Deep Brain Stimulation and Tremor

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Summary: Deep brain stimulation (DBS) has been used to treat various tremor disorders for several decades. Medication-resistant, disabling essential tremor (ET) is the most common tremor disorder treated with DBS. The treatment has been consistently reported to result in significant benefit in upper extremity, as well as head and voice tremor, all of which were improved more dramatically with bilateral procedures. These benefits have been demonstrated to be sustained for up to 7 years. DBS has also been shown to be beneficial for the tremor associated with multiple sclerosis and post-traumatic tremor; however, fewer cases have been reported and the benefit is less consistent, less dramatic, and more transient than that seen with ET. The ventral intermediate nucleus of the thalamus is the most common DBS target for tremor disorders, but more recent studies have demonstrated benefits in tremor from DBS of the subthalamic area, primarily the zona incerta. Surgical complications are relatively uncommon and are generally less frequent than those seen with thalamotomy. Stimulation-related effects are usually mild and resolve with adjustment of stimulation parameters. DBS is thus a relatively safe and effective treatment for tremor disorders, particularly for medication-resistant, disabling ET, but may also have some role in medication-resistant, disabling tremor associated with multiple sclerosis and traumatic head injury. **Key Words:** Deep brain stimulation, tremor, essential tremor, primary writing tremor, multiple sclerosis tremor, post-traumatic tremor.

INTRODUCTION

Tremor is a rhythmic, involuntary oscillation that can affect the upper and lower extremities, head, face, jaw, tongue, voice, and trunk. There are several types of tremor, including resting, postural, action, and intention tremors. Multiple neurological disorders involve tremor; the most common are essential tremor (ET) and Parkinson's disease.[1] Pharmacologic treatments for tremor are limited and often result in inconsistent or no benefit. It is estimated that only about 50% of ET patients respond to pharmacologic treatments; in Parkinson's disease, tremor is the most difficult cardinal symptom to control, and other forms of tremor such as primary writing tremor, the tremor of multiple sclerosis (MS) and post-traumatic tremor are even more difficult to treat.[2–5]

In the 1960s, the ventral intermediate nucleus (Vim) of the thalamus was found to be the most effective target for ablative surgical treatment of tremor. During this same period, it was observed that the high-frequency stimulation used for targeting during lesioning of the thalamus significantly reduced tremor and that tremor recurred once the stimulation was discontinued.[6] Further research in the 1980s[7] provided additional evidence that deep brain stimulation (DBS) of the Vim of the thalamus significantly reduced tremor, which set the groundwork for the approval of DBS of the thalamus for the treatment of essential and parkinsonian tremor in 1997. Several studies have demonstrated that DBS of the thalamus has comparable control of tremor with fewer side effects, compared with thalamotomy, especially with bilateral procedures, and DBS is therefore currently the treatment of choice for medication-resistant tremor.[8–10] This review focuses on the results of DBS for various forms of tremor, including ET, primary writing tremor, the tremor of MS, and post-traumatic tremor. Parkinsonian tremor is discussed in a separate section of this issue, dedicated to Parkinson's disease.

ESSENTIAL TREMOR

Essential tremor is the most common tremor disorder. It can present from childhood throughout adulthood, but is most common among older adults. It has been estimated that 5% of persons over the age of 60 are affected

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by ET, which is characterized by a 4-Hz to 12-Hz postural or kinetic tremor. The tremor most commonly affects the upper extremities but the head, voice, trunk, and lower extremities can also be affected. The most common pharmacologic treatments are primidone and beta-adrenergic blockers such as propranolol or atenolol, but other medications such as gabapentin or topiramate and other antiepileptics or benzodiazepines can be beneficial in some patients. Unfortunately, these pharmacologic treatments are successful in only about 50% of ET patients.[2] DBS of the Vim of the thalamus is an effective treatment option for ET patients with medication-resistant tremor experiencing significant disability. DBS candidates should not have any other medical conditions that would increase the risk of a surgical procedure.

At present, the Vim of the thalamus is the most commonly targeted site for DBS in medication-resistant, disabling ET. There have been multiple reports of the benefits of DBS of the Vim of the thalamus for the treatment of ET.[7,11–24] Table 1 summarizes selected long-term studies of Vim DBS for ET. The first North American multicenter study[11] of unilateral DBS of the thalamus in 29 ET patients demonstrated a significant improvement in contralateral hand tremor of approximately 60% and an improvement of between 43% and 68% in activities of daily living such as writing, drawing and pouring, 3 and 12 months after surgery. At 3 months after surgery, approximately 79% of the ET patients reported marked improvement, 10% reported moderate improvement, 3% reported mild improvement, and 7% were unchanged. Mean amplitude at 3 months was 3.0 V, frequency was 162 Hz, and pulse width was 117 μs. None of these settings were significantly changed at 12 months. Complications were combined with an additional 24 patients with parkinsonian tremor. One patient had generalized seizures, two had skin infections, and one had skin erosion. Stimulation-related adverse effects were mild and resolved with stimulation parameter adjustments.[11]

Five-year outcomes were reported for 15 of these patients with unilateral implants and for 7 patients with bilateral implants.[12] In the patients with unilateral implants, there were improvements of 75% in targeted hand tremor, 46% in overall tremor, 51% in activities of daily living, 57% in drawing, and 44% in pouring. In the seven patients with bilateral implants, at 5 years there were improvements of 65% in left-handed tremor, 86% in right-handed tremor, 78% in overall tremor, and 36% in activities of daily living. Stimulation parameters were not significantly different at 5 years from those at 12 months. Of 45 patients with either ET or parkinsonian tremor, surgical revisions were performed in 27% and stimulation-related adverse events occurred in 10%.[12]

The most common adverse events in ET patients with unilateral implants were paresthesia (56%), pain (33%), asthenia (22%), dysarthria (17%), incoordination (17%), abnormal thinking (17%), headache (17%), depression (11%), and hallucinations (11%). In ET patients with bilateral implants, the most common adverse events were dysarthria (63%), incoordination (38%), pain (25%), paresthesia (25%), asthenia (25%), insomnia (25%), abnormal gait (25%), hypophonia (25%), somnolence (25%), dysphagia (13%), and abnormal thinking (13%).[12]

A multicenter European study of 37 ET patients evaluated 12 months after thalamic DBS[13] and the long-term follow-up of these patients[14] had similar results to those of the North American multicenter studies.[11,12] Kinetic and postural tremor of the upper extremities and activities of daily living were improved by more than 75% at 12 months, relative to baseline. In addition, head tremor was improved by 15% with unilateral implants and by 85% in those implanted bilaterally. Similarly, voice tremor was improved by 33% with unilateral implants and by 40% with bilateral implants.

The average amplitude for all electrodes at 12 months was 2.4 V, which was significantly greater than the initial amplitude of 1.9 V. Frequency and pulse width were not significantly different at 12 months, compared with the initial settings. Adverse events reported included those for 73 patients receiving thalamic DBS for parkinsonian tremor. Two patients had subdural hematomas and one patient had an intracerebral hematoma, all of which resolved without treatment; two had subcutaneous hematomas that were evacuated; and the DBS system was temporarily removed in two patients because of infection. Stimulation-related adverse events were mild and resolved with adjustments of stimulation parameters.[13]

Data were available for 19 of these ET patients, 12 unilateral and 7 bilateral, after an average of 6.5 years.[14] There continued to be significant improvements in overall tremor and kinetic and postural tremor of the upper extremities compared to baseline; however, the degree of improvement was reduced by 13% to 21%, relative to the 12-month follow-up. Activities of daily living were also significantly improved at long-term follow-up, compared with the baseline, but there was a 41% worsening, relative to the improvement seen at 12 months. Improvements in head tremor were increased to 45% for those with unilateral implants and the 85% improvement for those with bilateral implants was maintained at long-term follow-up. Improvements in voice tremor were reduced from 33% at 12 months to 25% at long-term follow-up in the unilateral group, but in the bilateral group improvements increased from 40% at 12 months to 60% at the long-term follow-up.[14]

The mean amplitude of all implanted electrodes was 2.6 V at 6 years, which was 0.3 V higher than at 12 months. At 6 years, mean frequency had increased by about 10 Hz and mean pulse width had increased by about 3 μs, relative to the 12-month visit. The most common stimulation-related adverse events were pares-

TABLE 1. *Selected Long-Term Studies of Thalamic Deep Brain Stimulation for Treatment of Essential Tremor (Percent Improvement Compared to Baseline)*

Study	*n* (u/b)	Age, yr	Follow-up, mo	Overall Tremor	Hand Tremor	Functional Ability*	ADLs	Head	Voice	Stimulation Parameter Settings‡		
										Ampl, V	Freq, Hz	PW, μs
Koller et al.[11] (1997)	29/0	67	12	—	~60%	48%–63%	—	—	—	3.0	153	86
Pahwa et al.[12] (2006)	15/7	71	60	46% (u); 78% (b)	75% (u); 65%–86% (b)	44%–57% (u); 35%–57% (b)	51% (u); 36% (b)	—	—	3.6, 3.6, 3.2	158, 155, 153	111, 111, 129
Limousin et al.[13] (1999)	28/9	63	12	55%	>75%	44%	80%	15% (u); 85% (b)	33% (u); 40% (b)	2.4	164	84
Sydow et al.[14] (2003)	12/7	62	80	41%	50%–70%	37%	39%	45% (u); 85% (b)	25% (u); 60% (b)	2.6	173	89
Koller et al.[26] (1999)	20/0	72	12	42%	—	—	—	50%	—	3.1	158	67
Koller et al.[15] (2001)	25/0	72	22–69	50%	78%	—	—	—	—	3.6	161	100
Putzke et al.[16] (2004)	29/23	72	3–36	—	>83%	—	>63%	15%–51% (u); 39%–79% (b)†	15%–51% (u); 39%–79% (b)†	3.0	171	88
Putzke et al.[25] (2005)	0/22	70	29	—	80%–91%	—	69%–86%	90%–100%	65%–100%	2.8, 2.4	168, 159	97, 97

ADLs = activities of daily living; Ampl = amplitude; b = bilateral; Freq = frequency; PW = pulse width; u = unilateral.
*Writing, drawing, pouring. †Reported as midline tremor. ‡Amplitude, frequency, and pulse width presented for longest follow-up; presented for unilateral and bilateral separately, with bilateral procedures presented as first and second side unless values were based on the mean of all implanted electrodes, in which case there is just one value for each parameter.

thesia, gait disorders, headache, and dysarthria, which was more common with bilateral procedures. One patient had additional surgery to reposition the lead; loss of effect occurred in two patients; infection, erosion, and skin irritation each occurred in two patients; severe dystonia led to stimulation discontinuation in one patient; and intermittent stimulation occurred in one patient.

Another study[16] reported 52 ET patients (23 bilateral) up to 36 months after thalamic DBS. There was no decrease in tremor control over time, with patients maintaining a minimum improvement of 83% in upper extremity tremor and 63% in activities of daily living. After 3 months, stimulation parameters were not significantly changed. At 3 years, mean amplitude for all electrodes was 3.0 V, mean frequency was 171 Hz, and mean pulse width was 88 μs. Stimulation-related adverse events included dysarthria (40%), disequilibrium (31%), motor disturbance (24%) and paresthesia (16%). Eight leads were repositioned due to loss of effect, two leads were replaced due to breakage, and one patient experienced infection requiring device removal.[16]

An additional report[25] examined specifically the effects on midline tremor in 22 ET patients from this cohort, at an average of 29 months after staged bilateral implants. There was a significant mean increase in midline tremor suppression of 81% between the first and second implant. More specifically, during a follow-up period of 3 years there was a minimum improvement in head tremor of 90% and a minimum improvement in voice tremor of 65% with bilateral thalamic DBS. Stimulation parameters were not significantly different at the 1-year, 2-year, and 3-year visits, and there were no significant changes in the first electrode settings after the second electrode was implanted. Because these were staged bilateral procedures, adverse events were compared after the first and second surgeries. The only significant difference was an increase in dysarthria, which occurred in 27% of patients with bilateral implants and in none of the patients with unilateral implants.[25]

Several studies have reported improvements in head or voice tremor in patients who received thalamic DBS for hand tremor (Table 1).[13,14,16,25,26] In these studies, improvements in head tremor ranged from 15% to 51% for unilateral procedures and 39% to 100% for bilateral procedures. Similarly, improvements in voice tremor ranged from 15% to 51% for unilateral procedures and 39% to 100% for those with bilateral procedures. One report described two ET patients that received bilateral thalamic DBS for isolated head tremor.[27] Complete resolution of head tremor was reported at 9 months.

A few reports have suggested that stimulation of the subthalamic area may be superior to thalamic stimulation. In one report,[28] an ET patient with severe medication-resistant proximal postural tremor unresponsive to thalamotomy received unilateral DBS in the subthalamic area, targeting the zona incerta. Complete resolution of the tremor was reported, and there were no adverse events that did not resolve with stimulation adjustments. In a second article,[29] the same investigators reported eight ET patients with medication-resistant proximal tremor who received unilateral DBS of the posterior part of the subthalamic white matter which included the zona incerta and prelemniscal radiation. They reported a mean improvement of 81% in both distal and proximal arm tremor, as well as an improvement in head and voice tremor. No major complications were reported.[29]

Another study reported four ET patients with medication-resistant tremor who received bilateral DBS of the subthalamic region.[30] At 12 months after surgery, there were improvements of 81% in overall tremor, 83% in upper extremity tremor, 89% in activities of daily living, 67% in drawing spirals, 77% in pouring water, 58% in line drawing, and 68% in handwriting. In two patients who had severe head tremor at baseline, the tremor resolved at the 12-month follow-up. There were no surgical- or stimulation-related complications and no signs of tolerance. Stimulation parameters did not change between 6 weeks and 12 months after surgery (amplitude 1.8 V, frequency 170 Hz, and pulse width 109 μs). Further research is necessary to compare DBS of the subthalamic area and DBS of the Vim of the thalamus for ET.

In summary, multiple long-term studies ranging from 1 to 7 years have demonstrated improvements in hand tremor ranging from 50% to 91%. These studies have also shown significant improvements in head and voice tremor, ranging from 15% to 100%; however, these improvements were more pronounced with bilateral procedures. Although improvements were maintained long-term, they were often lesser than the initial improvements. It is unclear if this is related to disease progression, tolerance, or some other phenomenon. Stimulation parameters were similar across studies, with amplitudes ranging from 2.4 V to 4.4 V, frequency ranging from 143 Hz to 173 Hz and pulse width ranging from 67 μs to 138 μs. In the majority of studies, minimal, nonsignificant changes in parameter settings were reported after the 3-month assessment. Stimulation-related adverse events were generally mild and resolved with adjustments of parameter settings; however, dysarthria was consistently shown to be more common with bilateral procedures. Surgical complications were rare and generally led to no permanent deficits. Device complications such as erosion and lead breakage occurred in a small percentage of patients in most reports and were resolved with additional surgical procedures. In conclusion, Vim DBS has been shown to be an effective, long-term treatment for medication-resistant, disabling ET.

PRIMARY WRITING TREMOR

Primary writing tremor is a task-specific focal tremor that occurs predominately during writing, or when the hand is in the position used for writing. It is not clear if it is a form of ET, dystonia, a combination of both, or unrelated to either. Medications such as propranolol, primidone, and anticholinergics may be beneficial, and some relief has been seen with botulinum toxin injections.[5] When medical options have been exhausted, thalamic DBS may be an option for disabling primary writing tremor. Unilateral DBS of the Vim of the thalamus was performed in a case of medication-resistant, disabling primary writing tremor.[31] At 1 year after the procedure, the patient had almost complete tremor resolution, and was able to write without difficulty. The stimulator was used only when needed for writing, remaining off the rest of the time. After 3 months, the stimulation parameters remained constant (amplitude 2.2 V, frequency 130 Hz, pulse width 60 μs). There were no complications reported.[31]

A second, similar case report[32] found that unilateral DBS of the Vim of the thalamus provided nearly complete relief of tremor in a patient with medication-resistant, disabling primary writing tremor. Stimulation parameters were amplitude of 1.5 V, frequency of 150 Hz, and pulse width of 120 μs; however, neither duration of effect nor length of follow-up were reported. There were no complications reported. Although there are limited data available, initial reports suggest that DBS of the Vim of the thalamus is an effective treatment for primary writing tremor.

MULTIPLE SCLEROSIS

Tremor is commonly seen in MS, given that approximately 80% of patients have cerebellar or brainstem lesions. The tremor is generally a large-amplitude, 2.5-Hz to 7-Hz postural, kinetic, or intention tremor that most commonly affects the upper extremities, although the lower extremities, head, neck, or trunk can be affected. It is important to differentiate tremor from dysmetria or ataxia, which can also be present with MS but which do not have the rhythmic component seen with true tremor and do not respond to DBS. MS tremor is often refractory to medications, but in some cases propranolol or clonazepam can be beneficial.[1,5] DBS of the Vim of the thalamus may be an option in some MS patients with medication-resistant, disabling tremor.

The results of thalamic DBS on MS tremor are often inconsistent, transient, and less dramatic than those seen with ET or parkinsonian tremor.[7,9] There are several concerns regarding the use of DBS to control MS tremor. First, the other symptoms of MS may be causing much more disability than the tremor, leading to unrealistic expectations about the outcome of DBS. In addition, persons with MS may have altered neuroanatomy or neurophysiology due to MS that may make DBS targeting more difficult. Patients should be stable for at least 1 year prior to surgery, to make sure that the tremor is not likely to resolve spontaneously. DBS should not be attempted in cases with severe cerebellar syndrome or significant lesions in the thalamus.[5]

Several studies have examined the effects of thalamic DBS on MS tremor (Table 2).[33–38] The majority of these were single-center studies with small sample sizes. One study reported unilateral DBS of the Vim in 13 MS patients (11 relapsing progressive; 2 relapsing remitting) after a follow-up of up to 26 months.[33] All patients were diagnosed with severe cerebellar tremor due to MS. There was a decrease in tremor amplitude in all patients and long-term reduction of tremor in 69%. Functional disability was improved in 92%, and those with unilateral tremor improved to a greater extent than those with bilateral tremor. Frequent stimulation parameter adjustments were necessary. There were no serious complications; three patients relapsed within 12 months of the surgery, but in each case this was typical of their MS prior to surgery.[33]

In a study of 15 MS patients (10 relapsing remitting; 5 chronic progressive), of whom 14 received unilateral

TABLE 2. *Selected Studies of Unilateral Deep Brain Stimulation of the Thalamus for Tremor in Patients with Multiple Sclerosis*

Study	*N*	Follow-up (mo)	Outcome
Geny et al.[33] (1996)	13	8 to 26	69% had some sustained benefit.
Montgomery et al.[34] (1999)	14	<3 to >12	100% had some sustained benefit in all types of tremor.
Berk et al.[37] (2002)	12	12	At 2 months: improvements in resting (58%), postural (57%), kinetic (70%) and overall tremor (63%). At 12 months: improvement in postural (56%), kinetic (67%) and overall tremor (60%). Minimal to no improvements in ADLs, and improvements not sustained.
Schulder et al.[36] (2003)	9	9 to 54	100% had improved tremor compared to baseline; 33% had sustained functional benefit.

ADLs = activities of daily living.

thalamic DBS, resting, postural, and kinetic tremor were significantly reduced.[34] Sustained benefit occurred in all patients, but frequent stimulator adjustments were necessary to avoid tolerance; these adjustments had no consistent pattern, however, and did not involve merely increasing the parameter settings at each adjustment. The procedure was not completed in one patient because of intracerebral hematoma, and one patient had a significant worsening of MS symptoms 3 days after surgery.[34]

In a study of 12 MS patients (1 primary progressive; 10 secondary progressive; 1 relapsing remitting), results of unilateral DBS of the thalamus were reported at 2 and 12 months after surgery.[37] There were significant improvements in resting, postural, kinetic, and overall tremor at 2 months and sustained improvements in postural, kinetic, and overall tremor at 12 months. At 2 months, there were significant improvements in feeding, but other ADLs were improved minimally or not at all; the improvements in feeding were not maintained at 12 months. One patient was explanted after 2 months because of infection, and another died after 7 months from causes related to MS progression. Paresthesia was the most common stimulation-related adverse event.[37]

One study examined the long-term effects of thalamic stimulation in nine MS patients an average of 32 months after surgery.[36] All patients experienced a sustained reduction in tremor; however, other symptoms of MS were either unchanged or worsened with time. One-third of patients had sustained functional improvement from DBS. In three patients, MS symptoms worsened within 1 month of DBS. The only complication reported was a mild decline in memory in one patient.

A review of the literature[38] identified 14 studies that reported a total of 75 MS patients who received unilateral thalamic DBS. The follow-up periods ranged from less than 3 months to greater than 12 months. Some improvement in tremor and activities of daily living were seen in the majority of the studies. Data on improvements in tremor were available in 12 of the reports, including a total of 65 patients, of whom 88% were determined to have reduced tremor compared to before the surgery. Six studies provided data on activities of daily living, including 25 patients, of whom 76% were reported to have some improvement. Of the 75 patients in the 14 studies, 5 had intracerebral hemorrhages, 2 had seizures, and 1 had an implantable pulse generator–related infection requiring eventual device removal. The most common adverse event related to stimulation was paresthesia, which generally was mild and transient. Other adverse events included dysarthria, disequilibrium, and limb weakness. Six of the 14 studies, representing 38 patients, reported changes in MS; 18% had a worsening of MS symptoms.

Another review of the literature[39] identified 13 studies reporting the use of DBS for MS tremor in a total of 97 patients. The review focused on adverse events and initial improvements in tremor and functional ability. In these studies, there was one death due to MS progression, three intracerebral hemorrhages, one intracerebral hematoma, and two thalmocapsular hematomas; seven patients had an MS relapse after DBS. An initial improvement in tremor was reported in 93 of the 97 patients (96%). Assessments of functional ability were available for 54 patients, of whom 46 had some initial improvement (85%). There were no studies in this review reporting data after 12 months. These results were compared with results from 11 reports of thalamotomy for MS tremor, which led to the conclusion that the two procedures are comparable in terms of safety and efficacy. Advantages of DBS included the ability to adjust stimulation parameters to improve efficacy and reduce adverse effects, the reversibility of the procedure, and reduced adverse effects with bilateral procedures compared to thalamotomy.

The preceding reports all involved DBS of the Vim of the thalamus for MS tremor. One additional report included 15 MS patients who received DBS that targeted both the ventralis oralis posterior nucleus of the thalamus and the zona incerta.[40] Data were available for 10 patients, with a mean follow-up of 15 months. There was a 64% improvement in postural tremor and a 36% improvement in intention tremor. Adverse events for the whole cohort ($n = 15$) included transient hemiparesis, seizure, and dysarthria each in one patient, and wound infections in two patients. Three patients required battery replacements. Given the inconsistent and often short-term benefits of DBS of the thalamic Vim for MS tremor, further research is necessary to determine the most effective target for tremor associated with MS.

In summary, there are limited data available from relatively small, single-center studies of the effects of DBS on MS tremor. These studies consistently show some initial improvement in MS tremor after DBS for the majority of patients, improvement that has been reported to be maintained long-term in some patients. The majority of reports, however, also highlight the fact that the progression of other symptoms of MS often leads to significant disability that overshadows the improvements in tremor. Further research is necessary to determine the appropriate DBS target and long-term benefits of DBS for MS tremor.

POST-TRAUMATIC TREMOR

Post-traumatic tremor is the most common movement disorder that results from severe head trauma. It can occur within a month or years after the actual trauma and can include resting, postural, kinetic, and intention tremor. The combination of resting, postural, and intention tremor is often referred to as Holmes tremor or

midbrain tremor. The tremor almost exclusively affects the upper extremities, but the head and trunk can be affected, though rarely. Post-traumatic tremor is generally resistant to medications; however, propranolol, primidone, dopaminergic therapies, benzodiazepines, anticholinergics, and botulinum toxin have been reported to be effective in some patients.

In medication-resistant, disabling post-traumatic tremor, DBS may be an option. There are several concerns with performing DBS in a patient with post-traumatic tremor, in that there is generally widespread damage to the brain and the presence of multiple other symptoms that might limit the benefit of DBS, such as psychological and cognitive deficits, ataxia, dysarthria, paresis, and oculomotor deficits. In cases where DBS is determined to be an option, it should be performed no sooner than 1 year after tremor presentation, when it is clear that the tremor is not likely to spontaneously lessen or resolve.[41]

Only a few reports have described DBS for post-traumatic tremor, with limited details and follow-up periods.[41] In one case with post-traumatic unilateral postural, kinetic, and resting tremor that was causing significant functional disability, DBS of the Vim of the thalamus significantly reduced tremor and improved functional ability for at least 10 months.[42] In another case, post-traumatic action tremor was significantly reduced with Vim DBS, with no associated complications.[43] Finally, one report suggests that two leads may better control post-traumatic Holmes tremor.[44] In this case, two leads were implanted on the same side of the brain, one placed on the border of the Vim and ventralis oralis posterior thalamic nuclei, and the other placed on the border of the ventralis oralis posterior and anterior thalamic nuclei. The lead in the Vim of the thalamus was activated first and suppressed the tremor, but not to an extent to improve functional ability, and this effect lessened during the first 2 months. After 2 months, the other lead was activated, and marked improvement in both tremor and functional ability were achieved; these effects were sustained to the last follow-up, at 12 months. Further research on the most effective target and potential benefits of DBS for post-traumatic tremor is warranted.

SUMMARY

Deep brain stimulation of the Vim of the thalamus has been demonstrated in multiple studies to be an effective treatment for medication-resistant, disabling ET. Significant improvements in upper extremity, head, and voice tremor have been consistently reported, both initially and up to 7 years after surgery. Permanent morbidity is rare, and complications related to the stimulation are generally mild and most often eliminated with stimulation parameter adjustments. A few small reports have demonstrated that the subthalamic area is an effective target in controlling ET. Further studies are necessary to determine the best site for the treatment of medication-resistant, disabling ET.

Several studies have reported the use of DBS for other forms of tremor, including primary writing tremor, MS tremor, and post-traumatic tremor. Only a few case reports have demonstrated significant improvement in primary writing tremor after Vim DBS; however, these reports are preliminary and follow-up is limited. Several small studies have reported the effects of thalamic DBS on MS tremor. The majority of these studies demonstrated a reduction in MS tremor, which was sustained in most patients. In contrast, improvements in functional ability were less consistent and were most often not maintained long-term, which is likely related to increased disability due to the progression of other MS symptoms. Limited data are also available for DBS for post-traumatic tremor. A few case reports have shown some benefit with DBS; however, few details are provided, limited follow-up is available, and the most effective target site has not been determined. Further research is necessary to determine the utility of DBS for MS and post-traumatic tremor.

REFERENCES

1. Deuschl G, Bain P, Brin M; Ad Hoc Scientific Committee. Consensus statement of the Movement Disorder Society on Tremor. Mov Disord 1998;13 Suppl 3:2–23.
2. Lyons KE, Pahwa R, Comella CL, et al. Benefits and risks of pharmacological treatments for essential tremor. Drug Saf 2003; 26:461–481.
3. Olanow CW, Watts RL, Koller WC. An algorithm (decision tree) for the management of Parkinson's disease (2001): treatment guidelines. Neurology 2001;56(11 Suppl 5):S1–S88.
4. Pahwa R, Lyons KE. Essential tremor: differential diagnosis and current therapy. Am J Med 2003;115:134–142.
5. Deuschl G, Bain P. Deep brain stimulation for trauma [correction of trauma]: patient selection and evaluation. Mov Disord 2002; 17(Suppl 3):S102–S111.
6. Hassler R, Riechert T, Mundinger F, Umbach W, Ganglberger JA. Physiological observations in stereotaxic operations in extrapyramidal motor disturbances. Brain 1960;83:337–350.
7. Benabid AL, Pollak P, Gao D, et al. Chronic electrical stimulation of the ventralis intermedius nucleus of the thalamus as a treatment of movement disorders. J Neurosurg 1996;84:203–214.
8. Tasker RR. Deep brain stimulation is preferable to thalamotomy for tremor suppression. Surg Neurol 1998;49:145–153; discussion 153–154.
9. Schuurman PR, Bosch DA, Bossuyt PM, et al. A comparison of continuous thalamic stimulation and thalamotomy for suppression of severe tremor. N Engl J Med 2000;342:461–468.
10. Pahwa R, Lyons KE, Wilkinson SB, et al. Comparison of thalamotomy to deep brain stimulation of the thalamus in essential tremor. Mov Disord 2001;16:140–143.
11. Koller W, Pahwa R, Busenbark K, et al. High-frequency unilateral thalamic stimulation in the treatment of essential and parkinsonian tremor. Ann Neurol 1997;42:292–299.
12. Pahwa R, Lyons KE, Wilkinson SB, et al. Long-term evaluation of deep brain stimulation of the thalamus. J Neurosurg 2006;104: 506–512.
13. Limousin P, Speelman JD, Gielen F, Janssens M. Multicentre European study of thalamic stimulation in parkinsonian and essential tremor. J Neurol Neurosurg Psychiatry 1999;66:289–296.

14. Sydow O, Thobois S, Alesch F, Speelman JD. Multicentre European study of thalamic stimulation in essential tremor: a six year follow up. J Neurol Neurosurg Psychiatry 2003;74:1387–1391.
15. Koller WC, Lyons KE, Wilkinson SB, Troster AI, Pahwa R. Long-term safety and efficacy of unilateral deep brain stimulation of the thalamus in essential tremor. Mov Disord 2001;16:464–468.
16. Putzke JD, Wharen RE Jr, Obwegeser AA, et al. Thalamic deep brain stimulation for essential tremor: recommendations for long-term outcome analysis. Can J Neurol Sci 2004;31:333–342.
17. Ondo W, Jankovic J, Schwartz K, Almaguer M, Simpson RK. Unilateral thalamic deep brain stimulation for refractory essential tremor and Parkinson's disease tremor. Neurology 1998;51:1063–1069.
18. Blond S, Siegfried J. Thalamic stimulation for the treatment of tremor and other movement disorders. Acta Neurochir Suppl 1991; 52:109–111.
19. Alesch F, Pinter MM, Helscher RJ, Fertl L, Benabid AL, Koos WT. Stimulation of the ventral intermediate thalamic nucleus in tremor dominated Parkinson's disease and essential tremor. Acta Neurochir 1995;136:75–81.
20. Hariz GM, Bergenheim AT, Hariz MI, Lindberg M. Assessment of ability/disability in patients treated with chronic thalamic stimulation for tremor. Mov Disord 1998;13:78–83.
21. Kumar K, Kelly M, Toth C. Deep brain stimulation of the ventral intermediate nucleus of the thalamus for control of tremors in Parkinson's disease and essential tremor. Stereotact Funct Neurosurg 1999;72:47–61.
22. Krauss JK, Simpson RK Jr, Ondo WG, Pohle T, Burgunder JM, Jankovic J. Concepts and methods in chronic thalamic stimulation for treatment of tremor: technique and application. Neurosurgery 2001;48:535–541; discussion 541–533.
23. Rehncrona S, Johnels B, Widner H, Tornqvist AL, Hariz M, Sydow O. Long-term efficacy of thalamic deep brain stimulation for tremor: double-blind assessments. Mov Disord 2003;18:163–170.
24. Putzke JD, Wharen RE Jr, Wszolek ZK, Turk MF, Strongosky AJ, Uitti RJ. Thalamic deep brain stimulation for tremor-predominant Parkinson's disease. Parkinsonism Relat Disord 2003;10:81–88.
25. Putzke JD, Uitti RJ, Obwegeser AA, Wszolek ZK, Wharen RE. Bilateral thalamic deep brain stimulation: midline tremor control. J Neurol Neurosurg Psychiatry 2005;76:684–690.
26. Koller WC, Lyons KE, Wilkinson SB, Pahwa R. Efficacy of unilateral deep brain stimulation of the VIM nucleus of the thalamus for essential head tremor. Mov Disord 1999;14:847–850.
27. Berk C, Honey CR. Bilateral thalamic deep brain stimulation for the treatment of head tremor: report of two cases. J Neurosurg 2002;96:615–618.
28. Kitagawa M, Murata J, Kikuchi S, et al. Deep brain stimulation of subthalamic area for severe proximal tremor. Neurology 2000; 55:114–116.
29. Murata J, Kitagawa M, Uesugi H, et al. Electrical stimulation of the posterior subthalamic area for the treatment of intractable proximal tremor. J Neurosurg 2003;99:708–715.
30. Plaha P, Patel NK, Gill SS. Stimulation of the subthalamic region for essential tremor. J Neurosurg 2004;101:48–54.
31. Minguez-Castellanos A, Carnero-Pardo C, Gómez-Camello A, et al. Primary writing tremor treated by chronic thalamic stimulation. Mov Disord 1999;14:1030–1033.
32. Racette BA, Dowling J, Randle J, Mink JW. Thalamic stimulation for primary writing tremor. J Neurol 2001;248:380–382.
33. Geny C, Nguyen JP, Pollin B, et al. Improvement of severe postural cerebellar tremor in multiple sclerosis by chronic thalamic stimulation. Mov Disord 1996;11:489–494.
34. Montgomery EB Jr, Baker KB, Kinkel RP, Barnett G. Chronic thalamic stimulation for the tremor of multiple sclerosis. Neurology 1999;53:625–628.
35. Schulder M, Sernas T, Mahalick D, Adler R, Cook S. Thalamic stimulation in patients with multiple sclerosis. Stereotact Funct Neurosurg 1999;72:196–201.
36. Schulder M, Sernas TJ, Karimi R. Thalamic stimulation in patients with multiple sclerosis: long-term follow-up. Stereotact Funct Neurosurg 2003;80:48–55.
37. Berk C, Carr J, Sinden M, Martzke J, Honey CR. Thalamic deep brain stimulation for the treatment of tremor due to multiple sclerosis: a prospective study of tremor and quality of life. J Neurosurg 2002;97:815–820.
38. Wishart HA, Roberts DW, Roth RM, et al. Chronic deep brain stimulation for the treatment of tremor in multiple sclerosis: review and case reports. J Neurol Neurosurg Psychiatry 2003;74:1392–1397.
39. Yap L, Kouyialis A, Varma TR. Stereotactic neurosurgery for disabling tremor in multiple sclerosis: thalamotomy or deep brain stimulation? Br J Neurosurg 2007;21:349–354.
40. Nandi D, Aziz TZ. Deep brain stimulation in the management of neuropathic pain and multiple sclerosis tremor. J Clin Neurophysiol 2004;21:31–39.
41. Krauss JK, Jankovic J. Head injury and posttraumatic movement disorders. Neurosurgery 2002;50:927–939; discussion 939–940.
42. Broggi G, Brock S, Franzini A, Geminiani G. A case of posttraumatic tremor treated by chronic stimulation of the thalamus. Mov Disord 1993;8:206–208.
43. Umemura A, Samadani U, Jaggi JL, Hurtig HI, Baltuch GH. Thalamic deep brain stimulation for posttraumatic action tremor. Clin Neurol Neurosurg 2004;106:280–283.
44. Foote KD, Okun MS. Ventralis intermedius plus ventralis oralis anterior and posterior deep brain stimulation for posttraumatic Holmes tremor: two leads may be better than one: technical note. Neurosurgery 2005;56(2 Suppl):E445.