EDITORIAL

Tremor, thalamotomy, and cognition

Ying Meng, MD, and Nir Lipsman, MD, PhD

Sunnybrook Health Sciences Centre, Division of Neurosurgery, University of Toronto, Ontario, Canada

ESSENTIAL tremor (ET) is the most common movement disorder and, contrary to widespread belief, is not an exclusively monosymptomatic motor-circuit condition. Neurocognitive studies of patients with ET have consistently shown a decrease in multiple domains of executive function, such as spatial processing, working memory, and language.^{5,8} The pathophysiology of this is complex and could be linked to contributions from dysfunction in the fronto-thalamic-cerebellar loops as part of a cerebellar cognitive affective syndrome (CCAS).⁵ As a result, surgical interventions within the thalamus, especially on the dominant side, can put already vulnerable patients at risk for further cognitive deterioration.

Surgical strategies in patients with refractory motor symptoms, including ET, are rapidly evolving. To the currently available options, namely radiofrequency thalamotomy and deep brain stimulation (DBS), we can now add less invasive procedures, such as Gamma Knife radiosurgery and MR-guided focused ultrasound (MRgFUS). Common to all of these is intervention within the ventral intermediate nucleus (Vim) of the thalamus, an operation leading to significant improvement in tremor and quality of life (QOL), but one whose side-effect profile can include neurocognitive and other effects.⁷ In the context of an emerging surgical strategy, it is critical to study not only its putative benefits but also, and perhaps more importantly, its potential pitfalls. In their paper, Jung et al. report on the first study to specifically address neurocognitive changes after MRgFUS thalamotomy for medically refractory ET.⁶

In high-intensity MRgFUS, ultrasound penetrates the skull from multiple sources to converge on a discrete intracranial target, raising tissue temperature and generating a thermocoagulative lesion. The advantages of MRgFUS are real-time image guidance and the ability to raise temperatures to sublesional levels to assess for adverse events prior to generating a permanent lesion. These operations

have the additional advantage of shorter recovery times, lower infection rates, and no need for long-term programming and battery replacement. Compared with those of stereotactic radiosurgery, the bioeffects of ultrasound are nonionizing and immediate, allowing the surgeon to adjust the targeting in real time. While medically refractory ET is the procedure's first clinically approved indication in the central nervous system, high-intensity MRgFUS is also being investigated for tremor-dominant Parkinson disease, chronic pain, obsessive-compulsive disorder, and major depressive disorder, among others.

While the clinical effects of MRgFUS on tremor and resultant QOL have been characterized, the influence of the procedure on neurocognitive symptoms is unknown—and important to determine. Jung et al. report tremor, neurocognitive, and QOL assessment in 20 patients with ET who underwent left-sided MRgFUS thalamotomy.⁶ The Seoul Neuropsychological Screening Battery (SNSB), commonly used in Korea for dementia and other neurological disorders, was applied to test domains of attention, language, visuospatial function, verbal memory, and frontal executive function.¹ A blinded assessor administered the test at baseline and 6 months after treatment. Quality of life was measured via the Quality of Life in Essential Tremor Questionnaire (QUEST). Jung and colleagues' most important finding was that scores on all domains of the SNSB did not significantly decline after treatment, with statistically significant improvements in certain aspects, such as the Korean version of the Boston Naming Test and memory functions.

These results are certainly interesting and raise important points about measuring and following more than just motor scores in ET patients postoperatively. Common adverse events following MRgFUS procedures can be divided into those that occur during the procedure (nausea or dizziness) and those that occur postoperatively (paresis and gait disturbances). Sensory disturbances can

result from encroachment on the sensory relay posterior to the Vim, whereas gait and weakness occur with laterally placed lesions. Although the majority of these events are transient, some are not and can have significant impacts on functioning, notwithstanding the impact on tremor. Neuropsychological effects are even less well characterized. Speech disturbances, reported as dysarthria, are documented at an incidence from 0% to 7% in several MRgFUS ET studies.^{3,4,9} By comparison, a meta-analysis of radiofrequency thalamotomy and thalamic DBS for ET showed respective rates of approximately 4.5% and 10.3% verbal problems after unilateral treatment.² Importantly, with DBS, side effects can be improved or controlled with adjustments to stimulation parameters.

Given Jung et al.'s results and the procedure's putative advantages in visualizing lesion size and tissue temperature, it is tempting to think that MRgFUS thalamotomy is somehow unique in having a neurocognitive benefit for patients; however, the authors concede that the noted improvements could be attributable to learning effects on retest and that the relatively small sample size renders broad conclusions difficult. Nevertheless, we applaud the authors for addressing a critical, and as yet unanswered, question in the MRgFUS and surgical ET literature. Indeed, with the growing number of technologies available to treat ET, now and in the future, the side-effect profile of these interventions will be as, if not more, important as tremor improvement in determining which procedure patients and their surgeons will choose.

<https://thejns.org/doi/abs/10.3171/2017.11.FOCUS17682>

References

1. Ahn HJ, Chin J, Park A, Lee BH, Suh MK, Seo SW, et al: Seoul Neuropsychological Screening Battery-Dementia Version (SNSB-D): a useful tool for assessing and monitoring

cognitive impairments in dementia patients. **J Korean Med Sci** **25**:1071–1076, 2010

2. Alomar S, King NKK, Tam J, Bari AA, Hamani C, Lozano AM: Speech and language adverse effects after thalamotomy and deep brain stimulation in patients with movement disorders: a meta-analysis. **Mov Disord Off J Mov Disord Soc** **32**:53–63, 2017
3. Elias WJ, Lipsman N, Ondo WG, Ghanouni P, Kim YG, Lee W, et al: A randomized trial of focused ultrasound thalamotomy for essential tremor. **N Engl J Med** **375**:730–739, 2016
4. Huss DS, Dallapiazza RF, Shah BB, Harrison MB, Diamond J, Elias WJ: Functional assessment and quality of life in essential tremor with bilateral or unilateral DBS and focused ultrasound thalamotomy. **Mov Disord Off J Mov Disord Soc** **30**:1937–1943, 2015
5. Janicki SC, Cosentino S, Louis ED: The cognitive side of essential tremor: what are the therapeutic implications? **Ther Adv Neurol Disord** **6**:353–368, 2013
6. Jung NY, Park CK, Chang WS, Jung HH, Chang JW: Effects on cognition and quality of life with unilateral magnetic resonance-guided focused ultrasound thalamotomy for essential tremor. **Neurosurg Focus** **44**(2):E8, 2018
7. Schuurman PR, Bruins J, Merkus MP, Bosch DA, Speelman JD: A comparison of neuropsychological effects of thalamotomy and thalamic stimulation. **Neurology** **59**:1232–1239, 2002
8. Sinoff G, Badarny S: Mild cognitive impairment, dementia, and affective disorders in essential tremor: a prospective study. **Tremor Other Hyperkinet Mov (N Y)** **4**:227, 2014
9. Zaaroor M, Sinai A, Goldsher D, Eran A, Nassar M, Schlesinger I: Magnetic resonance-guided focused ultrasound thalamotomy for tremor: a report of 30 Parkinson's disease and essential tremor cases. **J Neurosurg** **128**:202–210, 2018

Disclosures

The authors report no conflict of interest.