Deep brain stimulation for dystonia

TO THE EDITOR: The authors of a recent paper in the Journal of Neurosurgery suggest that subthalamic nucleus (STN) deep brain stimulation (DBS) for dystonia is superior to pallidal DBS (Schjerling L, Hjermind LE, Jespersen B, et al: A randomized double-blind crossover trial comparing subthalamic and pallidal deep brain stimulation for dystonia. Clinical article. J Neurosurg 119:1537–1545, December 2013). Microelectrode recording (MER) was employed to guide lead implantation for both nuclei. A crossover design with 6 months’ stimulation at each target was planned, with blinded clinical evaluation after each stimulation period. Only 8 of the 12 included patients completed the study protocol.

Figure 2 presents a diagram of lead location within the globus pallidus internus (GPi) that is based on postoperative imaging. This figure contradicts the claim that “Most electrodes were positioned near the intended location (… posteroventral in the GPi)…” In this figure, also chosen to grace the cover of the December issue of the journal, the majority of leads lie outside the posterolateral third of the nucleus and a number are within the anterior-medial third of the internal pallidal segment.1

Despite the use of MER, the majority of pallidal leads do not appear to have reached the intended anatomical target. The conclusion that STN DBS may be more efficacious for dystonia than posteroventral GPi DBS is therefore inaccurate. However, an alternative conclusion does present itself: correct interpretation of postoperative stereotactic imaging documenting actual (as opposed to intended) lead location is an essential part of every DBS procedure.

LUDVIC ZRINZO, M.D., Ph.D., F.R.C.S. Ed. (Neuro Surg.)1,2
PATRIC BLOMSTEDT, M.D., Ph.D.,3
MARWAN HARIZ, M.D., Ph.D.1,3
1 UCL Institute of Neurology
University College London
London, United Kingdom
2 National Hospital for Neurology and Neurosurgery
London, United Kingdom
3 Umeå University
Umeå, Sweden

Disclosure

Mr. Zrinzo and Prof. Hariz report having received travel expenses and honoraria from Medtronic and St. Jude Medical for speaking at meetings. Prof. Blomstedt reports stock ownership in Mithridaticum AB.

Reference


RESPONSE: We would like to thank Zrinzo, Blomstedt, and Hariz for their interest in our article, demonstrating that the STN may be an interesting target for DBS in dystonia, in comparison with the current standard, stimulation of the GPi. In our study, we implanted DBS electrodes bilaterally in the STN and the GPi in 12 patients with dystonia. In a randomized double-blind trial, 2 periods of stimulation of either target were compared. There was clinical effect of stimulation in either target, but no statistically significant difference in the clinical effect between the 2 targets. There was a trend indicating superior effect of STN stimulation, and in some patients superior effect was obtained by simultaneous stimulation of both the STN and the GPi.

The strength of our study is that it is a randomized controlled study. The weakness of the study is, as pointed out by Zrinzo et al., that the study population was rather small. We were careful not to conclude beyond the statement that DBS of the STN in our study proved to be a safe and promising target in the treatment of patients with dystonia. We did not, as indicated by Zrinzo et al., claim that STN stimulation was superior to GPi stimulation in dystonia.

Zrinzo et al. question whether the placement of electrodes within the GPi in our study was in the correct part of the GPi for optimal effect in dystonia. We find the precise location of the electrodes within a given nucleus to be very important and therefore welcome the debate. Our study started in 2002, and since then the awareness that posteroventral placement of electrodes within the GPi is optimal has increased. In our study, postoperative MRI demonstrated that in 2 patients the electrodes passed more anteriorly, and although one of those patients had marked effect on dystonic symptoms, both patients experienced suboptimal effect compared to the effect achieved with STN placement. In all the other patients, the electrodes passed through the center or posterior portion of the GPi. It should be noted that with a classical trajectory from the coronal suture, an electrode passing through the center of the GPi terminates in the posteroventral portion (Fig. 1).

We are aware of the important article co-authored by Zrinzo and Hariz, two of the authors of this letter to the editor: “Effect of electrode contact location on clinical efficacy of pallidal deep brain stimulation in primary generalised dystonia,” published in 2007.1 In that article, it was concluded that posteroventral stimulation provided the best overall effect of dystonic symptoms, a statement that we agree with.

As this discussion reveals, correct localization of electrodes in the GPi is more complex than in the STN. This supports one of the conclusions in our article, that...
Deep brain stimulation without microelectrode recording

To The Editor: With regard to optimal targeting for deep brain stimulation (DBS) and the use of microelectrode recordings (MERs), Burchiel et al.1 (Burchiel KJ, McCartney S, Lee A, et al: Accuracy of deep brain stimulation electrode placement using intraoperative computed tomography without microelectrode recording. Clinical article. J Neurosurg 119:301–306, August 2013) and numerous other authors2 have made important contributions to the debate, but unfortunately have made serious logical errors. First, with respect to the repeated use of the term “accuracy,” the more appropriate term is “precision.” The latter refers to the reproducibility of the action and the former refers to the validity of the action; that is, how often the action results in the true condition. For example, an action can place a DBS lead in the wrong position but do it with a high degree of reproducibility. For these authors to use the term “accuracy” appropriately, they would have to assume that the initial targeting was exactly the valid target. Therein lies the second error.

The valid target is that which results in the maximum benefit and the minimum risk. It is not a foregone conclusion that the anatomical targets available on MRI or CT studies have a one-to-one correspondence to the valid target as defined. To be sure, determining the accuracy relative to the valid target is highly problematic. One option is to use a more accessible surrogate such as the physiologically defined optimal target.3 Such studies raise questions as to the variability of the physiologically defined optimal target and anatomical targets that can be visualized on MRI or CT—which relates to the third error, the presumption that the valid targets can be visualized on MRI or CT studies.

For any imaging (including electrophysiological imaging) to be useful, the target must have some contrast with adjacent nontargets in the physical modality used by the scan, be it proton density, radiodensity, or patterns of neuronal action potential discharges. Contrary to the presumption of Burchiel et al.4 and many others, the subthalamic nucleus is not the target. Rather, it is the sensorimotor region of the subthalamic nucleus and the other regions of the subthalamic nucleus that must be avoided. There is nothing on the MRI or CT studies that can differentiate the sensorimotor region from the others, whereas MERs can. This is tacitly admitted by Burchiel et al. and many others by their having to resort to coordinates relative to the anterior and posterior commissure for their targeting in the case of thalamic DBS.

The sources of error that affect accuracy and precision are multiple, including those arising from the methods and those inherent in the intrinsic biological variability. The problem is that as of yet there has been no way to differentiate the contributions made by the various sources of error. The critical issue is that improved surgical techniques may reduce one source of error but not the others, and if the biological variability is significant, then MERs are the only way currently to deal with that variability.

Most reasonable persons would agree that the use of MERs increases the risks and costs of DBS surgery. However, the use of MERs may reduce the risk of reoperation in the event of failed placement or (possibly worse) only partial benefit that makes it difficult to recommend lead revision. But the risks are only one aspect of the decision whether and how to pursue DBS. The other side of the equation is benefit, and how the surgical methodologies impact benefit. Unfortunately, this question is very difficult to answer.5 Furthermore, development of systems that will enable any neurosurgeon anywhere to provide image-guided and MER-mapped DBS lead placement by offloading the required expertise is nearly complete, thus obviating one concern about MERs reducing accessibility.

All sides of the continuing open debate have limitations. For the future resolution of this important question, premises (both implicit and explicit) and arguments must be clearly and accurately stated.

Erwin B. Montgomery Jr., M.D.
Greenville Neuromodulation Center
Greenville, PA