The symptomatic and functional outcome of stereotactic thalamotomy for medically intractable essential tremor

MARC S. GOLDMAN, M.D., J. ERIC AHLSKOG, M.D., PH.D., AND PATRICK J. KELLY, M.D.

Departments of Neurosurgery and Neurology, Mayo Clinic, Rochester, Minnesota

Eight patients with medically refractory disabling essential tremor underwent ventralis lateralis (VL) thalamotomies; the procedure was unilateral in seven cases and bilateral (staged) in the other. Contralateral tremor remained absent or markedly reduced in all patients at the time of the most recent follow-up examinations, at a mean of 17.3 months after surgery. Disability was determined by a modified form of an established rating scale for tremor, and was reduced from a mean score of 21.1 (moderate grade) to 3.9 (absent grade) (p < 0.001). Interestingly, voice tremor was abolished or significantly improved in 71.4% of patients with preoperative voice tremor. This feature has not been reported previously. Persistent surgical morbidity was limited to two patients with mild dysarthria and one with a mild cognitive impairment. There were no surgically related deaths. It is concluded that stereotactic VL thalamotomy is a treatment option for medically intractable disabling essential tremor.

KEY WORDS • tremor • thalamotomy • stereotaxis • movement disorder • voice tremor

Essential tremor is defined as a postural and action tremor that is absent when the patient is at rest and is not associated with other neurological deficits. It affects more than 5 million individuals over the age of 40 years in the United States. For a small percentage of patients, the tremor is severe, debilitating, and refractory to medical management. Stereotactic surgical therapy for movement disorders has been accepted as a reasonable option for selected cases since the 1960's. However, studies of objective symptomatic outcome following ventralis lateralis (VL) thalamotomy in essential tremor are not commonly reported, and functional outcome has not been investigated previously.

Unlike other movement disorders where functional improvement may not accompany symptomatic improvement after thalamotomy, essential tremor is a monosymptomatic disorder that provides a unique opportunity for significant functional improvement with effective treatment. This study explored the symptomatic and functional impact of thalamotomy on patients with unequivocal severe essential tremor.

Clinical Material and Methods

Case Material

Stereotactic VL thalamotomies were performed on 73 patients at the Mayo Clinic between September, 1984, and March, 1991, for the treatment of medically refractory movement disorders. Eight of these patients underwent stereotactic thalamotomies for disabling essential tremor, including one patient who was treated by staged bilateral stereotactic thalamotomies for bilateral severe tremor. One patient was excluded from analysis; the VL thalamotomy was aborted because evoked responses in the ventralis posterior (VP) thalamus could not be obtained during attempts at electrophysiological localization. The clinical characteristics of each patient are listed in Table I.

Patient Evaluation

The mean age of the eight patients at the time of surgery was 46.6 years (range 18 to 69 years). Although women were not excluded, all patients were men. The age at onset of tremor ranged from 5 to 60 years (mean 25.5 years) and the preoperative duration of tremor ranged from 5 to 55 years (mean 21.1 years). Positive family histories of tremor were present in all cases where obtainable (one patient was adopted). Stereotactic VL thalamotomies were performed on the left side in six patients and on the right side in one; one patient received staged bilateral thalamotomies.

General neurological examinations, psychometric evaluations, speech pathology evaluations, and neuro-radiological studies (computerized tomography (CT) or magnetic resonance (MR) imaging) were performed.
Stereotactic thalamotomy

TABLE 1
Clinical characteristics of eight patients referred for thalamotomy with essential tremor

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Side of Lesion</th>
<th>Family History</th>
<th>Tremor*</th>
<th>Follow-Up Period (mos)</th>
<th>Morbidity</th>
<th>Disability Score†</th>
<th>Preop</th>
<th>Postop</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>33, M</td>
<td>lt</td>
<td>?</td>
<td></td>
<td>+2, +3</td>
<td>0 0</td>
<td>1</td>
<td>hyposthesia</td>
<td>22</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>69, M</td>
<td>lt</td>
<td>+</td>
<td></td>
<td>+2</td>
<td>0 0</td>
<td>3</td>
<td>attention deficit</td>
<td>21</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>68, M</td>
<td>lt</td>
<td>+2, +3</td>
<td></td>
<td></td>
<td>0 0, +1</td>
<td>3</td>
<td>attention deficit</td>
<td>21</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>44, M</td>
<td>lt</td>
<td>+</td>
<td></td>
<td>+2</td>
<td>0 0</td>
<td>50</td>
<td>ataxic dysarthria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4‡</td>
<td>45, M</td>
<td>rt</td>
<td>+</td>
<td></td>
<td>+3</td>
<td>0 0, +1, +2</td>
<td>43</td>
<td>ataxic dysarthria</td>
<td>19</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>22, M</td>
<td>lt</td>
<td>+</td>
<td></td>
<td>+2</td>
<td>0 0, +1</td>
<td>4</td>
<td>anomic dysphasia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>68, M</td>
<td>lt</td>
<td>+3</td>
<td></td>
<td>0 0, +1</td>
<td>8</td>
<td>23</td>
<td>verbal cognitive deficit</td>
<td>22</td>
<td>5</td>
</tr>
<tr>
<td>7</td>
<td>18, M</td>
<td>rt</td>
<td>+</td>
<td></td>
<td>+3</td>
<td>0 0</td>
<td>43</td>
<td>—</td>
<td>23</td>
<td>10</td>
</tr>
<tr>
<td>8</td>
<td>51, M</td>
<td>lt</td>
<td>+2, +3</td>
<td></td>
<td>0 0</td>
<td>1</td>
<td>20</td>
<td>verbal cognitive deficit</td>
<td>60</td>
<td>0</td>
</tr>
</tbody>
</table>

* Tremor: grade 0 = absent; +1 = mild; +2 = moderate; +3 = marked; +4 = very severe; immediate = immediately postoperative; follow-up = at subsequent follow-up examination(s).
† Tremor disability score: no disability = 0; maximum severe disability = 28.
‡ Second of staged bilateral thalamotomies.
§ This patient underwent disability evaluation after the second of his staged bilateral procedures.

Preoperatively and repeated during the 1st postoperative week. All of these measures were repeated 3 months postoperatively and at successive follow-up visits as circumstances permitted. Videotaped documentation of the tremor and selected segments of the neurological examination were performed preoperatively and at each postoperative evaluation. Tremor was graded on a four-point scale (0 = absent; 4 = very severe) with respect to each component: rest, static, action, and terminal accentuation.

Preoperative and postoperative disability was graded in seven patients according to a modified form of the clinical rating scale for tremor developed by Fahn, et al. One patient was unavailable for completion of his disability evaluation. The disability scale represented the composite score of a four-point grading system (0 = no disability; 4 = maximum severe disability) which evaluated specific areas of function: handwriting, speaking, solid and liquid feeding, hygiene, dressing, and working. The maximum possible score (reflecting the maximum disability) was 28. From this score, disability could be graded as absent (0 to 7 points), mild (8 to 14 points), moderate (15 to 21 points), or severe (22 to 28 points).

Postoperative neurological morbidity was defined as a new deficit or worsened preoperative deficit. If present, this was labeled transient or persistent depending on its existence at the most recent follow-up examination.

Surgical Procedure

The stereotactic thalamotomy procedure has been described in detail previously. Briefly, patients were initially placed in a stereotactic head frame and underwent stereotactic CT scanning and/or MR imaging. With the use of the stereotactic atlas, thalamic landmarks were superimposed by computer on the patient’s scans and the approximate location of the VL thalamus was estimated. Stereotactic anteroposterior and lateral metrizamide ventriculography was performed to establish landmarks and lesion coordinates. This was done through a burr hole 12 cm from the nasion and 2.5 cm from the midline, using a catheter stereotactically placed at the foramen of Monro.

The y (anteroposterior) and z (rostrocaudal) coordinates of the lesion site were then calculated from the ventriculogram as follows. A line was drawn from the anterior commissure (AC) to the posterior commissure (PC). A perpendicular line from the floor of the lateral ventricles to the midpoint of the AC-PC line defined the thalamic height. A line perpendicular to this was drawn to a line drawn perpendicular to the AC-PC line at the AC. An oblique was drawn from a point on this line corresponding to the junction between the middle and posterior thirds of the AC-PC line to the midpoint of the posterior third of the AC-PC line. A parallel line 5 mm above the AC-PC line completed the quadrilateral that defined the VP thalamus. A line parallel to the oblique line defined the area of the ventralis intermedius (VIM) thalamus, and a line parallel to the oblique from the junction of the middle and posterior thirds of the AC-PC line defined the area of the ventralis oralis posterior (VOP) thalamus. The y and z coordinates of the lesion site were placed at the VOP/VIM interface approximately 2.5 cm above the AC-PC line.

The laterality of the lesion (x coordinate) was estimated initially at 11.5 mm from the lateral wall of third ventricle. This was electrophysiologically confirmed and
M. S. Goldman, J. E. Ahlskog, and P. J. Kelly

TABLE 2

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Postop Voice Tremor</th>
<th>Follow-Up Period (mos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NC</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>NC</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>++</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>NC</td>
<td>50</td>
</tr>
<tr>
<td>5</td>
<td>++</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>+</td>
<td>8</td>
</tr>
<tr>
<td>8</td>
<td>++</td>
<td>1</td>
</tr>
</tbody>
</table>

* NC = no change; ++ = tremor abolished.

FIG. 1. Graph showing preoperative and postoperative disability scores after ventralis lateralis thalamotomy for medically intractable disabling essential tremor. Asterisk = final score after second step of staged bilateral thalamotomies.

Operative Results

Tremor

The contralateral upper-extremity tremor was completely abolished after each of the nine thalamotomy procedures in eight patients (Table 1). Follow-up examination (mean 17.3 months, range 1 to 50 months) revealed continued absence of upper-limb tremor in four patients and marked tremor reduction in three patients undergoing unilateral thalamotomy. The patient receiving staged bilateral thalamotomies was tremor-free in his upper extremities except for minimal residual tremor in his nondominant left hand, persisting at his 50-month follow-up examination. Disability scores (Table 1) were markedly improved at follow-up examination in all seven patients undergoing this assessment. The mean disability score was reduced from 21.1 (moderate grade) to 3.9 (no disability, p < 0.001) (Fig. 1).

Speech

Preoperative voice tremor was detected in seven of the eight patients. All patients with voice tremor had received left-sided thalamotomies and were righthanded. Following thalamotomy, voice tremor was abolished in three patients and improved in one (reduced or abolished in 57.2% of patients, Table 2). At follow-up examination (mean 10 months, range 1 to 50 months, after surgery) voice tremor was absent in three patients and reduced in two. One patient (Case 4) displayed delayed improvement in voice tremor during the interval between his staged bilateral procedures.

Medications

At the time of last follow-up visit (mean 17.3 months postoperatively), two patients required no medications for tremor and three patients were taking medications for the tremor corresponding to the unoperated side only. Of these latter three patients, one was taking a reduced dose of his preoperative medicine and two were receiving methazolamide exclusively. Two patients were taking reduced doses of their preoperative medication for residual targeted tremor. Medication data were unavailable in one patient. In no case could postoperative tremor improvement be attributed to a change in medication.

Morbidity

There were no deaths and no permanent postoperative morbidity in this group of patients. A mild persistent dysarthria was noted in two patients and a mild verbal cognitive deficit persisted in one patient. The deficits in these patients were demonstrated only at formal speech or psychometric evaluation and were clinically nonsymptomatic. All patients who experienced persistent deficits were older than 65 years and received left-sided lesions (two patients) or had undergone staged bilateral procedures (one patient). Transient deficits were uniformly mild and generally had resolved by the time of hospital discharge. These included extremity hypesthesias (two patients), dysarthrias (two patients), anomic dysphasia (one patient), extremity dyspraxia (one patient), attention deficits (two patients), and a verbal cognitive deficit (one patient). Many of these distributions in language, speech, and cognition were subtle and only demonstrable at formal speech pathology and psychometric evaluations.

Discussion

Essential tremor of the upper limbs often responds to medical therapy; however, the response is typically incomplete and response failures are common. A small but significant subset of essential tremor patients who
Stereotactic thalamotomy

fail medical therapy are sufficiently disabled by their condition to justify considering them for thalamotomy.

Literature Review

Stereotactic thalamotomy for the treatment of what was possibly essential tremor (“tremor of attitude”), was first described in the French literature in 1960. Guiot, et al., Wertheimer, et al., and Thurel, et al. reported excellent results in single patients following stereotactic lesions placed in the VL thalamus, VL thalamus and subthalamus, and internal capsules, respectively. In 1962, Cooper reported successful treatment of “heredofamilial tremor” following stereotactic VL thalamotomy in three patients. Laitinen in 1965 described improvement or resolution of essential tremor in seven of nine patients undergoing stereotactic electrocautery or leukotomy lesioning at various intracranial sites. The early-onset “cerebellar tremors” that responded to stereotactic centrum medianum lesions described by Adams and Rutkin, also in 1965, may have been essential tremor. Between 1965 and 1969, Obrador and Dierssen, Blacker, et al., and Bertrand, et al., described good results in a total of 47 of 50 patients undergoing thalamotomy for essential tremor. Van Manen published a stereotactic surgical series of 52 hereditary action tremors in 1974, but the actual number with essential tremor was not stated. In 1982, Ohye, et al., reported stereotactic Vim thalamotomy in 15 cases of essential tremor with complete or nearly complete tremor arrest in all cases. Recently, Mohadjer, et al., reported good long-term results of stereotactic thalamotomy in the treatment of essential tremor in a large population (104 patients) with a long follow-up period (mean 8.6 years). However, in this series the diagnostic criteria were not defined, family histories were not documented, multiple targeting methods and sites were utilized, and the postoperative examinations were limited.

Analysis of Current Series

The shortcomings of the above-mentioned surgical series include small patient populations, poorly defined or undefined inclusion criteria, non-uniform surgical techniques and/or surgical target sites, and surgical outcome analyses mixing essential tremor cases with other tremor types. In the present series, strict and explicit diagnostic guidelines were utilized as a basis for inclusion. The surgical methods were uniform, with one neurosurgeon (P.J.K.) performing all of the procedures. The analysis of outcome in this study employed several measures, including assessment from videotapes and functional disability rating. In addition, patients underwent formal speech pathology evaluations both before surgery to assess voice tremor and after surgery to assess beneficial as well as adverse effects of thalamotomy on speech and language.

Essential voice tremor was noted by speech pathology assessment and formal review of recorded speech samples in seven of our patients prior to surgery. It is interesting to note that voice tremor seemed to be lateralized in that it was not detected in patients requiring lesions in the nondominant hemisphere. Voice tremor was not severe in any of the patients, but was clearly detectable. It was completely abolished by left-sided thalamotomy in three patients and noted to be substantially reduced in two others at the time of last follow-up examination. These preliminary results suggest that thalamotomy might be a therapeutic modality for patients with severe refractory voice tremor. A surgical therapeutic alternative would be welcomed by many patients with voice tremor since typically this condition is relatively refractory to treatment with medications.

Conclusions

We followed eight patients with severe preoperative essential tremor for a mean of 17.3 months after VL thalamotomy. In all patients, there was persistent complete or nearly complete abatement of the contralateral tremor. Interestingly, voice tremor was ablated or significantly improved in 71.4% of cases. Almost all patients were able to discontinue or reduce the dose of medications taken for their targeted tremor. Moderate and severe disability were objectively reduced to mild or no disability in all cases. There was no surgical mortality and persistent neurological morbidity was rare, mild, and not debilitating. As in other series, increased age (in association with dominant hemispheric lesions) and bilateral procedures were found to increase the risk of persistent postoperative deficit. Transient deficits were more common and probably reflected perilesional edema or were induced by perioperative medications including anticonvulsant drugs (often with supratherapeutic blood levels). Stereotactic VL thalamotomy for medically intractable debilitating essential tremor typically carries low surgical risk and can be a dramatically effective treatment option for properly selected patients.

Acknowledgments

The authors thank Cathy Hunt, R.N., and Mary Hanenberger for their expert assistance in data collection and manuscript preparation, respectively.

References


M. S. Goldman, J. E. Ahlskog, and P. J. Kelly

Manuscript received August 14, 1991. Accepted in final form November 18, 1991.
Address reprint requests to: Patrick J. Kelly, M.D., Department of Neurosurgery, Mayo Clinic, Rochester, Minnesota 55905.