Neurosurgical forum
Letters to the editor

Deep Brain Stimulation


Abstract

Object. The effects of thalamic deep brain stimulation (DBS) on essential tremor (ET) and Parkinson disease (PD) have been well documented, but there is a paucity of long-term data. The aim of this study was to evaluate the long-term safety and efficacy of DBS of the ventralis intermedius nucleus (VIM) of the thalamus for PD and ET.

Methods. Thirty-eight of 45 patients enrolled at five sites completed a 5-year follow-up study. There were 26 patients with ET and 19 with PD undergoing 29 unilateral (18 ET/11 PD) and 16 bilateral (eight ET/eight PD) procedures. Patients with ET were evaluated using the Tremor Rating Scale, and patients with PD were evaluated using the Unified Parkinson’s Disease Rating Scale. The mean age of patients with ET was 70.2 years and 66.3 years in patients with PD. Unilaterally implanted patients with ET had a 75% improvement of the targeted hand tremor; those with bilateral implants had a 65% improvement in the left hand and 86% in the right compared with baseline. Parkinsonian patients with unilateral implants had an 85% improvement in the targeted hand tremor and those with bilateral implants had a 100% improvement in the left hand and 90% improvement in the right. Common DBS-related adverse events in patients receiving unilateral implants were paresthesia (45%) and pain (41%), and in patients receiving implants bilaterally dysarthria (75%) and balance difficulties (56%) occurred. Device-related surgical revisions other than IPG replacements occurred in 12 (27%) of the 45 patients.

Conclusions. Thalamic stimulation is safe and effective for the long-term management of essential and parkinsonian tremors. Bilateral stimulation can cause dysarthria and incoordination and should be used cautiously.

The authors used a multicenter study design in pooling and analysis of data from five sites. They demonstrated long-term tremor control with thalamic DBS in patients with either ET or PD. In their 26 patients with ET, the mean motor tremor score improvement in the stimulation on state compared with baseline was 46% with unilateral and 78% with bilateral stimulation. Activities of daily living (ADL) improved by 51 and 36%, respectively. In the 19 patients with PD, the Unified Parkinson’s Disease Rating Scale tremor subscore improved by 56% after unilateral and by 88% after bilateral stimulation. Cardinal PD features other than tremor did not change significantly after thalamic DBS.

Between 1997 and 2005, we implanted 143 thalamic DBS electrodes in 105 patients, including 83 with ET, 20 with tremor-predominant PD, and two with multiple sclerosis. Like Pahwa and colleagues and other authors,6,11 we have observed a good tremor response in both groups of patients. Unilateral VIM stimulation provided our patients with an excellent improvement in contralateral upper- and lower-extremity tremor and ADL.7,8 Overall, in patients with PD, 90% improvement in mean tremor scores and 47% improvement in ADL were observed 3 years after surgery.8 Both resting and postural tremor improved significantly with stimulation. In patients with ET, tremor in the contralateral upper extremity improved by 87% and in the contralateral lower extremity by 100%. Midline tremor improved by 76% with unilateral stimulation and by 84% with bilateral stimulation.7 Our surgical revision rate of 23% (excluding implantable pulse generator replacement) is close to the rate observed by Pahwa and coauthors6 (27%). The majority of revisions involved lead fractures related to the extension lead, which have been nearly eliminated since the availability of a lower-profile extension lead.

We are surprised by the relatively high percentage of side effects described in the cited article and would disagree with the authors’ recommendations against bilateral implantation due to the high potential for speech and gait difficulties. For example, in ET, the authors reported dysarthria in 63% of patients treated with bilateral stimulation and paresthesias in 56% of patients treated with unilateral stimulation. Analogous values in our series of ET patients were 27% for dysarthria and 5% for paresthesias. The frequency of side effects related to DBS observed by Pahwa and colleagues is also higher than in other reported series.2,11 Theoretically, four factors could contribute to this discrepancy. First may be operative technique. We use the same coordinates for VIM and stereotactic magnetic resonance imaging targeting with intraoperative stimulation tests. After the first 23 implanted electrodes, however, we abandoned performing routine microelectrode recording (because of its limited utility and potential for a microthalamotomy effect that can interfere with evaluation of the DBS electrode). The location of the most distant active contact in our reported series5 was 14.5 mm lateral to the midline, 7.1 mm anterior to the posterior commissure, and 0.7 mm above anterior commissure–posterior commissure plane, which corresponds with the anterior margin of the VIM. The location of active electrode contacts was not provided in the article by Pahwa and associates.6 It would be useful to know the final active contact location for comparative purposes (especially comparison of side effects) across centers.

The second reason for observed differences in side effects could relate to implantable pulse generator programming. The mean pulse width values used by Pahwa et al.6 in patients with ET and PD were almost 130 μsec and 140 μsec, respectively. Many authors, as well as our group, typically employ pulse widths in the range of 60–90 μsec.1,5,7,8,11 We can speculate that in VIM DBS, as in subthalamic nucleus stimulation,10 the increase of the pulse width causes a narrowing of the therapeutic window. The latter is defined as the difference between the intensity threshold of the stimulus for onset of the side effects and the intensity value necessary to obtain required clinical effect. It is intriguing that in subthalamic nucleus stimulation, paresthesias and dysarthria were found to be the most common side effects related to increasing pulse width (at constant amplitude and fre-
frequency), a finding that was attributed to a wider spread of current. A third possible factor, contributing to the differences in side effects after VIM DBS, could be staging of the neurosurgical procedure. We have adopted an approach that typically entails staging procedures with at least a 3-month interval (between unilateral and subsequent contralateral procedures). We believe that this approach may help to identify some patients who benefit enough from a unilateral procedure not to require a second, contralateral surgery, at least not immediately. We also expect that a time interval between two stages (if applied) will favor functional compensation and recovery of the patient and diminish negative consequences associated with a second procedure.

A final factor may relate to varying levels of scrutiny for adverse effects. While we specifically inquire regarding paresthesias and evaluate speech, perhaps the multicenter group employed a more elaborate rating scale for such adverse effects that was not published within the article.

Although our reported follow-up duration (3 years) was shorter than a portion of the series published (5 years), this difference in duration of follow up probably does not contribute substantively to the difference in results. Tremor control with VIM DBS tends to be stable over time. However, with increased duration of follow up, the number of adverse events and revisions (particularly device-related ones) could increase in our series.

In conclusion, in contrast to the authors’ recommendations, our experience (as well as that of others) suggests that bilateral stimulation, perhaps in a staged approach, is an effective and safe procedure for appropriate patients.

**References**


**RESPONSE:** Slowinski and colleagues indicate that they are surprised by the higher percentage of side effects reported in our article compared to their series of thalamic DBS patients. There are several points not addressed by Slowinski et al. that may account for this discrepancy. The subjects in our study were operated on between 1993 and 1997, and were among the first patients to receive thalamic DBS in the US. Because this study was done as an investigational study of DBS for tremor under regulation of the Food and Drug Administration (FDA), a very detailed accounting of adverse events was required. In fact, any adverse event that occurred during the conduct of the trial was noted even if that particular effect, such as paresthesia or dysarthria, later resolved with additional programming. As indicated in the letter of Slowinski et al., their patients were operated on from 1997 to 2005, and were therefore not part of an investigational FDA-regulated study requiring such thorough accounting of adverse events.

Slowinski and colleagues state that they disagree with our recommendation against bilateral implantation. It should be clarified that we did not recommend against bilateral DBS. We suggested that for ET patients, bilateral thalamic DBS should be considered with caution because of potential adverse events, and that thalamic DBS for PD is not generally recommended as a unilateral or bilateral procedure due to the progression of other PD symptoms not well controlled by thalamic DBS.

Four factors were mentioned by Slowinski et al. that they felt could account for the higher percentage of adverse events in our study. The first is related to the location of the contacts. This information was not collected as part of our study and was therefore not reported. They also raise a point about the parameter settings, particularly the pulse widths that we reported. As mentioned previously, this study involved the first patients receiving thalamic DBS in the US; at that time, the most appropriate parameter settings had not yet been determined. In addition, our study was a multicenter study, which may have increased the range of programming values selected, given that no guidelines for the most appropriate settings were available. However, it should be clarified that the mean pulse width for ET subjects in our study was 130 μsec only for the second surgical side; for unilateral procedures and the first side of bilateral procedures, it was 111 μsec. The bilateral procedures in our study were also all staged, with the second side not being operated on until at least 6 months after the first side. An additional, more elaborate rating scale for adverse events was not used in this study.

In summary, we believe that the differences between our experience and the Mayo Clinic experience are primarily...