Disputes & Debates: Editors' Choice

Steven Galetta, MD, FAAN, Section Editor

Editors' note: Clinical outcomes of asleep vs awake deep brain stimulation for Parkinson disease

In "Clinical outcomes of asleep vs awake deep brain stimulation for Parkinson disease," authors Brodsky et al. aimed 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. They found that asleep DBS for PD was associated with improved motor outcomes over 6 months, on par with, or better than, awake DBS, and was superior with regard to speech fluency and quality of life. In the accompanying editorial, Drs. Aziz and Hariz point out that microelectrode recording (MER) should be reserved as a tool for scientific research on basal ganglia neuronal activity. The authors explain that well-visualized targets, such as the subthalamic nucleus and internal globus pallidus (GPi), can also be done while the patient is fully asleep and without MER. Commenting on the Brodsky et al. article, Dr. Sidiropoulos requests comparison between image-guided DBS surgery and MER-guided surgery and questions why the asleep group was more shifted towards GPi as a target compared to the awake cohort. Commenting on the editorial, Dr. Sidiropoulos also suggests that accurate thalamic targeting for tremor using image-guided techniques is more challenging. Dr. Aziz, author of the editorial, agrees that the subdivisions of the thalamus are not so clearly visualized. He explains, however, that using image-guided approaches is emerging and thalamic targets can be extrapolated from visualization of the red nucleus and the posterior subthalamic area. Dr. Tröster also commented on the article. He asks for several clarifications regarding verbal fluency scores data, correlation between verbal fluency scores and 39-item Parkinson's Disease Questionnaire (PDQ-39) cognition and communication scores, and the effect on the Dementia Rating Scale (DRS). Brodsky et al. explain that Controlled Oral Word Association Test (COWAT) standard scores were used and that the longitudinal mixed-effects models were evaluated and confirmed previous findings. They clarify that statistical analysis of the correlation between the COWAT speech fluency scores and the cognition and communication subscores of the PDQ-39 was not performed, but that the improvement in both cohorts was significant. Finally, they explain that while the DRS is influenced by speech fluency, there were enough other factors in the DRS that counterbalanced the improvement in speech that was seen in the asleep DBS group.

Chafic Karam, MD, and Steven Galetta, MD

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

Christos Sidiropoulos (East Lansing)

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We congratulate Brodsky et al.¹ for the well-designed study, despite its limitations that the authors clearly stated in the article's discussion. The article adds further support to existing data² on the validity of image-guided deep brain stimulation surgery as an emerging, and probably more advantageous, approach to the standard microelectrode recording (MER)-guided surgery.

Author disclosures are available upon request (journal@neurology.org).

It would be helpful if the authors provided data on the comparative targeting accuracy of the 2 approaches, taking into account the 2 different targets as well as stimulation measures. The authors also did not specify whether or not the raters of the motor scoring were blinded. Moreover, the asleep group was more shifted towards internal globus pallidus (GPi) as a target compared to the awake cohort. Could the authors provide a comment on this?

The accompanying editorial by Drs. Aziz and Hariz³ suggested that MER may have its best place as a tool for basal ganglia research. While many neurosurgeons are relying more on image-guided approaches for subthalamic nucleus and GPi targeting, accurate thalamic targeting for tremor using such approaches is more challenging and will probably take longer to establish despite accumulating evidence on its feasibility and clinical efficacy.⁴

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2. Chen T, Mirzadeh Z, Ponce FA. “Asleep” deep brain stimulation surgery: a critical review of the literature. *World Neurosurg* 2017;105:191–198.
3. Aziz TZ, Hariz M. To sleep or not to sleep during deep brain stimulation surgery for Parkinson disease? *Neurology* 2017;89:1938–1939.
4. Chen T, Mirzadeh Z, Chapple KM, et al. Intraoperative test stimulation versus stereotactic accuracy as a surgical end point: a comparison of essential tremor outcomes after ventral intermediate nucleus deep brain stimulation. *J Neurosurg Epub* 2017 Oct 13.

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

Tipu Z. Aziz (Oxford, UK)

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In our editorial on the article by Brodsky et al.,¹ Dr. Hariz and I point out that microelectrode recording (MER) is, at best, becoming a research tool. That has been my stance for many years.² Well-visualized targets, such as the subthalamic nucleus (STN) and internal globus pallidus, can also be done while the patient is fully asleep and without MER, as Brodsky et al. demonstrated most convincingly.

I agree the subdivisions of the thalamus are not so clearly visualized; to overcome this uncertainty of placement, awake stimulation is preferred. Even then, sporadic reports of successful implantation of deep brain stimulation leads while asleep and using image-guided approaches are emerging as the thalamic target can be approached extrapolating from visualization of the red nucleus and STN (namely the posterior subthalamic area).³ This may be closer to hand than Prof. Sidropoulos believes.

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

Alexander I. Tröster (Phoenix)

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Brodsky et al.¹ compared verbal fluency, aspects of cognition, and quality of life after asleep and awake deep brain stimulation (DBS) in Parkinson disease. Awake DBS is associated with

significant perioperative discomfort in 40% or more of patients.² It is possible that anticipated discomfort contributes to the reluctance to undergo surgery expressed by 50% of patients (who are not referred for surgery despite appropriateness of DBS).³ Although good motor outcomes are attainable by asleep DBS,⁴ little is known about differences between the 2 methods in cognitive and quality of life outcomes.⁵ Brodsky et al.¹ reported that verbal fluency improved after asleep DBS and that speech and quality of life outcomes were superior after asleep vs awake DBS. Only the change scores were presented for each group and then compared. It would be helpful to know the preoperative and postoperative scores of the groups, as well as the effect size associated with the interaction terms between group and time. Such data would better allow consideration of potential preoperative differences between the groups and whether these differences are accentuated after surgery. In addition, the clinical significance of fluency data is difficult to interpret as change is measured in points. Do these points refer to the number of words or a standardized score? Furthermore, were the verbal fluency changes correlated with change in the 39-item Parkinson's Disease Questionnaire cognition and communication scores? Why might the fluency changes not have manifested in Dementia Rating Scale total score changes, which are heavily influenced by fluency (20 of 144 points)?

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

Matthew A. Brodsky (Portland)

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We thank Dr. Tröster for the thoughtful comments on our article.¹ To clarify, Controlled Oral Word Association Test (COWAT) scores were standard scores instead of raw word counts, reflected in the means and SDs pre and post deep brain stimulation (DBS) for categorical fluency (awake pre-DBS: 47.95 ± 7.28 , awake post-DBS: 42.94 ± 10.45 ; asleep pre-DBS: 97.61 ± 17.1 , asleep post-DBS: 96.95 ± 15.5) and phonemic fluency (awake pre-DBS: 47.95 ± 7.28 , awake post-DBS: 42.94 ± 10.45 ; asleep pre-DBS: 97.61 ± 17.1 , asleep post-DBS: 96.95 ± 15.5).

Knowing the absolute discrepancies on our change models, baseline values were included in all models presented. Addressing Dr. Tröster's reservations, longitudinal mixed-effects models evaluated and confirmed previous findings. The awake cohort exhibited reduced verbal fluency at follow-up (categorical: $t = -4.67$, $p < 0.001$; phonemic: $t = -3.55$, $p < 0.001$) but heavily attenuated in the asleep cohort (categorical: $t = 4.10$, $p < 0.001$; phonemic: $t = 2.40$, $p = 0.019$). These effects were observed despite profound baseline score differences between cohorts (categorical: $t = 17.9$; phonemic: $t = 16.1$).

Statistical analysis of the correlation between the COWAT speech fluency scores and the cognition and communication subscores of the 39-item Parkinson's Disease Questionnaire was not performed, but improvement in both cohorts was significant.

We agree that the Dementia Rating Scale (DRS) is influenced by speech fluency, but there were clearly enough other factors in the DRS that counterbalanced the improvement in speech seen in the asleep DBS group.

1. Brodsky MA, Anderson S, Murchison C, et al. Clinical outcomes of asleep vs awake deep brain stimulation for Parkinson disease. *Neurology* 2017;89:1944–1950.

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CORRECTION

Age-dependent white matter inflammation and cognitive impairment in the TgAPP21 rat model of Alzheimer disease

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In the poster abstract “Age-dependent white matter inflammation and cognitive impairment in the TgAPP21 rat model of Alzheimer disease” by A. Levit et al.,¹ the second author “Andrew Gibson” is missing from the byline. Mr. Gibson reports no disclosures and is affiliated with the Department of Anatomy & Cell Biology and Schulich School of Medicine and Dentistry at University of Western Ontario. The authors regret the omission.

Reference

1. Levit A, Allman BL, Nagalingam R, Hachinski V, Whitehead SN. Age-dependent white matter inflammation and cognitive impairment in the TgAPP21 rat model of Alzheimer disease. *Neurology* 2018;90:P2.184.

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Age-dependent white matter inflammation and cognitive impairment in the TgAPP21 rat model of Alzheimer disease

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