Bilateral thalamic deep brain stimulation for the treatment of head tremor

Report of two cases

CAGLAR BERK, M.D., AND CHRISTOPHER R. HONEY, M.D., D.PHIL., F.R.C.S.(C)

Surgical Centre for Movement Disorders, University of British Columbia, Vancouver, British Columbia, Canada

Isolated head tremor is rare, but can be disabling. The authors’ experience with the treatment of limb tremor due to essential tremor led them to consider using bilateral thalamic deep brain stimulation (DBS) in two patients presenting only with disabling head tremor.

One patient exhibited no peripheral tremor and the other displayed only a slight upper-limb tremor. Both patients underwent placement of units that apply simultaneous bilateral thalamic DBS. Surgical targets were verified by using intraoperative macrostimulation, and the stimulators were implanted during the same surgery. Patients were videotaped preoperatively and at 2, 4, 6, and 9 months postoperatively during periods in which the stimulators were turned on and off. Videotapes were randomized and rated for resting, postural, and action tremors according to the Fahn clinical rating scale for tremor. Because this scale is not designed for head tremor, the patients were also evaluated on the basis of a functional scale that reflected their quality of life and the amount of disability caused by head tremor.

Both patients experienced no tremor after their stimulators were turned on and properly adjusted at the 6th postoperative week. The patients were followed for a total of 9 months and results remained stable throughout this period. No complications were encountered.

Bilateral thalamic DBS appears to be an effective and safe treatment for isolated head tremor in patients with essential tremor. The authors present a scale for the functional assessment of head tremor.

Case Report

Case 1

This 43-year-old right-handed woman began to experience head tremor when she was 34 years of age. It began as a several-week episode of head shaking that spontaneously disappeared. The head shaking recurred when she was 39 years old and slowly progressed in both frequency and intensity. At presentation, she displayed a no–no type of head tremor, but no tremor in her upper limbs. She had received several botox injections in her neck muscles without benefit, and her current medication regimen consisted of propranolol 120 mg/day and primidone 125 mg/day. The patient’s tremor increased with stress and was responsive to alcohol. It interfered with her work because it caused eye-strain while she worked at a computer and social embarrassment while interacting with clients. We believe she has essential tremor (at her latest follow-up examination she displayed a subtle right-arm tremor when the stimulator was turned off).

Magnetic resonance images did not reveal any structural abnormalities.

Case 2

This 41-year-old right-handed woman first experienced tremors when she was 4 years of age. The tremors progressed in frequency and intensity throughout her life. In this case there was a strong family history of essential tremor.
or affecting a great uncle and the patient’s son. She presented with the following symptoms: a no–no head tremor, voice tremor, a left upper-limb tremor, and a right upper-limb tremor that only occurred in response to stress. The tremors were responsive to alcohol and all were worsened by stress. The limb tremor occurred with posture and intention, but was absent during rest. The patient’s head tremor resulted in headaches, eye strain, and fatigue, causing her to stop working as a computer administrator. Her current medication regimen consisted of propranolol 80 mg/day and primidone 125 mg/day.

Similar to Case 1, magnetic resonance images did not reveal any structural abnormalities.

Surgical Procedure

Both patients were admitted to the hospital on the morning of surgery and discharged home the following day. Thalamic targets were calculated on the basis of axial computerized tomography scans obtained after the patient’s head had been placed within a stereotactic frame (CRW-FN; Radionics, Inc., Burlington, MA). Coordinates for the Vim nucleus were selected at the vertical level of the line connecting the anterior and posterior commissures, 10 mm lateral from the edge of the third ventricle, and one third to one quarter the distance between the posterior and anterior commissures. Placement of electrodes (lead model 3475; Medtronic, Inc., Minneapolis, MN) was performed after a local anesthetic agent had been given to the patient and the final position had been confirmed by macroelectrode stimulation. We implanted one stimulator in the nondominant side first and inserted another in the contralateral side during the same operation. After general anesthesia had been induced, the impulse generator (Kineta model 3746; Medtronic, Inc.) was implanted. The patients received intravenous antibiotic medications (cefazolin 1 g every 8 hours) for 24 hours before they were discharged from the hospital. Stimulation was begun 6 weeks later.

Preoperative and Postoperative Assessment

Patients were evaluated preoperatively and at 2, 4, 6, and 9 months postoperatively. At these times videotapes of the patients’ movements were randomized and scored for resting, postural, and action tremor on a scale of increasing severity ranging from a score of 0 to a score of 4. Voice tremor was also scored on a scale ranging from 0 to 4. Head tremor was assessed using our proposed scale (Table 1) of increasing severity, which also ranged from 0 to 4.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
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<tbody>
<tr>
<td>0</td>
<td>no tremor</td>
</tr>
<tr>
<td>1</td>
<td>tremulous feeling</td>
</tr>
<tr>
<td>2</td>
<td>mild tremor; tremor is occasional &amp; does not interfere w/ social or professional activities</td>
</tr>
<tr>
<td>3</td>
<td>moderate tremor; tremor is constant &amp; occasionally interferes w/ social or professional activities</td>
</tr>
<tr>
<td>4</td>
<td>severe tremor; tremor always interferes w/ social or professional activities and activities of daily living (feeding, grooming, &amp; so forth)</td>
</tr>
</tbody>
</table>

Voice tremor is manifested by rhythmic alterations in the pitch and volume of vowel sounds, making these sounds usually reduced.18 Although life expectancy in patients with Parkinsonian tremor in August 1997. At least 4000 patients have undergone stimulator implantation in North America, and approximately 10,000 patients around the world.41 Reported benefits of reduced limb tremor in response to thalamic DBS for patients with essential tremor vary from 55 to 93%.1,10,16,22,31 Although head tremor is a common finding in cases of advanced essential tremor, it is usually not considered a sole indication for surgical treatment. Essential tremor usually affects the head, neck, voice, and upper extremities. It does not affect the eyes and is rarely symptomatic in the lower extremities.6 Head tremor may be horizontal (no–no) or vertical (yes–yes), and spontaneous fluctuations between directions are occasionally seen. Looking downwards may exacerbate the tremor. Voice tremor is manifested by rhythmic alterations in the pitch and volume of vowel sounds, making these sounds difficult to sustain.15 Although life expectancy in patients with essential tremor is normal, the sensitivity of life is certainly reduced.

Propranolol and other β-adrenergic blockers are clearly effective in suppressing essential tremor. Primidone is also effective, but sedation and dys equilibrium are common side effects.6,11,15 Failure to respond to one of these drugs were also evaluated for cognitive changes by undergoing a battery of neuropsychological tests preoperatively and at 2 and 4 months postoperatively (data not presented).

Results

The scores presented in Table 2 were obtained preoperatively and at the latest (9 month) postoperative assessment. Both patients demonstrated complete resolution of their head tremor in response to bilateral thalamic DBS. The benefits were seen at the first follow-up examination and remained stable throughout the follow-up period. A microthalamotomy effect from the electrode implantation was observed during surgery in both cases. Head tremor was temporarily reduced in both patients for several weeks. There have been no adverse effects such as paresthesia, dysarthria, dysphagia, infection, or cognitive changes.

Discussion

Unilateral thalamic DBS was approved by the United States Food and Drug Administration for essential and Parkinsonian tremor in August 1997. At least 4000 patients have undergone stimulator implantation in North America, and approximately 10,000 patients around the world.41 Reported benefits of reduced limb tremor in response to thalamic DBS for patients with essential tremor vary from 55 to 93%.1,10,16,22,31 Although head tremor is a common finding in cases of advanced essential tremor, it is usually not considered a sole indication for surgical treatment.

Functional scale for head tremor

<table>
<thead>
<tr>
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<th>Description</th>
</tr>
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<tbody>
<tr>
<td>0</td>
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<td>4</td>
<td>severe tremor; tremor always interferes w/ social or professional activities and activities of daily living (feeding, grooming, &amp; so forth)</td>
</tr>
</tbody>
</table>

Tremor scores for the worst affected upper limb, voice, and head preoperatively and 9 months postoperatively with DBS turned on* |

<table>
<thead>
<tr>
<th></th>
<th>Case 1</th>
<th>Case 2</th>
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<tbody>
<tr>
<td></td>
<td>Preop</td>
<td>9 Mos</td>
</tr>
<tr>
<td>resting</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>postural</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>action</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>voice</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>head</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>

* Scores for head tremor are based on the scale shown in Table 1; other scores are based on the Fahn clinical rating scale.
Bilateral thalamic DBS for treatment of head tremor

does not preclude a beneficial response to the other, and some patients may require a combination of the two agents.\textsuperscript{6,15} It is estimated that less than 50% of patients with essential tremor who present for treatment can be adequately treated with currently available medications and, in the long run, many patients become surgical candidates.\textsuperscript{12}

In many clinical studies chronic high-frequency stimulation of the thalamus has been shown to reduce essential tremor.\textsuperscript{1–4,10,13,16,21,27} Deep brain stimulation offers several potential benefits over traditional ablative stereotactic surgery. Thalamic stimulation and thalatomy are almost equally effective for tremor suppression, but thalamic DBS carries less risk of peri- and postoperative morbidity and results in greater improvement in function.\textsuperscript{9,25,29,31} Deep brain stimulation can be performed bilaterally without significant risk of morbidity,\textsuperscript{23} whereas bilateral thalatomy is associated with a high prevalence of speech and cognitive impairment.\textsuperscript{1,17,19,20,26,30} We did not observe any of these possible side effects in either patient. This may be due to the low amplitude settings (1–2.5 V/185 Hz), which were sufficient to control the head tremor. Initial paresthesia, which occurred when the stimulator was turned on and which subsided within seconds, was not considered to be a side effect. Optimal targeting is crucial to avoid possible side effects from the high stimulator amplitudes needed to compensate for suboptimal lead placement.

The very similar results of lesioning and high-frequency stimulation do not prove that DBS inactivates cells. The mechanism by which high-frequency electrical stimulation inhibits tremor is unknown. Proposed mechanisms include the following: 1) stimulation of γ-aminobutyric acid inhibitory cells in the thalamus that normally suppress tremor generators; 2) a nonphysiological synchronous discharge that is incomprehensible to target neurons; and 3) a depolarization block.\textsuperscript{24}

Chronic high-frequency stimulation of the thalamus has been used to treat tremor caused by Parkinson disease, essential tremor, and others. Although other sites can be successfully stimulated in Parkinson disease (for example, the pallidum or the subthalamic nucleus), the thalamus is the only target accepted for essential tremor. The motor thalamus can be divided into three distinct regions according to its afferent pathways. There is a cerebellar receiving area (Vim nucleus) with afferents from the deep cerebellar nuclei, a pallidal receiving area (ventral oral posterior and ventral oral anterior nuclei) with afferents from the motor (posterolateral) area of the pallidum via the ansa lenticularis and fasciculus reticularis, and a nigral receiving area with afferents from the substantia nigra pars reticulata. Tremor cells can be easily identified using microelectrode recordings and are found within the Vim nucleus and also the ventral oral posterior nucleus to a lesser extent. Surgical lesioning or long-term high-frequency stimulation in the region in which tremor cells are recorded correlate with long-term tremor relief. Therefore, the Vim nucleus seems to be a rational target to control tremor, either by lesioning or by exerting DBS.

The multicenter European trial demonstrated that unilateral DBS did not significantly improve head and voice tremor at 1 year postimplantation, although there was a trend toward improvement.\textsuperscript{10} Because voice and head tremor are usually the result of a bilateral process, bilateral DBS would be expected to be more effective.\textsuperscript{9,21,32} This has been confirmed in a few series.\textsuperscript{19,21,28} There is a small cohort of patients in whom head tremor is the only disabling symptom.\textsuperscript{12,21} We believe that these patients can benefit from bilateral thalamic DBS and substantiate this belief by presenting two patients who are free from symptoms following this procedure. Simultaneous bilateral thalamic DBS appears to be a safe and highly effective treatment for patients in whom head tremor is the presenting or only symptom.

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Address reprint requests to: Christopher R. Honey, M.D., D.Phil., Surgical Centre for Movement Disorders, University of British Columbia, Suite 325, 700 West 10th Avenue, Vancouver, BC, V5Z 4E5, Canada. email: choney@interchange.ubc.ca.