133.4	750	900
5	51	42	NA	NA	42	987.5	NA	300
6	37	28	NA	NA	28	1100	NA	1033.4
7	11	14	14	14	31	301.5	0	450
8	25	23	21	21	33	600.0	400	600
9	41	38	34	34	56	350.0	400	300
Mean ($\pm$ SE)	37.6 $\pm$ 4.3	31.6 $\pm$ 4.1	32.9 $\pm$ 12.5	32.9 $\pm$ 12.5	36.8 $\pm$ 16.4	761.9 $\pm$ 116.5	439.3 $\pm$ 125.9	603.7 $\pm$ 118.3
% change		-16%	-12.5%	-12.5%	-2.1%		-42.3%	-20.8%
<i>P</i> -value*		0.03*	0.04*	0.04*	0.42		0.08	0.13

* Statistically significant values. *P*-values were calculated by comparing the motor score from baseline to each follow-up period.

F/U indicates follow-up; LED, levodopa equivalent dose; NA, not available; PD, Parkinson disease; SE, standard error; UPDRS, Unified Parkinson Disease Rating Scale.

TABLE 3

Comparison of UPDRS Part II (ADL) and PDQ-39 Scores From Baseline to 6 Months and Last Follow-up

	Preoperative	6 mo	1 y	Last F/U
UPDRS				
PDQ-39				
Part II	19.4 ± 2.4	13.7 ± 1.6 [*]	15.0 ± 2.4	21.6 ± 2.6
Mobility	42.2 ± 9.3	34.7 ± 8.4	25.4 ± 5.3	43.6 ± 7.5
ADL	44.0 ± 7.0	22.7 ± 4.5 [*]	26.8 ± 3.0	36.1 ± 5.3
Emotional	32.0 ± 5.0	12.5 ± 4.8 [*]	17.3 ± 4.7	16.2 ± 3.8 [*]
Stigma	35.4 ± 9.8	8.4 ± 3.9 [*]	9.8 ± 5.1 [*]	19.4 ± 6.9 [*]
Social	7.4 ± 2.9	9.2 ± 4.9	7.1 ± 3.8	13.0 ± 4.0
Cognition	39.6 ± 10.1	20.9 ± 5.7	16.1 ± 5.1	31.9 ± 4.1
Community	35.2 ± 9.5	21.3 ± 5.4	28.6 ± 6.8	38.0 ± 5.4
Discomfort	46.3 ± 9.4	36.1 ± 7.5	28.6 ± 6.0	30.6 ± 7.7

^{*} Statistically significant ($P < 0.05$); mean and standard error shown.

ADL indicates activity of daily living; F/U, follow-up; UPDRS, Unified Parkinson Disease Rating Scale; PDQ, Parkinson disease questionnaire.

TABLE 4

UPDRS Subscores, Dyskinesia Rating Scale Scores, PGIS, and CGIS

Dyskinesia Rating Scale			UPDRS Part IV				UPDRS Part II		UPDRS Part III		PGIS	CGIS
Case	Total Scores		Item 32 (Dyskinesia)		Item 39 (Off Periods)		Item 16 (Tremor)		Item 20 (Resting Tremor)			
	Preoperative	Postoperative	Preoperative	Postoperative	Preoperative	Postoperative	Preoperative	Postoperative	Preoperative (UE/LE)	Postoperative (UE/LE)		
Dyskinesia patients												
1	3	0	2	1	—	—	—	—	—	—	1	1
2	3.5	1	2	1	—	—	—	—	—	—	1	1
3	3.5	0	2	0	—	—	—	—	—	—	2	2
4	2	0	2	1	—	—	—	—	—	—	1	1
5	2	0	2	0	—	—	—	—	—	—	1	1
Motor fluctuation patients												
6	—	—	—	—	2	0	—	—	—	—	2	2
Medication-refractory tremor patients												
7	—	—	—	—	—	—	3	0	—	2/0	2	2
8	—	—	—	—	—	—	4	1	—	3/0	1	1
9	—	—	—	—	—	—	2	1	—	3/1	2	2

CGIS indicates Clinician Global Impression Scale; Item 32, duration of dyskinesia; Item 39, duration of off periods; LE, contralateral lower extremity; PGIS, Patient Global Impression Scale; Preoperative, Baseline off medication state; UE, contralateral upper extremity; UPDRS, Unified Parkinson's Disease Rating Scale. Dyskinesia rating scale ranges 0 to 5 with 5 being the worst.