Thalamic deep brain stimulation for the treatment of head, voice, and bilateral limb tremor

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Object. In published series of patients who undergo deep brain stimulation (DBS) of the thalamus the effects of unilateral stimulation on contralateral limb tremor have been reported. The authors detail their experience with bilateral thalamic DBS in the treatment of head, voice, and bilateral limb tremor and compare it with earlier studies of unilateral stimulation.

Methods. Twenty-three patients (six with Parkinson’s disease, 15 with essential tremor, and two with multiple sclerosis) underwent 19 bilateral DBS procedures (nine staged, 10 simultaneous) and four procedures contralateral to thalamotomy to control tremor of the head in 10, voice in seven, and limbs in 20 patients. Limb tremor improvement was graded as follows: 4, no tremor; 3, stress-induced tremor; 2, functional improvement; 1, no functional improvement; and 0, persistent tremor. Improvement of head or voice tremor was graded as follows: 4, greater than 75%; 3, between 50% and 75%; 2, between 25% and 50%; 1, less than 25%; and 0, no improvement. The mean follow-up period was 10 months.

Twenty-two patients (96%) demonstrated improved tremor at the last follow-up review. Of 20 patients with bilateral limb tremor, 17 (85%) improved to Grades 3 and 4, two patients (10%) with multiple sclerosis improved to Grade 3, and one (5%) exhibited tremor recurrence 8 months later. Nine (90%) of 10 patients with severe head tremor improved to Grades 4 or 3. Seven patients (30%) developed dysarthria, and seven (30%) developed disequilibrium; symptoms reversed in the majority of patients after the stimulation parameters were changed. One patient (4%) developed mild memory decline. There were no deaths.

Conclusions. The following findings are reported: 1) bilateral thalamic DBS and stimulation contralateral to thalamotomy are safe; 2) staging the procedure does not reduce the risk of dysarthria or gait disequilibrium; and 3) head and voice tremor are primary indications for bilateral DBS.

Keywords • deep brain stimulation • Parkinson’s disease • thalamotomy • tremor

Deep brain stimulation (DBS) of the ventralis intermedius nucleus (Vim) is an effective treatment of limb tremor accompanying Parkinson’s disease, essential tremor, and multiple sclerosis. In most studies of DBS of the Vim, the results of unilateral thalamic stimulation for the control of contralateral limb tremor have been reported. Deep brain stimulation is approved by the United States Food and Drug Administration for the unilateral implantation of electrodes in the Vim to control tremor of the contralateral limb.

Some patients require bilateral thalamic surgery to control axial tremor or tremor in both upper extremities. For these patients, bilateral thalamotomy can be performed, but is generally discouraged because of its association with a relatively high risk of postoperative dysarthria, disequilibrium, and cognitive deficits. Although bilateral DBS is currently advocated for these patients, published data on the safety of this procedure or of DBS contralateral to thalamotomy are limited. In addition, data are scarce on the effect of thalamic DBS on head and voice tremor. This study addresses both issues.

Clinical Material and Methods

Patient Population

From September 1997 through September 1998, 23 consecutive patients underwent bilateral thalamic surgery to control tremor, and they constitute the population of this study. All patients signed informed consent forms. Tremor was associated with Parkinson’s disease in six patients, essential tremor in 15, and multiple sclerosis in two. Nine patients underwent staged bilateral DBS procedures 3 to 8 months apart, 10 underwent simultaneous procedures, and four underwent a thalamotomy procedure followed by contralateral DBS 7 to 15 months later. The indications for surgery were tremor of the head in 10 patients, voice in seven, and bilateral limbs in 20.

Surgical Technique

A Cosman-Roberts-Wells (CRW) halo frame (Radiionics, Burlington, MA) was fixed to the patient’s skull roughly parallel to the anterior commissure (AC)—posteri-
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or commissure (PC) plane. After mounting the CRW computerized tomography (CT) localizer onto the CRW frame, 3-mm-thick axial CT scans were obtained parallel to the AC–PC plane. The spatial coordinates of the localizer rods, AC, PC, and a point on the falx were obtained using the CT scanner software (General Electric, Milwaukee, WI). The target was the Vim, which was localized as follows: 25% of the AC–PC distance anterior to the PC, 11.5 mm lateral to the wall of the third ventricle, and at the intercommissural line. The spatial coordinates of the thalamic target were calculated by using personal computer software that corrects for frame tilts.

With the patient receiving local anesthesia, a 3-mm twist-drill hole was created, through which a brain cannula was inserted 12 mm short of the target at a trajectory relative to the AC–PC plane (85° in the coronal plane and 60° in the sagittal plane). A 1.1 × 2-mm electrode (Radiomics) was advanced to the target, which was stimulated at 2, 50, and 100 Hz. The electrode was then replaced by a quadripolar deep brain stimulator (Activa; Medtronic, Minneapolis, MN), implanted such that the distal electrode was positioned beneath the thalamic target. Multiple combinations of bipolar stimulation were performed at a frequency of 185 Hz and a pulse width of 60 msec. The final position of the deep brain electrode was determined by the clinical findings of tremor arrest and proximity to the sensory thalamus and the internal capsule, as described by several investigators. The electrode was fixed to the skull, using a plating system previously described. After closure of the skin incision, the CRW headframe was removed, the patient was intubated, and general anesthesia was administered. The scalp wound was reopened and the deep brain electrode was attached to an extension wire, which was connected to the pulse generator (ITREL II; Medtronic) implanted inferior to the clavicle. When bilateral deep brain electrodes were implanted, each was connected to a separate pulse generator. The pulse generator was programmed 10 days postimplantation or when tremor recurred in patients who developed a microthalamotomy effect.

Postoperative Assessment

Improvement in limb tremor was graded as follows: 4, no tremor; 3, only stress-induced tremor; 2, functional improvement; 1, no functional improvement; and 0, persistent tremor. Head and voice tremor improvement was graded as follows: 4, greater than 75% improvement; 3, greater than 50% improvement; 2, greater than 25% improvement; 1, less than 25% improvement; and 0, no improvement. Voice tremor was evaluated for articulation of specific words and sentences and the ability to maintain an “aah” sound for 5 seconds. The mean follow-up period was 10 months. Statistical significance, calculated on the basis of the Fisher exact test, was set at a probability value of less than 0.05.

Results

Tremor Control

Twenty-two patients (96%) demonstrated improved tremor at the last follow-up review. Seventeen (85%) of 20 patients with bilateral limb tremor improved to Grade 4 (eight patients) or Grade 3 (nine patients), two patients (10%) with multiple sclerosis improved to Grade 2, and one patient (5%) with Parkinson’s disease improved to Grade 4 initially but lost tremor control 8 months later, 2 weeks after implantation of a contralateral deep brain electrode. Nine (90%) of 10 patients with severe head tremor improved to Grade 4 (five patients) or Grade 3 (four patients), and the other patient improved to Grade 2. Six (86%) of seven patients with voice tremor improved to Grade 3 and the remaining patient improved to Grade 2.

Postoperative Complications

Dysarthria developed in seven patients (30%) after programming of the pulse generator: in three (33%) of nine patients who underwent staged DBS, in three (30%) of 10 patients who underwent simultaneous DBS, and in one (25%) of four patients who underwent the procedure contralateral to thalamotomy. The difference was not statistically significant. Postoperative CT scans demonstrating the absence of hemorrhage or infarction were obtained in all patients. In five of the seven patients, dysarthria resolved after reprogramming, with good control of tremor. In two patients, dysarthria resolved after reprogramming, but tremor control declined. These two patients preferred the initial program, which produced mild dysarthria but good tremor control.

Disequilibrium, manifested as a feeling of being unstable on the feet, frequent falls, swaying to one side during walking, losing balance during turning, or loss of the ability to perform tandem walking, developed in seven patients (30%) after programming: in three (33%) of nine patients who underwent staged DBS, in three (30%) of 10 patients who underwent simultaneous DBS, and in one (25%) of four patients who underwent the procedure contralateral to thalamotomy. The difference was not statistically significant. Postoperative CT scans demonstrating the absence of hemorrhage or infarction were obtained in all patients. In two of the seven patients the gait imbalance resolved after reprogramming, with good tremor control. In three patients, gait imbalance resolved after reprogramming, but tremor control declined; these three patients preferred the initial program, which produced good tremor control with mild gait imbalance (for example, unsteadiness during sudden movements, worsening of tandem walking, mild swaying to one side, but without falling). In two patients (one undergoing staged DBS, the other a procedure contralateral to thalamotomy), gait imbalance improved yet persisted despite multiple changes in the stimulation parameters. These two patients swayed mildly to one side during walking, could not perform tandem walking, and reported frequent falls. Both patients occasionally use a cane for ambulation.

One patient (4%) developed mild short-term memory loss after simultaneous bilateral DBS. Postoperative CT scans did not demonstrate intracranial hemorrhage or obvious infarction. It was not clear whether memory deterioration was the effect of stimulation or microthalamotomy, because the patient refused a change in the stimulation parameters, which had achieved good tremor control. Four patients (20%) experienced a mild shock in the infra-
clavicular area when the pulse generator was turned on, but did not require revision. None of the patients died, and none had intracranial hemorrhage, infarction, or infection.

Discussion

This study addresses two issues: one is the safety of bilateral thalamic surgery, including staged bilateral DBS, simultaneous bilateral DBS, and DBS contralateral to a previous thalamotomy. The second issue is the effectiveness of this procedure in controlling tremor of the head and voice. The following discussion provides an analysis of each of these issues.

Bilateral Thalamic Surgery

Bilateral thalamic ablative surgery (that is, bilateral thalamotomy) has generally been discouraged because of its association with a relatively high risk of postoperative speech, balance, and cognitive deficits. Because the effect of stimulation on neural tissue is generally reversible, nonablative bilateral thalamic surgery is preferred for patients who experience functional limitations related to tremor that involves both upper extremities. These patients can undergo thalamotomy or DBS to control the dominant or most affected limb, followed a few months later by thalamotomy or DBS to control tremor of the contralateral limb. Alternatively, simultaneous DBS can be performed; however, data are scarce comparing the safety of staged versus simultaneous bilateral procedures and of bilateral compared with DBS contralateral to thalamotomy. Most information is obtained from studies by Benabid, et al., who reported postoperative dysarthria in 14 (28%) of 51 patients in France who underwent bilateral DBS and in four (40%) of 10 patients who underwent DBS contralateral to a previous thalamotomy. Postoperative disequilibrium occurred in six (12%) of 51 patients who underwent bilateral DBS and in three (30%) of 10 patients who underwent DBS contralateral to a previous thalamotomy. Although these complications usually subsided after the programming parameters were changed, Benabid, et al., concluded that bilateral DBS was safer than DBS contralateral to a previous thalamotomy. No analysis was provided comparing staged and simultaneous bilateral DBS.

In our series of 19 patients who underwent bilateral DBS, four patients (21%) developed postoperative dysarthria, four (21%) developed postoperative disequilibrium, and two (11%) developed both dysarthria and disequilibrium. The risk of dysarthria in our series is similar to that reported by Benabid, et al., but the risk of disequilibrium is higher. We believe that the difference reflects our inclusion of any postoperative gait worsening as a complication, even if it was considered subtle by the patient; however, we cannot rule out the possibility of a different intracranial electrode placement. In contrast with the results of Benabid, et al., our preliminary experience with four patients who underwent DBS after a previous thalamotomy has been favorable, with a risk of dysarthria and disequilibrium similar to that associated with unilateral thalamic DBS. However, more patients are required before this issue is resolved.

In our series, staged and simultaneous bilateral DBS had similar complication rates. There are advantages and disadvantages for each procedure. Simultaneous bilateral DBS promptly controls the tremor of both limbs, avoiding a second surgery with its associated potential perioperative complications. On the other hand, staged bilateral DBS avoids the risks of potential simultaneous bilateral intracranial hemorrhage or infection. In addition, staging bilateral DBS allows patients the opportunity to evaluate the need for surgical control of tremor of the untreated limb, thus avoiding potential complications associated with bilateral thalamic surgery. In our experience, however, most patients who had bilateral upper extremity tremor and who underwent unilateral thalamic surgery returned for surgical control of the untreated side. The majority of patients who developed complications such as mild dysarthria and disequilibrium chose to keep the same stimulation parameters if tremor control could not be achieved otherwise.

In our series, one patient (4%) developed short-term memory decline after simultaneous DBS, but refused to change the stimulation parameters that had achieved good tremor control. It is not clear whether this complication resulted from a bilateral microthalamotomy effect or from stimulation of both thalamic regions. Benabid, et al., reported the absence of gross neuropsychological deficits after bilateral DBS; however, a detailed postoperative neuropsychological evaluation demonstrated a slight decline in verbal performance when the left Vim was stimulated, and in spatial performance when the right Vim was stimulated. We cannot comment on these findings, because we did not perform detailed postoperative neuropsychological testing.

Head and Voice Tremor

In a recent national interactive satellite broadcast evaluating thalamic DBS for tremor control (Current and Emerging Therapies in Tremor Management, Medtronic, October 1, 1998), tremor of the voice was not considered a primary indication for surgery. This recommendation was based on the findings of Carpenter, et al., who reported improvements of 1 to 3 points on a 5-point scale in four of seven patients who underwent surgery to control hand tremor but who also had tremor of the voice. Based on our experience, we disagree with this recommendation and consider severe voice tremor a primary indication for bilateral DBS. In our study, six (86%) of seven patients who had severe voice tremor had greater than 50% improvement after bilateral simultaneous DBS. Although voice tremor did not totally subside in any patient, all seven patients reported the ability to carry on conversations postoperatively that had not been possible preoperatively. The difference in the results may be related to the type of surgery. In the series reported by Carpenter, et al., only two of seven patients underwent bilateral DBS, with the most improvement occurring in one of these patients. Based on the bilateral nature of voice control,21,26 we recommend simultaneous bilateral DBS for patients who experience significant voice tremor.

Similar to voice tremor, head tremor is usually the result of a bilateral pathological intracranial process; therefore, bilateral DBS is expected to yield better results than unilateral treatment. Data on this subject are scarce in the literature. In our series, nine (90%) of 10 patients with
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head tremor experienced greater than 50% improvement after simultaneous bilateral DBS (seven patients), staged bilateral DBS (one patient), and stimulation contralateral to a previous thalamotomy (one patient). One patient with multiple sclerosis had greater than 75% improvement in head tremor after DBS electrodes were implanted contralateral to a previous thalamotomy, but this had decreased to 25% 1 year later. Although head tremor did not subside totally in any patient, all 10 considered the improvement in their head tremor to be significant. Based on our experience, we consider severe head tremor a primary indication for surgery and recommend simultaneous bilateral DBS for its treatment.

Other Potential Intracranial Targets

In several series the effects of pallidotomy, pallidal stimulation, and stimulation of the subthalamic nucleus on the tremor of the contralateral limb in patients with Parkinson’s disease have been reported.30 Pallidotomy improves contralateral limb tremor by more than 50% in the majority of patients, but rarely abolishes it.31 Bilateral pallidotomy, like bilateral thalamotomy, is associated with an increased risk of dysarthria.32 Alternatively, bilateral pallidal stimulation can be performed with good, but inferior tremor control compared with Vim stimulation in patients with tremor-predominant Parkinson’s disease.3,2,14,23 Subthalamic nucleus stimulation effectively controls contralateral limb tremor in patients with Parkinson’s disease, with a success rate similar to that achieved by Vim stimulation, and with the added benefit of improved bradykinesia and rigidity.18,19,28 The early experience with bilateral subthalamic nucleus stimulation suggests that this may be a better target for tremor control than Vim stimulation in patients with tremor-predominant Parkinson’s disease.18 Currently, Vim stimulation remains the best treatment for patients with essential tremor.

Conclusions

On the basis of our experience, we conclude the following: 1) that bilateral DBS is safe; 2) that DBS contralateral to a previous thalamotomy is safe; 3) that when bilateral DBS is performed, staging the procedure does not reduce postoperative complications; 4) that although complications such as dysarthria and disequilibrium are usually reversed by changing stimulation parameters, some patients may thus lose good tremor control, and most will choose stimulation parameters that best control tremor despite persistent mild dysarthria and disequilibrium; and 5) that severe head and voice tremor are primary indications for simultaneous bilateral Vim DBS.

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