Symptomatic and functional outcome of stereotactic ventralis lateralis thalamotomy for intention tremor

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In the past, intention tremor has responded well to selected neuroablative procedures; however, objective symptomatic and functional outcomes of ventralis lateralis (VL) thalamotomy specifically for intention tremor in the post-computerized tomography era has rarely been reported. This series explored the symptomatic and functional impact of VL thalamotomy on 14 patients presenting at the Mayo Clinic with severe, refractory intention tremor due to multiple sclerosis (five patients), trauma (four patients), or stroke (five patients). General neurological examinations, psychometric evaluations, speech pathology assessments, and neuroradiological scans were performed. Pre- and postoperative disability were graded according to a modified form of an established rating scale for tremor. All patients received VL radiofrequency thalamotomies utilizing neurophysiological recording and stimulation control. Contralateral targeted upper-extremity tremor remained symptomatically absent or markedly reduced in 81.8% of cases (mean follow-up period 23.4 months). The median disability score was reduced by 12 points (0.02 < p < 0.05). Persistent surgical morbidity was limited to two patients with mild, nondisabling dysarthrias. One elderly patient died of pulmonary complications 2 weeks postoperatively. There were no reported surgically induced exacerbations in multiple sclerosis; however, some of these patients exhibited difficulties with electrophysiological localization. These results compare favorably with those reported in the literature and confirm that stereotactic VL thalamotomy for debilitating intention tremor carries a low surgical risk and can be an effective treatment option for properly selected patients.

Key Words • intention tremor • tremor • thalamotomy • stereotaxis • movement disorder

A kinetic tremor, also called “intention tremor,” due to pathology of the cerebellorubral system was first described in 1904 by Holmes.15 Denny-Brown6 coined the term “rubral tremor,” referring to a characteristic tremor produced by midbrain dysfunction due to multiple sclerosis, stroke, severe head injury, tumor, or toxins. This is a 2- to 2.5-Hz, irregular, kinetic tremor that appears weeks to months after injury to the superior cerebellar peduncle, midbrain tegmentum, or posterior thalamus, and is associated with paresis, plastic rigidity, dystonic posturing, and often hemianesthesia.66

Surgical therapy for movement disorders has been accepted as a reasonable option for selected cases since the early 1960’s.29 In the past, intention tremor has responded well to selected neuroablative procedures;6,16,20,23,35 however, objective symptomatic and functional outcome of ventralis lateralis (VL) thalamotomy specifically for intention tremor in the post-computerized tomography (CT) era is reported only rarely. This study explores the symptomatic and functional impact of thalamotomy on patients with intention tremor evaluated with modern neuroradiological imaging techniques.

Clinical Material and Methods

Patient Population

A total of 73 patients underwent stereotactic VL thalamotomy at the Mayo Clinic from September, 1984, to March, 1991, for the treatment of medically refractory dyskinesias. Fourteen of these patients had medically refractory, debilitating secondary intention tremor due to multiple sclerosis (five patients), trauma (four patients), or stroke (five patients). Table 1 lists the clinical characteristics of these patients. There were seven males and seven females whose mean age was 40.4 years (range 15 to 72 years). The mean preoperative duration of symptoms was 11 years (range 10 months to 34 years). Associated symptoms included spastic paresis in eight patients, diplopia in one, ataxia
TABLE 1
Clinical characteristics of 14 patients referred for thalamotomy with intention tremor*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs.)</th>
<th>Sex</th>
<th>Etiology</th>
<th>Side of Lesion</th>
<th>Tremor Rating†</th>
<th>Disability Rating‡</th>
<th>Follow-Up Interval (mos)</th>
<th>Morbidity</th>
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* MS = multiple sclerosis; PT = posttraumatic; CVA = postinfarction; X = unavailable for completion of disability evaluation; NA = not applicable.
† Tremor rated on a scale of 0 (absent) to +4 (severe).
‡ Disability rated on a scale of 0 (none) to +4 (severe) in six different areas of function, for a maximum possible score of 24.

in six, and cognitive difficulties in one. There were five right-sided and seven left-sided thalamotomies; two procedures were aborted, one due to transient extremity weakness following probe placement (Case 5) and one due to failure to obtain adequate evoked responses required for target localization (Case 2). Multiple sclerosis was the tremor etiology in both cases.

Pre- and Postoperative Evaluation

General neurological examinations, psychometric evaluations, speech pathology assessments, and neuroradiological scans (CT or magnetic resonance (MR) imaging) were performed preoperatively and repeated during the 1st week postoperatively. The complete evaluation was repeated at the patient's first follow-up appointment 3 months postoperatively and at successive visits as circumstances permitted. Videotaped documentation of the tremor and selected segments of the neurological examination was obtained preoperatively and at each postoperative evaluation. Tremor was graded on a four-point scale (0 = no tremor, 4 = severe tremor) with respect to each of the following components: rest, static, action, and terminal accentuation.

Preoperative (retrospectively) and postoperative disability were graded according to a modified form of the clinical rating scale developed by Fahn, et al.,10 for tremor. The disability scale represented the composite score of a four-point grading system (0 = none, 4 = severe disability) that evaluated specific areas of function: handwriting, solid and liquid feeding, hygiene, dressing, and working. The maximum possible score (reflecting maximum disability) was 24 points.

Postoperative neurological morbidity was defined as a new deficit or a worsened preoperative deficit and was labeled "transient" or "persistent" depending on its status at the most recent follow-up examination.

Operative Procedure

The target coordinates were first approximated using stereotactic CT scans, MR images, and positive-contrast ventriculography, and were precisely localized with neurophysiological recording and stimulation control. The following procedure was used at our institution.20–22

The patient was placed in a stereotactic headframe with an attached localization system, and stereotactic CT and/or MR imaging was performed. Slices 5 mm thick and overlapping at 3-mm intervals were obtained through the region of the third ventricle. A computer-resident Schaltenbrand-Wahren stereotactic atlas was scaled to superimpose the individual thalamic nuclei 2.5 mm above and parallel to a line connecting the anterior and posterior commissures (AC-PC line). The VL nucleus was targeted on a computer display console and the stereotactic coordinates were calculated.

The patient was then placed on the operating table and the headframe positioned in an arc-quadrant stereotactic system.* With the patient under local anesthesia, a burr hole was made 12 cm posterior to the nasion and 2.5 cm from the midline. The foramen of Monro was placed at the system's focal point and a cannula was introduced stereotactically. The VL nucleus was moved into the focal point, and a positive-contrast

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A radiofrequency lesioning probe (with a 1.6-mm diameter and a 3-mm exposed tip) was passed to the target coordinates. A low-frequency low-amplitude stimulus drove the tremor and a high-frequency high-amplitude stimulus ablated the tremor in a reversible fashion. The temperature-monitored electrode was heated to 42°C for 60 seconds to create a temporary lesion. The patient was examined for strength, tremor, coordination, speech, and language (when appropriate) and, if no untoward effects were discovered, the probe was heated to 70°C for 60 seconds to generate a permanent lesion 4 mm in diameter and 4.5 mm long. The probe was allowed to cool to body temperature and withdrawn.

Statistical Analysis

The paired t-test and the sign rank test were used for statistical analysis. The level of significance was designated as 95%.

Results

Tremor

In the 12 thalamotomies performed, contralateral targeted upper-extremity tremor was completely abolished in 10 patients and nearly completely abolished in two. In the latter two cases, a preoperative grade +4 tremor was reduced to a postoperative grade +1 tremor (Cases 3 and 12). Follow-up examination (mean interval 23.4 months, range 0.5 to 55 months) was performed in 11 of the 12 patients undergoing thalamotomy and revealed an absence of upper-limb tremor (three patients) or only mild residual tremor (six patients) in 81.8% of cases. Five of the latter group experienced slight postoperative recurrences which, in general, represented a deterioration of only one tremor grade. In one patient (9.1%), an immediately ablated tremor recurred and reached preoperative grade (+3) (Case 8).

Disability

Nine patients underwent formal disability evaluation. Two patients were unavailable for completion of the disability questionnaire, two patients (mentioned above) did not complete the thalamotomy procedure, and one patient died 2 weeks postoperatively (Fig. 1). After thalamotomy, the median disability score was reduced by 12 points (range +2 to −19, 0.02 < p < 0.05) (Fig. 2). Stratifying the disability scores by etiology revealed that the only subgroup to attain a statistically significant reduction in disability score was the postinfarction patients (p = 0.02) (Fig. 3). The multiple sclerosis and posttrauma patients tended toward improved disability scores, but statistical significance was not reached in these small populations.

Morbidity

One patient died on postoperative Day 14 due to pulmonary complications (Case 14). He was a 72-year-
old man whose medical history was significant for myocardial infarction and who presented with a tremor after a left cerebral infarction. His preoperative grade +4 tremor was ablated completely at surgery and remained so until the time of his death due to aspiration pneumonia.

No permanent severe operative morbidity was seen in this group of patients. Formal speech pathology evaluations revealed persistent mild worsening of preoperative ataxic dysarthrias in two patients (Cases 1 and 11). Transient deficits were uniformly mild (detectable by formal psychometric or speech pathology evaluations only) and had generally resolved by the time of hospital discharge. These included mildly worsened preoperative dysarthrias in two patients (Cases 3 and 8) and a mild decline in verbal cognitive function in one patient (Case 7). Morbidity could not be correlated either to the side of the lesion or to tremor etiology in this series. No thalamotomy-induced relapses were reported in the five patients with multiple sclerosis.

**Discussion**

*Previous Reports*

A total of 204 patients have been described in the literature who underwent a stereotactic neuroablative procedure for intention tremors of specific etiologies (associated with multiple sclerosis, trauma, or infarct) (Table 2). There was immediate symptomatic ablation or significant improvement in 191 cases (94%); however, of the 127 patients followed symptomatically over time, these results persisted in only 88 (69%), implying a tremor recurrence rate of approximately 25%. The functional outcome of surgery was investigated in 58 patients and improvement was found in 30 (52%) of them. A total of 107 patients were evaluated for postoperative complications. A persistent new deficit or a worsened preoperative deficit was seen in 25 (23%).

*Multiple Sclerosis*

Intention tremor is one of the most severe symptoms of multiple sclerosis and the main reason for invalidism.\textsuperscript{14} Substantial symptomatic benefit from VL thalamotomy was demonstrated in most surgical series (Table 3).\textsuperscript{6,8,14,19,24,32,34,35} Between 1962 and 1987, a total of 131 patients underwent a stereotactic neuroablative procedure for tremor due to multiple sclerosis. There was immediate symptomatic ablation or significant improvement in 123 (94%). Among the 103 patients followed symptomatically over time, these excellent results persisted in 67 (65%), implying that tremor recurred in approximately 29%.

In contrast to cases of tremor from other etiologies, the long-term functional improvement was not as gratifying in these patients due to the progressive nature of their disease.\textsuperscript{28} Three series investigated functional outcome of stereotactic surgery in a total of 45 patients and found functional improvement in 20 (44%).\textsuperscript{14,24,34} Of 49 patients evaluated for postoperative complications, 11 (22%) showed a persistent new deficit or a worsened preoperative deficit. In one patient, surgery was believed to have induced a new relapse of the demyelinating process.

In the present series, no acute exacerbations of the demyelinating process were precipitated by surgery. Perioperative parenteral steroids may have been protective. As previously stated, this institution relied on meticulous electrophysiological confirmation of the target area, which could not be achieved for two patients due to sensory pathway deficits resulting from the disease. No lesioning was performed in these patients. The absence of sensory evoked responses in three patients may have been due to demyelination and perhaps nuclear reorganization.\textsuperscript{30}

*Posttraumatic Tremor*

Patients with severe head injury occasionally develop intention tremor as a late complication\textsuperscript{17,25} due to midbrain or cerebellar damage.\textsuperscript{31} Elevated supratentorial intracranial pressure causes stretching and tearing of the paramedian arteries in the upper brain stem,\textsuperscript{7} producing the characteristic syndrome of spastic hemiparesis, dysarthria, appendicular ataxia, and oculomotor

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**Fig. 2.** Block graph showing the pre- and postoperative median disability score for the 12 patients. This score was reduced after thalamotomy by 12 points (range +2 to -19). For scoring system, see text.

**Fig. 3.** Block graph stratifying the disability scores by etiology. The only subgroup to attain a statistically significant postoperative reduction in disability score comprised the postinfarction patients; however, the multiple sclerosis and posttraumatic patients tended toward improved disability. For scoring system, see text.
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| TABLE 2 |
|-------------------------|-------------------------------|--------------------------|-----------------------|--------------------------|
| Etiology | No. of Cases | Immediate Improvement | Improvement at Follow-Up† | Functional Improvement‡ | Persistent Deficit§ |
|-------------------------|-------------------------------|--------------------------|-----------------------|--------------------------|
| multiple sclerosis | 131 | 123 (94) | 67 (65) | 20 (44) | 11 (21) |
| postraumatic | 44 | 42 (96) | 9 (75) | 9 (90) | 10 (30) |
| stroke | 29 | 26 (90) | 12 (100) | 1 (33) | 4 (18) |
| totals | 204 | 191 (94) | 88 (69) | 30 (52) | 25 (23) |

* Numbers in parentheses denote percentages of patients evaluated for those data.  † A total of 127 patients were followed symptomatically over time.  ‡ The functional outcome of surgery was investigated in a total of 58 patients.  § A total of 107 patients were evaluated for postoperative complications.

| TABLE 3 |
|-------------------------|-------------------------------|--------------------------|-----------------------|--------------------------|
| Authors & Year | No. of Cases | Surgical Target | Immediate Improvement | Improvement at Follow-Up‡ | Functional Improvement‡ | Persistent Deficit§ |
|-------------------------|-------------------------------|--------------------------|-----------------------|--------------------------|
| Kravchenkó & Vašárgil, 1962 | 4 | VL | 4 (100) | 4 (100) | 4 (100) | 1 |
| Cooper, 1967 | 32 | VL | 31 (97) | 27 (84) | — | 2 |
| Samra, et al., 1970 | 25 | VL | 20 (80) | — | — | — |
| van Manen, 1974 | 4 | VL | 4 (100) | 0 | — | — |
| Riechert, et al., 1975 | 2 | VL, ZI | 2 (100) | 2 (100) | — | 1 |
| Kelly, 1980 | 3 | VL | 3 (100) | 0 | — | 0 |
| Specian & van Manen, 1984 | 11 | VL | 11 (100) | 9 (82) | 9 (82) | 6 |
| Kandell & Hondcrarian, 1985 | 20 | VL, ZI, FF | 18 (90) | 10 (50) | — | — |
| Hitchcock, et al., 1987 | 30 | — | 30 (100) | 15 (50) | 7 (23) | — |
| totals | 131 | 123 (94) | 67 (65) | 20 (44) | 11 (22) |

* VL = ventralis lateralis thalamus; ZI = zona incerta; FF = Forel's field; — = information not reported. Numbers in parentheses denote percentages of patients evaluated for those data.  † A total of 103 patients were followed symptomatically over time.  ‡ Functional outcome of surgery was investigated in a total of 45 patients.  § A total of 49 patients were evaluated for postoperative complications.

dysfunction. Typically, a static and kinetic tremor with a myoclonic or hemiballistic component appears at a mean interval of 6 weeks postictus as the ipsilateral hemiparesis improves. These are poorly responsive to medical management but may resolve spontaneously within a year.

Damage to the cerebellar vermis, hemispheres, and brachium conjunctivum leads to the postraumatic cerebellar syndrome of extremity tremor, dysarthria, voice tremor, ocular dysmetria, and ataxia, which was first described by Cantu. Gerstenbrand, et al., noted that this syndrome followed the apaplic state in many instances. Stein, et al., found that, as appendicular ataxia abated in some patients, intention tremor developed.

A total of 44 patients reported between 1960 and 1989 underwent a stereotactic neuroablative procedure (almost exclusively VL thalamotomy) for postraumatic tremor (Table 4). Immediate ablation or significant improvement of the tremor was noted in 42 (95%) of these patients. Tremor control persisted in nine (75%) of 12 patients followed symptomatically over time. Two series investigated functional outcome following surgery in 10 patients and found functional improvement in nine (90%). This trend was confirmed in the present study. A total of 33 patients were evaluated for postoperative complications; 10 (30%) of these showed a persistent new deficit or worsened preoperative deficit. The tendency of patients with postraumatic tremor to demonstrate slightly higher complication rates as shown above was not confirmed in the present series.

Because some postraumatic tremors resolve spontaneously, Andrew, et al., recommended an observation period of 1 year before thalamotomy was to be considered. However, they warned that postponing surgery for too long in young patients could delay development due to disuse of the affected extremity.

Postinfarction Tremor

Mesodiencephalic strokes in the territories of the thalamogeniculate, posteromedial choroidal, and posterolateral choroidal arteries result in tremor, myoclonus, chorea, and athetosis in combination with hemianesthesia, hemidysesthesia, hemiparesis, spasticity, hemianopsia, delusions, hallucinations, confusion, and altered level of consciousness.

A total of 29 patients reported between 1976 and 1987 underwent stereotactic VL thalamotomy for postinfarction tremor (Table 5). There was immediate symptomatic ablation or significant improvement in 26 (90%) of these patients. Follow-up study in 12
patients revealed persistent tremor control in all; no incidence of tremor recurrence was reported. In the present series, two of four patients experienced very mild tremor recurrence. One series investigated functional outcome of surgery in three patients, with functional improvement occurring in only one. Superimposed preoperative hemiparesis may have prevented noticeable functional improvement. In the present series, a statistically significant reduction in disability was achieved in all patients within this subgroup. Of 22 patients gathered from the literature who were evaluated for postoperative complications, four (18%) showed a persistent new deficit or worsened preoperative deficit.

Conclusions
The present series further supports the conclusion that most patients undergoing stereotactic thalamotomy for intention tremor enjoy significant immediate and long-term symptomatic relief, and that one-half to two-thirds of these patients will experience a significant improvement in function as well. Complications of thalamotomy are, at times, associated with improperly placed lesions. The frequency of these types of complications was greatly reduced with the introduction of stereotactic CT capabilities which afforded accurate localization of subcortical structures. This was dramatically illustrated in the present series, in which there was no severe persistent morbidity as compared to morbidity levels described in the predominantly pre-CT literature, which averaged 23% persistent deficits.

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References
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