

Clinical outcomes of asleep vs awake deep brain stimulation for Parkinson disease



Matthew A. Brodsky, MD
Shannon Anderson, PA-C
Charles Murchison, MS
Mara Seier, MD
Jennifer Wilhelm, DPT
Aaron Vederman, PhD
Kim J. Burchiel, MD

Correspondence to
Dr. Brodsky:
brodskym@ohsu.edu

ABSTRACT

Objective: To compare motor and nonmotor outcomes at 6 months of asleep deep brain stimulation (DBS) for Parkinson disease (PD) using intraoperative imaging guidance to confirm electrode placement vs awake DBS using microelectrode recording to confirm electrode placement.

Methods: DBS candidates with PD referred to Oregon Health & Science University underwent asleep DBS with imaging guidance. Six-month outcomes were compared to those of patients who previously underwent awake DBS by the same surgeon and center. Assessments included an “off”-levodopa Unified Parkinson’s Disease Rating Scale (UPDRS) II and III, the 39-item Parkinson’s Disease Questionnaire, motor diaries, and speech fluency.

Results: Thirty participants underwent asleep DBS and 39 underwent awake DBS. No difference was observed in improvement of UPDRS III ($+14.8 \pm 8.9$ vs $+17.6 \pm 12.3$ points, $p = 0.19$) or UPDRS II ($+9.3 \pm 2.7$ vs $+7.4 \pm 5.8$ points, $p = 0.16$). Improvement in “on” time without dyskinesia was superior in asleep DBS ($+6.4 \pm 3.0$ h/d vs $+1.7 \pm 1.2$ h/d, $p = 0.002$). Quality of life scores improved in both groups ($+18.8 \pm 9.4$ in awake, $+8.9 \pm 11.5$ in asleep). Improvement in summary index ($p = 0.004$) and subscores for cognition ($p = 0.011$) and communication ($p < 0.001$) were superior in asleep DBS. Speech outcomes were superior in asleep DBS, both in category ($+2.77 \pm 4.3$ points vs -6.31 ± 9.7 points ($p = 0.0012$) and phonemic fluency ($+1.0 \pm 8.2$ points vs -5.5 ± 9.6 points, $p = 0.038$).

Conclusions: Asleep DBS for PD improved motor outcomes over 6 months on par with or better than awake DBS, was superior with regard to speech fluency and quality of life, and should be an option considered for all patients who are candidates for this treatment.

Clinicaltrials.gov identifier: NCT01703598.

Classification of evidence: This study provides Class III evidence that for patients with PD undergoing DBS, asleep intraoperative CT imaging-guided implantation is not significantly different from awake microelectrode recording-guided implantation in improving motor outcomes at 6 months. *Neurology*® 2017;89:1944-1950

GLOSSARY

ADL = activities of daily living; **COWAT** = Controlled Oral Word Association Test; **DBS** = deep brain stimulation; **DRS-2** = Mattis Dementia Rating Scale-Second Edition; **GPI** = globus pallidus pars interna; **ICH** = intracerebral hemorrhage; **ICT** = intraoperative CT imaging; **iMRI** = intraoperative MRI; **MER** = microelectrode recording; **NSQIP** = National Surgical Quality Improvement Program; **OHSU** = Oregon Health & Science University; **OLS** = ordinary least squares; **PD** = Parkinson disease; **PDQ-39** = 39-item Parkinson’s Disease Questionnaire; **STN** = subthalamic nucleus; **UPDRS** = Unified Parkinson’s Disease Rating Scale.

Deep brain stimulation (DBS) for Parkinson disease (PD) is an established therapy for patients with advanced disease who have motor complications. Indications for DBS include frequent or unpredictable “on”/“off” motor fluctuations, disabling dyskinesia, or disabling tremor that is refractory to dopamine replacement medications. DBS for PD has traditionally been performed with the patient awake in the operating room to allow for microelectrode recording (MER) to accurately identify the target for placement of the stimulating electrode. This procedure involves placement of recording microelectrodes into the brain to identify the location and borders of

Editorial, page 1938

From the Departments of Neurology (M.A.B., S.A., C.M., M.S., J.W.) and Neurosurgery (A.V., K.J.B.), Oregon Health & Science University, Portland.

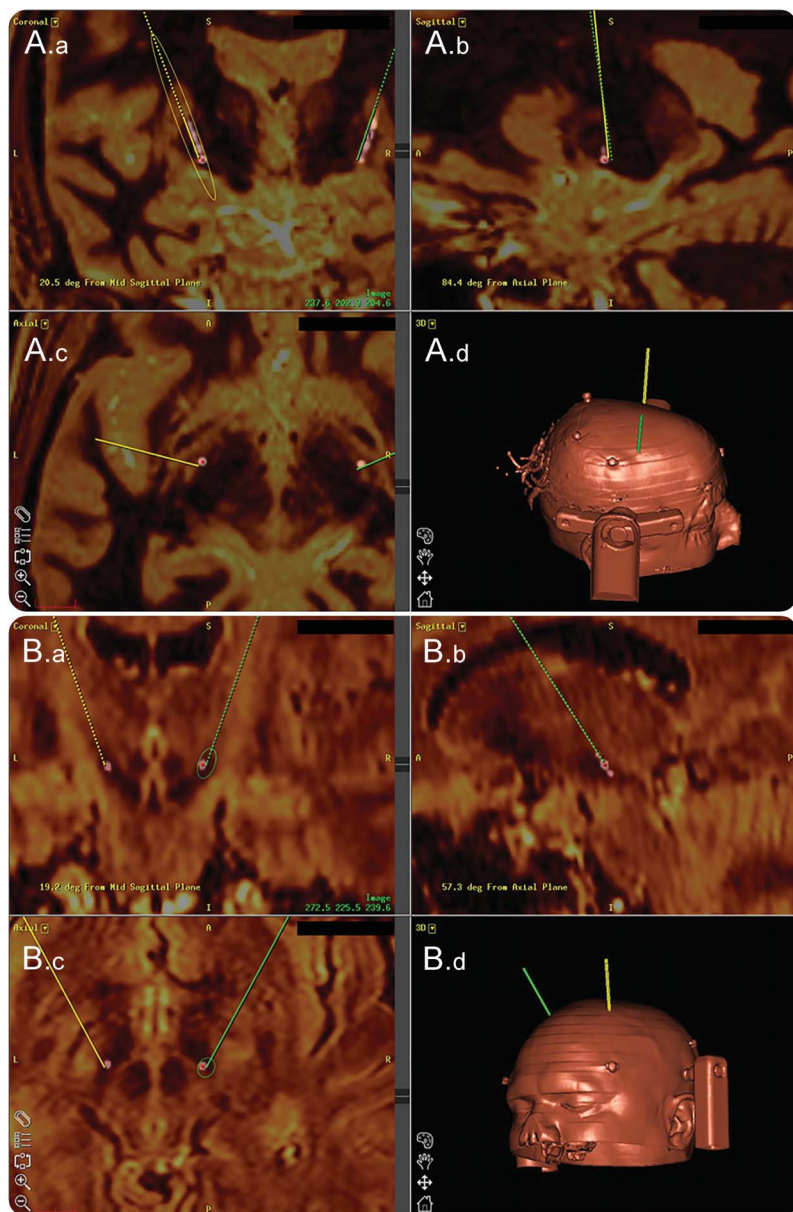
Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

either the subthalamic nucleus (STN) or globus pallidus pars interna (GPi), and often requires several passes into brain tissue to achieve a satisfactory result.¹

Newer methods of performing DBS with the patient asleep include the advent of intraoperative CT imaging (iCT) that has been coregistered with a preoperative 3T MRI to plan

the trajectory to avoid sulci and ventricles that are known to cause adverse events, visualize the planned target, and confirm lead placement with the stimulating electrode prior to the patient leaving the operating room. This allows the patient to be asleep from start to finish of the procedure. Accuracy of lead placement using this method is excellent,² with good outcomes³; however, meaningful clinical outcomes comparing asleep vs awake DBS performed by the same team at the same medical center have yet to be reported. This study aims to compare such outcomes.

Figure 1 Intraoperative image confirmation of globus pallidus pars interna (GPi) and subthalamic nucleus (STN) electrode placement



(A.a–A.d) Intraoperative image confirmation of GPi electrode placement. Fused images from preoperative 3T MRI with intraoperative CT show coronal (A.a), sagittal (A.b), and axial (A.c) views, with planned trajectory (yellow and green lines) and target confirmation (red points) in a GPi implant. (B.a–B.d) Intraoperative image confirmation of STN electrode placement. Fused images from preoperative 3T MRI with intraoperative CT show coronal (B.a), sagittal (B.b), and axial (B.c) views, with planned trajectory (yellow and green lines) and target confirmation (red points) in a STN implant.

METHODS The primary research question is whether there is a difference in motor outcomes at 6 months for patients with PD undergoing DBS awake using MER guidance vs asleep using intraoperative imaging guidance. The level of evidence assigned to this question is Class III.

Patients with idiopathic PD referred to Oregon Health & Science University's (OHSU) Movement Disorder Program for consideration of DBS were sequentially identified as potential participants.

Standard protocol approval, registrations, and patient consents. The study was approved by the OHSU institutional review board. Written informed consent was obtained from all participants in the study. The clinicaltrials.gov registration number is NCT01703598.

Baseline assessments included the Unified Parkinson's Disease Rating Scale (UPDRS) part II activities of daily living (ADL) scale, the 39-item Parkinson's Disease Questionnaire (PDQ-39), and a 72-hour motor diary. Participants underwent a baseline neurologic examination and were evaluated with the motor UPDRS (UPDRS III) by trained examiners (J.W., K.L.) in the practically defined "off" (after 12 hours without medication) and "on" levodopa state. Participants underwent cognitive testing including the Mattis Dementia Rating Scale–Second Edition (DRS-2) and the Controlled Oral Word Association Test (COWAT), which assesses phonemic fluency with the letter fluency task (FAS) and category fluency with the animal naming task.

Patients underwent implantation of DBS electrodes (Medtronic 3387; Minneapolis, MN) to the STN or GPi under general anesthesia by a single neurosurgeon (K.J.B.), using intraoperative imaging guidance using previously described techniques² (figure 1, A and B). Patients returned for programming optimization at 1, 2, and 3 months postimplant. At the 6-month postoperative visit, patients again completed the UPDRS part II, PDQ-39, and a 72-hour motor diary, alongside readministration of the same cognitive test battery. They were then evaluated by the same trained raters with the UPDRS III in the practically defined "off" and "on" levodopa state.

Patients in the awake DBS cohort consisted of those who were enrolled and participated in the Veterans Affairs Cooperative Studies Program 468 Study (NCT00056563)⁴ at OHSU. These participants underwent motor UPDRS examinations in the practically defined "off" and "on" levodopa state, completed motor diaries, the UPDRS part II, neuropsychological assessments (including the DRS-2 and COWAT), and the PDQ-39 at baseline. They then underwent DBS implantation in either the STN or GPi using intraoperative microelectrode recording and test

stimulation by the same neurosurgeon (K.J.B.). These participants likewise had their DBS programming optimized prior to their 6-month follow-up, at which point they underwent repeat motor UPDRS examinations and assessments with the UPDRS part II, PDQ-39, motor diaries, and neuropsychological testing.

The primary outcome was change in UPDRS III from baseline in the “off” levodopa state to 6 months postoperatively in the “off” levodopa/“on” DBS state in patients with PD who underwent asleep DBS with iCT compared to patients with PD who underwent awake DBS with MER. Secondary outcomes included change from baseline (pre DBS) to 6 months (with DBS “on”) in the “off” medication state of “on” time without dyskinesia, PDQ-39, UPDRS part II, DRS-2, Beck Depression Inventory II, and the verbal semantic and phonemic fluency scores of the COWAT. Potential adverse events were captured perioperatively and at each postoperative clinic visit.

Statistical analysis used ordinary least squares (OLS) regression to compare 6-month changes in study outcomes between participants who were asleep during DBS against those who were awake. Cohort comparisons using OLS modeling also corrected for age at study entry, sex, and study outcomes at baseline. When significant differences were not observed, equivalence of study outcomes was established by comparing mean outcomes in the asleep cohort against the defined 95% confidence interval boundaries in the awake group. Assumptions of normality were assessed across outcomes with log transformations applied as necessary and unequal variance was adjusted for using Welch correction. Standard diagnostics of the residuals were used to identify model outliers and remove any overly influential data points. Multiple model comparisons were accounted for using a stepwise Holm-

Bonferroni correction with contrasts considered significant at an adjusted $p < 0.05$.

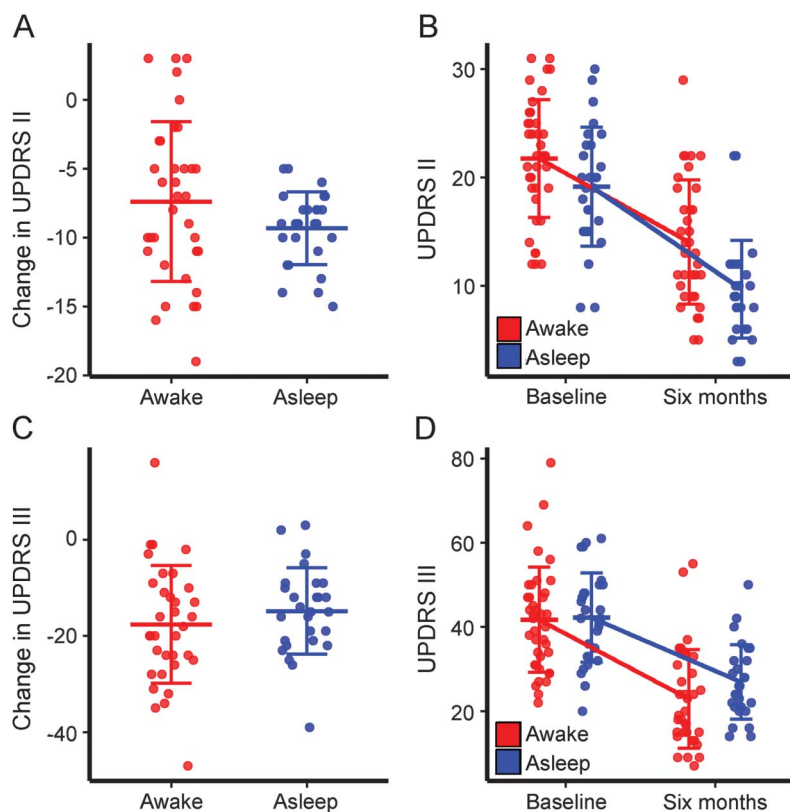
RESULTS Baseline demographics. Thirty participants underwent asleep DBS using iCT. Seven were implanted in the STN and 23 in the GPi. Their mean age was 63.7 ± 9.79 years; 20 were male and 10 female. Mean baseline “off” medication UPDRS III was 42.2 ± 10.6 . Thirty-nine participants who participated at OHSU in the cooperative trial underwent awake DBS using MER guidance.⁴ Eighteen were implanted in the STN and 21 in the GPi. Their mean age was 63.1 ± 7.61 years; 26 were male and 13 were female. Their mean baseline “off” medication UPDRS III was 41.7 ± 12.5 .

Primary outcome. Mean improvement in the “off” medication/“on” DBS UPDRS III at 6 months in the asleep group was 14.8 ± 8.9 , and in the awake group was 17.6 ± 12.26 . There was no difference in the change of UPDRS III from baseline to 6 months in the “off” medication/“on” DBS state between the awake MER-guided and asleep iCT-guided groups ($t = 1.32, p = 0.19$) (figure 2).

Secondary outcomes. ADL outcomes. The UPDRS part II ADL score improved in both the asleep (9.3 ± 2.7 points, $t = 18.4, p < 0.001$) and awake (7.4 ± 5.8 points, $t = 7.8, p < 0.001$) groups without significant difference based on cohort ($t = 1.60, p = 0.16$). Equivalence analysis identified a confidence interval for the expected change in ADL score for the awake MER-guided participants for 5.59 to 9.39 points. Based on this lower bound, asleep iCT-guided participants were found to have ADL changes that were specifically noninferior compared to the awake cohort ($t = 7.57, p < 0.001$) (figure 2).

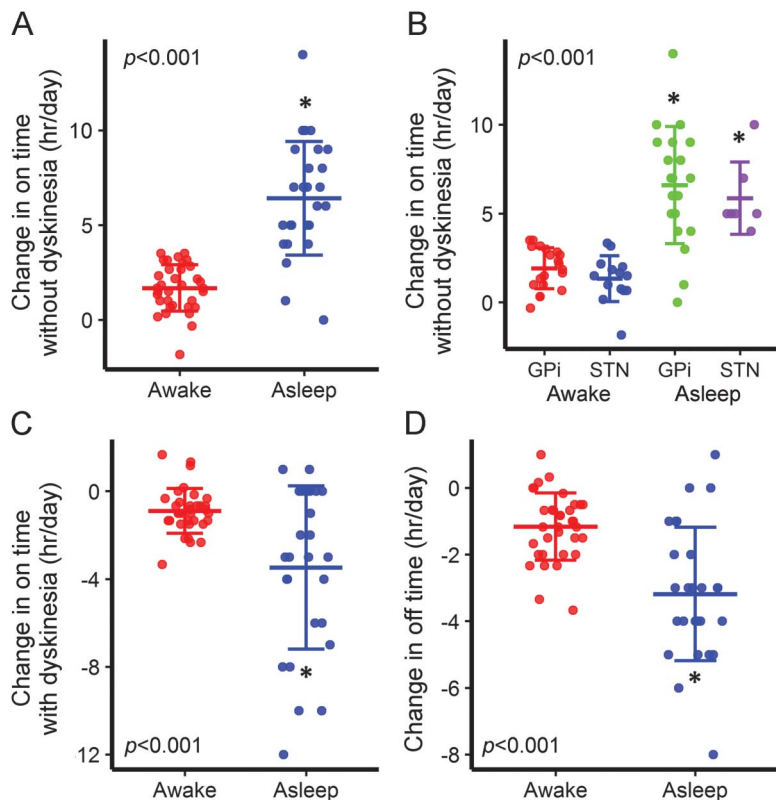
Motor diary outcomes. A total of 27 asleep participants (20 GPi, 7 STN) and 34 awake participants (20 GPi, 14 STN) completed motor diaries. Meaningful improvements in “on” time without dyskinesia were seen in both cohorts. The asleep patients had an increase in “on” time without dyskinesia by 6.4 ± 3.0 h/d ($t = 11.1, p < 0.001$) and a decrease in “on” time with dyskinesia by 3.5 ± 3.7 h/d ($t = 4.83, p < 0.001$). Although the awake group also had improvements in “on” time both without (1.7 ± 1.2 h/d increase, $t = 8.14, p < 0.001$) and with dyskinesia (0.9 ± 1.0 h/d decrease, $t = 5.2, p < 0.001$), these improvements were improved in the asleep participants (“on” with dyskinesia: $t = 8.58, p < 0.001$; “on” without dyskinesia: $t = 3.92, p = 0.0020$). Greater improvement in “on” time without dyskinesia in the asleep vs the awake group held up regardless of DBS target ($p < 0.001$). A reduction in “off” time was significant in both groups, with a reduction of 3.2 ± 2.0 h/d in the asleep cohort and 1.2 ± 1.0 h/d in the awake cohort, this

Figure 2 Motor examination and activities of daily living outcomes



Six-month change in Unified Parkinson’s Disease Rating Scale (UPDRS) part II (A, B) and III (C, D) in awake vs asleep deep brain stimulation.

Figure 3 Motor diary outcomes



Six-month change in 24-hour motor diaries in awake vs asleep deep brain stimulation. Change in “on” time without dyskinesia (A, B), with dyskinesia (C), and change in “off” time (D). GPi = globus pallidus pars interna; STN = subthalamic nucleus.

change again being superior in the asleep cohort ($t = 5.30$, $p < 0.001$) (figure 3).

Quality of life outcomes. Quality of life, based on the PDQ-39, improved in both the asleep and awake groups from baseline to 6 months. Patients in the asleep group improved by 18.8 ± 9.4 points on the mean PDQ-39 summary index score, significantly better than the 8.9 ± 11.5 point improvement in the awake group ($t = 3.71$, $p = 0.0040$). When subscores from the PDQ-39 were further analyzed, a greater improvement in the asleep group was seen for cognition ($t = 3.16$, $p = 0.011$) and communication ($t = 5.12$, $p < 0.001$) vs the awake group (figure 4).

Speech and cognitive outcomes. Participants undergoing asleep DBS fared better with regard to speech fluency. In the asleep group, category fluency improved on the COWAT animal naming task, by 2.77 ± 4.3 ($t = 3.00$, $p = 0.022$) points, while in the awake group category fluency worsened by 6.31 ± 9.7 points ($t = 3.90$, $p = 0.0021$), a difference observed to be significant between the 2 cohorts ($t = 4.11$, $p = 0.0012$). This cohort effect was observed even while controlling for DBS target ($t = 4.13$, $p = 0.0013$). Phonemic fluency as measured by the COWAT FAS test remained unchanged in the asleep DBS cohort

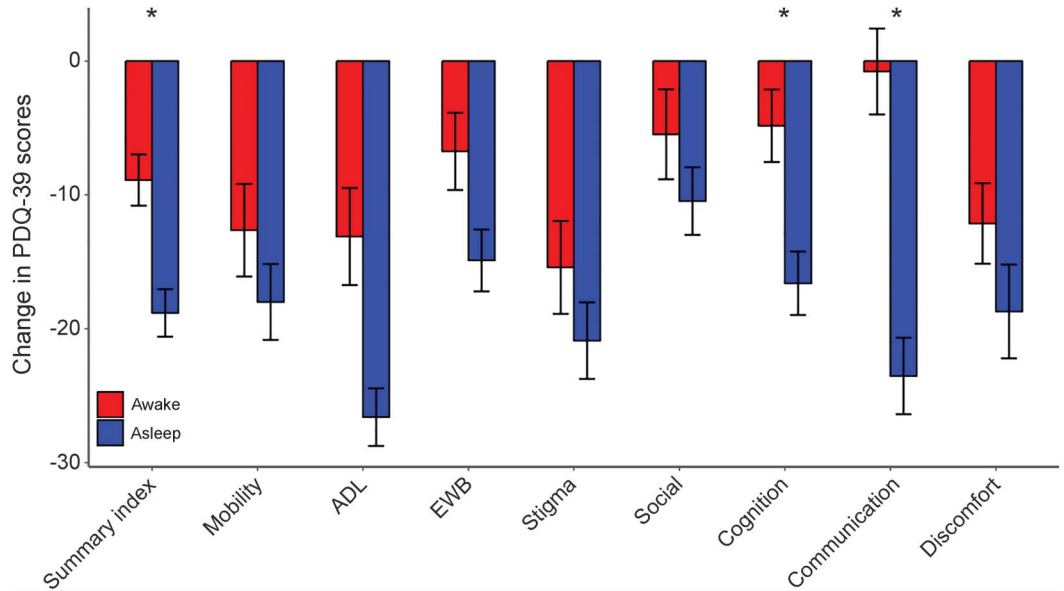
(1.0 ± 8.2 point improvement, $t = 0.45$, $p = 0.58$) and worsened in the awake DBS cohort (5.5 ± 9.6 point decline, $t = 3.42$, $p = 0.0072$), a significant difference between groups ($t = 2.39$, $p = 0.038$). Even while controlling for DBS target, this cohort-based difference was still significant ($t = 2.40$, $p = 0.038$). There was no observed difference based on target in the asleep cohort (GPi: 2.13 ± 7 point improvement, STN: 1.83 ± 11 point decline, $t = 0.87$, $p = 0.40$) (figure 5). Overall cognition as measured by the DRS-2 scores remained stable without change in both the asleep and awake cohorts ($p = 0.44$) and regardless of DBS target ($p = 0.78$).

Adverse events. In the awake DBS cohort, one patient developed a small venous hemorrhage secondary to a tear in the sagittal sinus. Postoperative MRI demonstrated DBS tips in the STN bilaterally, and the patient subsequently did well with DBS programming. In the asleep DBS cohort, one patient developed onset of left arm hemiballismus 4 months after STN DBS implantation, and evidence on imaging and cultures of an infection near the right DBS lead tip. He was subsequently explanted and treated with a course of antibiotics, and the hemiballismus resolved. A second patient had a perioperative small right frontal ischemic nonhemorrhagic infarct and a postoperative focal seizure, without subsequent sequelae.

DISCUSSION DBS is established as an important therapy for patients with PD who have motor fluctuations, dyskinesia, and disabling tremor. Frame-based stereotaxis and mapping of deep nuclei with MER has long been the gold standard for targeting DBS implantation.⁵ This methodology requires that the patient remain awake during the entire procedure, with the head in a fixed position for a prolonged period of time, causing significant discomfort. Furthermore, patients with PD must withhold their dopamine replacement medications for a minimum of 12 hours prior to the procedure, further adding to the degree of discomfort and anxiety related to surgery. The prospect of having an elective awake brain surgery is a barrier for many who are otherwise good candidates for this treatment.

Though supported by historical considerations, no Class I or II evidence exists that MER adds significant value to the DBS implant procedure. Often this procedure is accompanied by test stimulation with the patient awake to further verify target accuracy, further prolonging the duration of the procedure. With the advent of advanced MRI and CT, particularly intraoperative imaging, the argument for the continued use of MER during DBS implantation has been substantially weakened.

Figure 4 Quality of life outcomes



Six-month change in 39-item Parkinson's Disease Questionnaire (PDQ-39) scores in awake vs asleep deep brain stimulation. *Significant outcomes. ADL = activities of daily living subscore; EWB = emotional well-being subscore.

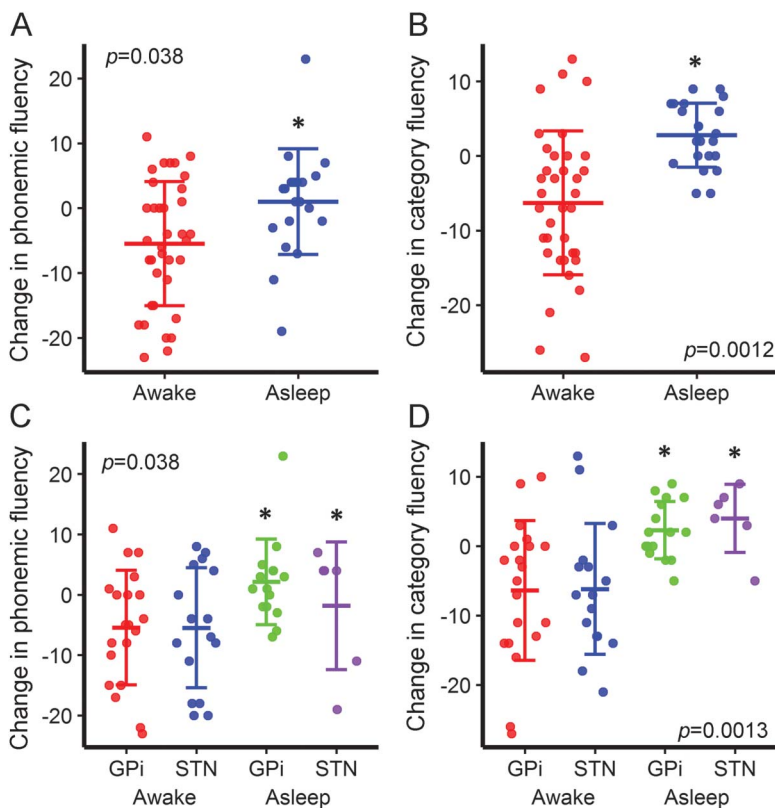
While the risk of a serious adverse event such as intracerebral hemorrhage (ICH) or infection remains low, it is not zero. Meta-analyses of surgical risk for

DBS have reported ICH rates of 3.2%–5%.^{6–8} Risk of ICH related to surgical technique includes use of MER, number of MER penetrations, and sulcal vs ventricular involvement by the trajectory.⁶ Multiple instrumented passes into the brain with the sharp tip of the recording microelectrode may contribute to risk of ICH, with the per-trajectory ICH rate estimated at 1.57%.⁹

ICH related to DBS may further be divided into asymptomatic, symptomatic, and resulting in permanent deficit or death, at reported rates of 1.9%, 2.1%, and 1.1%, respectively.⁶ The incidence of hemorrhage in studies adopting an image-guided and image-verified approach without MER was significantly lower than that reported with other operative techniques ($p < 0.001$ for total number of hemorrhages, $p < 0.001$ for asymptomatic hemorrhage, $p < 0.004$ for symptomatic hemorrhage, and $p = 0.001$ for hemorrhage leading to permanent deficit).⁶

While the risk of ICH remains low, other adverse effects such as worsening speech fluency remain relatively common.^{4,10} Both phonemic and category fluency worsened in our awake DBS cohort, but remained stable or improved in our asleep cohort. While adverse effects on speech from DBS have often been considered related to the stimulation itself, there is evidence that this effect may be due to instrumented passes and implantation of the inactive electrodes into the brain alone.¹¹ Thus, one might expect such side effects of DBS to be lessened with fewer instrumented passes into the brain. Although 73% of asleep participants received GPi implants, DBS target did not have a significant effect on speech outcomes in either cohort in our study.

Figure 5 Speech fluency outcomes



Six-month change in phonetic (A, C) and category (B, D) speech fluency scores in awake vs asleep deep brain stimulation. GPi = globus pallidus pars interna; STN = subthalamic nucleus.

Perhaps the most common argument for the use of MER is the sensitivity of this methodology in finding the precise target for implantation of DBS electrodes. A recent analysis of multiple databases between 2004 and 2013 revealed over 28,000 cases of DBS electrode placement, revision, and removal. Data from Medicare indicated that 15.2% of DBS procedures were for revision or removal. Similar analysis of the National Surgical Quality Improvement Program (NSQIP) dataset showed a 34.0% DBS removal or revision rate. The authors concluded that up to 48.5% of these revisions may have been due to improper targeting or lack of therapeutic effect.¹² Combining the Medicare and NSQIP datasets, the proportion of these procedures performed for a first-time DBS electrode implant with MER was 73.9%, compared to 10.8% without MER. Thus, the overwhelming majority of cases in the revision analysis were related to patients in whom MER had been specifically employed during the initial implant. This result suggests that the presumed location of DBS electrode implant using MER may not be as predictable as has been previously assumed.

In our study, patients undergoing asleep DBS using iCT targeting had significant improvements over 6 months in motor function, ADL, motor complications, and quality of life. When compared to patients who underwent awake DBS using MER targeting by the same surgeon at the same medical center, meaningful differences in motor outcomes were not seen. Overall cognitive performance was likewise preserved in both awake and asleep DBS cohorts. Importantly, there was a better outcome regarding both quality of life indices and speech fluency in the asleep DBS group when compared to the awake DBS group. Weighing the risk of all adverse effects from DBS has become ever more pertinent, given the increasing number of choices patients with PD have today in the ever-crowding field of pharmacologic delivery of dopaminergic drugs to reduce motor complications.^{13–18}

As the demand for this procedure is expected to rise with the increasing prevalence of PD worldwide, the cost of this procedure is also an important issue. Prolonged duration of the DBS procedure and neurophysiologic assessments with MER may add significantly to the cost of DBS. Operative time for awake DBS with bilateral implants typically ranges from 4 to 8 hours.^{19,20} Costs associated with asleep DBS at our center were lower than comparable academic health care centers performing awake DBS,²¹ likely due to shorter operative time and elimination of the need for MER.²² Intraoperative MRI (iMRI) is another method that has been used to target DBS electrode placement in the asleep patient; however, iMRI is a relatively more expensive and generally less available guidance

system at surgical centers performing DBS compared to iCT.

One shortcoming of our study is that our awake DBS cohort consisted of a historical control. Although every patient was operated on by the same surgeon at the same medical center, this study design does not have the rigor of a prospective randomized design. The preference for asleep DBS that is sought out at our center would have made prospective randomization to awake or asleep DBS a challenge.

This study demonstrates that asleep DBS for PD with iCT targeting improved motor outcomes over 6 months that were on par with, or better than, awake DBS at our center, and superior with regard to speech fluency and quality of life. Serious adverse events were uncommon in both groups, with the only ICH occurring in an awake DBS case. Asleep DBS allows for greater patient comfort, making this option more accessible for patients who otherwise might not choose it, and should be considered for all patients with PD who are candidates for this treatment.

AUTHOR CONTRIBUTIONS

Matthew Brodsky: study concept and design, organization and execution of the study, data acquisition and analysis, writing the first draft and revision of the manuscript. Shannon Anderson: organization and execution of the study, critical review and revision of the manuscript. Charles Murchison: data analysis, critical review and revision of the manuscript. Mara Seier: data acquisition, critical review and revision of the manuscript. Jennifer Wilhelm, data acquisition, critical review and revision of the manuscript. Aaron Vederman: data acquisition, critical review and revision of the manuscript. Kim Burchiel: execution of the study, critical review and revision of the manuscript.

ACKNOWLEDGMENT

The authors thank Kittima Leelaamornvichet, DPT, for performing ratings; Jaelyn Smith for data management; and the patients who participated in this study.

STUDY FUNDING

This study was funded, in part, by Medtronic.

DISCLOSURE

M. Brodsky: research grant, Medtronic. S. Anderson, C. Murchison, M. Seier, J. Wilhelm, A. Vederman, and K. Burchiel report no disclosures relevant to the manuscript. Go to Neurology.org for full disclosures.

Received April 21, 2017. Accepted in final form August 4, 2017.

REFERENCES

1. Starr PA, Christine CW, Theodosopoulos PV, et al. Implantation of deep brain stimulators into the subthalamic nucleus: technical approach and magnetic resonance imaging-verified lead locations. *J Neurosurg* 2002;97:370–387.
2. Burchiel KJ, McCartney S, Lee A, Raslan A. Accuracy of deep brain stimulation electrode placement using intraoperative computed tomography without microelectrode recording. *J Neurosurg* 2013;119:301–306.
3. Mirzadeh Z, Chapple K, Lambert M, et al. Parkinson's disease outcomes after intraoperative CT-guided “asleep”

- deep brain stimulation in the globus pallidus internus. *J Neurosurg* 2016;124:902–907.
4. Weaver F, Follett K, Stern M, et al. Bilateral deep brain stimulation vs best medical therapy for patients with advanced Parkinson disease. *JAMA* 2009;301:63–73.
 5. Israel Z, Burchiel K, eds. *Microelectrode Recording in Movement Disorder Surgery*, New York: Thieme Medical Publishers; 2005.
 6. Zrinzo L, Foltynie T, Limousin P, Hariz M. Reducing hemorrhagic complications in functional neurosurgery: a large case series and systematic literature review. *J Neurosurg* 2012;116:84–94.
 7. Kleiner-Fisman G, Herzog J, Fisman DN, et al. Subthalamic nucleus deep brain stimulation: summary and meta-analysis of outcomes. *Mov Disord* 2006;21(suppl 14):S290–S304.
 8. Videnovic A, Metman LV. Deep brain stimulation for Parkinson's disease: prevalence of adverse events and need for standardized reporting. *Mov Disord* 2008;23:343–349.
 9. Kimmelman J, Duckworth K, Ramsay T, Voss T, Ravina B, Emborg ME. Risk of surgical delivery to deep nuclei: a meta-analysis. *Mov Disord* 2011;26:1415–1421.
 10. Aldridge D, Theodoros D, Angwin A, Vogel A. Speech outcomes in Parkinson's disease after subthalamic nucleus deep brain stimulation: a systematic review. *Parkinsonism Relat Disord* 2016;33:3–11.
 11. Oken MS, Gallo BV, Mandybur G, et al. Subthalamic deep brain stimulation with a constant-current device in Parkinson's disease: an open-label randomized controlled trial. *Lancet Neurol* 2012;11:140–149.
 12. Rolston JD, Englot DJ, Starr PA, Larson PS. An unexpectedly high rate of revisions and removals in deep brain stimulation surgery: analysis of multiple databases. *Parkinsonism Relat Disord* 2016;33:72–77.
 13. Hauser RA, Hsu A, Kell S, et al. Extended-release carbidopa-levodopa (IPX066) compared with immediate-release carbidopa-levodopa in patients with Parkinson's disease and motor fluctuations: a phase 3 randomised, double-blind trial. *Lancet Neurol* 2013;12:346–356.
 14. LeWitt PA, Hauser RA, Grosset DG, et al. A randomized trial of inhaled levodopa (CVT-301) for motor fluctuations in Parkinson's disease. *Mov Disord* 2016;31:1356–1365.
 15. LeWitt PA, Friedman H, Giladi N, et al. Accordion pill carbidopa/levodopa for improved treatment of advanced Parkinson's disease symptoms [abstract]. *Mov Disord* 2012;27(suppl 1):408.
 16. Giladi N, Caraco Y, Gurevich T, et al. Pharmacokinetic profile of ND0612L (levodopa/carbidopa) for subcutaneous infusion in patients with moderate to severe Parkinson's disease. *Mov Disord* 2015;30(suppl 1):S87.
 17. Verhagen Metman L, Stover N, Chen C, Cowles VE, Sweeney M. Gastroretentive carbidopa/levodopa, DM-1992, for the treatment of advanced Parkinson's disease. *Mov Disord* 2015;30:1222–1228.
 18. Olanow CW, Kieburtz K, Odin P, et al. Continuous intrajejunal infusion of levodopa-carbidopa intestinal gel for patients with advanced Parkinson's disease: a randomised, controlled, double-blind, double-dummy study. *Lancet Neurol* 2014;13:141–149.
 19. Oh MY, Abosch A, Kim SH, Lang AE, Lozano AM. Long-term Hardware-related complications of deep brain stimulation. *Neurosurgery* 2002;50:1268–1276.
 20. Umemura A, Jaggi JL, Hurtig HI, et al. Deep brain stimulation for movement disorders: morbidity and mortality in 109 patients. *J Neurosurg* 2003;98:779–784.
 21. Jacob RL, Geddes J, McCartney S, Burchiel K. Cost analysis of awake versus asleep deep brain stimulation: a single academic health center experience. *J Neurosurg* 2016;124:1517–1523.
 22. McClelland SA III. Cost analysis of intraoperative microelectrode recording during subthalamic stimulation for Parkinson's disease. *Mov Disord* 2001;26:1422–1427.

20 Minutes Pack a Punch

Neurology[®] Podcasts

- Interviews with top experts on new clinical research in neurology
- Editorial comments on selected articles
- Convenient—listen during your commute, at your desk, or even at the gym
- On demand—it's there when you want it
- Fun and engaging
- New topic each week
- FREE

Listen now at www.aan.com/podcast

Neurology®

Clinical outcomes of asleep vs awake deep brain stimulation for Parkinson disease

Matthew A. Brodsky, Shannon Anderson, Charles Murchison, et al.

Neurology 2017;89;1944-1950 Published Online before print October 6, 2017

DOI 10.1212/WNL.0000000000004630

This information is current as of October 6, 2017

Updated Information & Services	including high resolution figures, can be found at: http://n.neurology.org/content/89/19/1944.full.html
Supplementary Material	Supplementary material can be found at: http://n.neurology.org/content/suppl/2017/10/07/WNL.0000000000004630.DC1
References	This article cites 21 articles, 0 of which you can access for free at: http://n.neurology.org/content/89/19/1944.full.html##ref-list-1
Citations	This article has been cited by 1 HighWire-hosted articles: http://n.neurology.org/content/89/19/1944.full.html##otherarticles
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): Parkinson's disease/Parkinsonism http://n.neurology.org/cgi/collection/parkinsons_disease_parkinsonism
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://n.neurology.org/misc/about.xhtml#permissions
Reprints	Information about ordering reprints can be found online: http://n.neurology.org/misc/addir.xhtml#reprintsus

Neurology® is the official journal of the American Academy of Neurology. Published continuously since 1951, it is now a weekly with 48 issues per year. Copyright © 2017 American Academy of Neurology. All rights reserved. Print ISSN: 0028-3878. Online ISSN: 1526-632X.

