

Case Report

Orthostatic Tremor Responds to Bilateral Thalamic Deep Brain Stimulation

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Abstract

Background: Orthostatic tremor (OT) is a disabling movement disorder manifested by postural and gait disturbance. Primarily a condition of elderly people, it can be progressive in up to 15% of patients. The primary treatments are medications that are often ineffective.

Case Report: A 75-year-old male presented with a 10-year history of progressive and disabling OT. He had tried various medications without significant benefits. He underwent bilateral thalamic Vim deep brain stimulation (DBS). At 30-month follow-up, he has had continued significant improvement of his OT.

Discussion: Bilateral thalamic DBS may be a viable option for medically refractory OT.

Keywords: Orthostatic tremor, deep brain stimulation, thalamus

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Introduction

Orthostatic tremor (OT) was first described in 1984 by Heilman.¹ He reported three patients who presented with leg and trunk tremor upon standing that was relieved by walking, sitting, lying down, or leaning against a wall or object.¹ OT most commonly affects middle-aged and elderly people. They most commonly describe unsteadiness in the legs and a fear of falling upon standing. However, in certain cases the symptoms can involve the trunk and upper extremities. There is a latency of several seconds or, rarely, a few minutes.^{2,3} Since the tremor can also be evoked by strong tonic contraction of the leg muscles and is, hence, not exclusively orthostatic, the term “shaky-legs syndrome” has been suggested.⁴ The latter term though does not take into account the involvement of the trunk and upper extremity muscles in some patients with OT. Psychological stress, slow walking, or standing on a narrow base may increase OT.⁵ Electromyography (EMG) shows high frequency 13–18 Hz tremor discharges in weight-bearing muscles, most prominently in the legs.

The most commonly used medication for OT is clonazepam,^{1,3} but many patients are unresponsive to it or are unable to tolerate the side effects. We previously reported the beneficial effects of gabapentin in patients with OT, including those who were unresponsive to

clonazepam.⁶ Other medications used in patients with OT include primidone, clonazepam, phenobarbital, valproic acid, propranolol, phenytoin, and carbamazepine.^{7–9} OT can profoundly impact the quality of life in those patients suffering from this condition and more effective treatments need to be developed.⁷ Pharmacological treatment of OT is the primary therapeutic option, but often with limited success.¹⁰ Deep brain stimulation of the ventralis intermedius nucleus of the thalamus may offer a treatment option for those patients with medically refractory and severely disabling OT.

Deep brain stimulation (DBS) has been reported as a treatment option in three cases of OT in the literature. Espay and colleagues reported two patients who underwent thalamic DBS for refractory OT.¹¹ However, only one of the two patients had sustained relief of symptoms. Guridi et al.¹² described a single case of a patient with severe medically refractory OT successfully treated with thalamic Vim DBS.

Case Report

We report a 75-year-old male with a 10-year history of progressive OT and unsuccessful medical treatment. He used a portable stool or cane when he had to stand in place. Upon standing, he would have the immediate onset of fine tremors in both legs. He could only stand in

place for 20 seconds at most before needing to sit, lean, or hold on to something. The patient had been initially trialed on acetazolamide and primidone over the course of 5 years prior to his referral to our institution. He tolerated the medications, but they were discontinued because of ineffectiveness. He was then started on topiramate, up to 50 mg twice per day, but discontinued because of side effects of anorexia and significant weight loss. He was subsequently begun on clonazepam, up to 0.5 mg twice per day, but was discontinued because of sedation. Gabapentin and then valproic acid were trialed without any improvement in his symptoms. The severity of the side effects of the clonazepam and topiramate and the ineffectiveness of the other medications resulted in referral for consideration of DBS surgery.

Pre-operative surface EMG showed 13 Hz tremors of the lower extremities upon standing, which spread upwards to his paraspinal, truncal, and upper limb muscles. The patient underwent bilateral thalamic DBS. The target coordinates were based upon the midcommissural point and 11.5 mm lateral to the wall of the ipsilateral third ventricle. Intraoperative electrophysiology was performed to locate and confirm the leg portion of the Vim nucleus. Microelectrode recordings were followed by microstimulation looking for sensory side effects in the contralateral leg. In the right brain, leg side effects were noted at 13 mm lateral to the ipsilateral wall of the third ventricle, whereas in the left brain, final laterality was 11.5 mm. Macrostimulation was carried out to further refine final electrode placement based upon intraoperative improvement of contralateral leg tremor. This was assisted by surface EMG recordings of the legs, asking the patient to push down on each leg against resistance or on a footboard (Figure 1). Final electrode placement per side was determined based on stimulation side effects (sensory symptoms in the contralateral leg) and improvement of the contralateral leg tremor on surface EMG with macrostimulation (Figure 2).

One month following surgery, initial programming was done. The left Implantable Programmable Generator (IPG) settings were: contacts 0 and 1(-); contact 2(+); amplitude 4 volts; pulse width

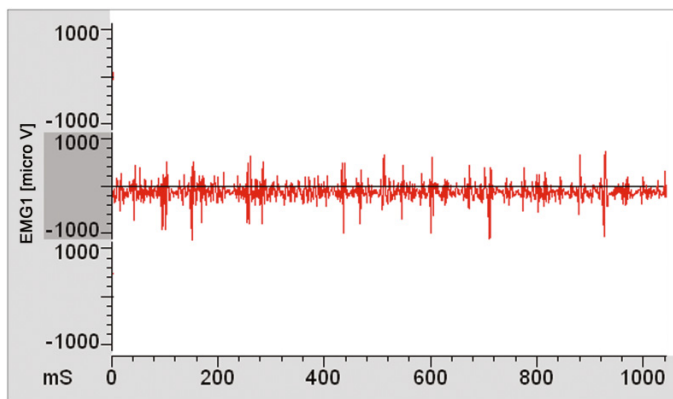


Figure 1. Pre-operative surface EMG of the right anterior tibialis in the movement neurophysiology laboratory shows well-formed, continuous, and rhythmic 13 Hz tremor bursts, which are noted immediately upon standing in place from a seated position. The tracing shows a 2-second epoch.

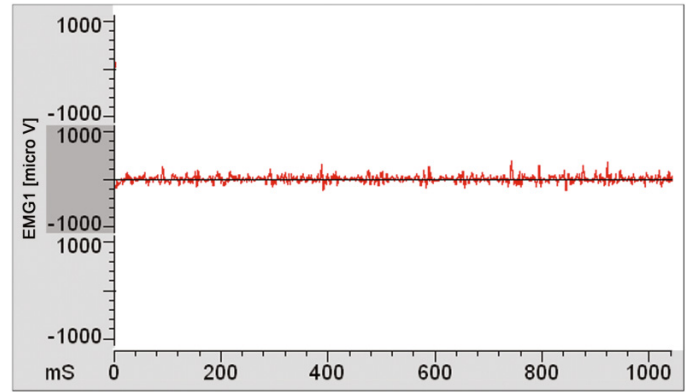


Figure 2. 3-month postoperative surface EMG of the right anterior tibialis in the movement neurophysiology laboratory demonstrates less continuous, less rhythmic, and slower frequency (5–10 Hz) tremor bursts. The tracing shows a 2-second epoch.

60 milliseconds; and frequency 185 Hz. The right IPG settings were: contact 4(-); contact 5(+); amplitude 2.5 volts; pulse width 90 milliseconds; and frequency 185 Hz.

He reported an 80% subjective improvement of his OT in the left leg and 50% improvement in the right leg. He was able to stand in place for 7 minutes before needing to sit. He no longer required his portable stool/cane. A repeat surface EMG study was performed 3 months post-DBS. On standing from a seated position, there was immediate onset of tremor in the lower extremities on surface EMG, although the tremor bursts were less continuous, less rhythmic, and often showing bursts of slower frequency than the previous 13 Hz tremor seen pre-operatively (Figures 3–4). At 11 months post-DBS, the patient developed an infection and skin erosion around the IPG, which required removal of the pulse generator. Interestingly, it took 1 month before he returned to baseline severity of his OT. A new pulse generator was placed 2 months later, resulting in prompt improvement of his OT. The patient has been followed at our institution by the treating movement disorders neurologist and implanting neurosurgeon. Since surgery, the patient has had 19 visits to the DBS clinic

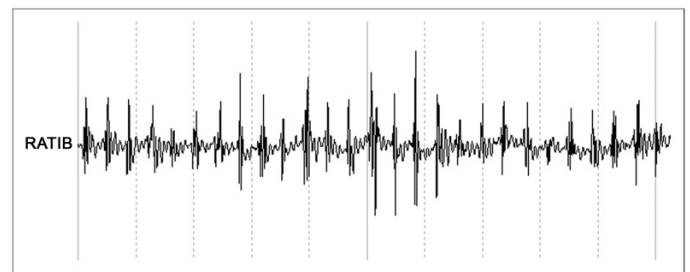


Figure 3. Intraoperative surface EMG recordings of the right anterior tibialis prior to stimulation with the patient supine in the operating table shows irregular 12–15 Hz tremor bursts while having the patient push down on the leg against resistance. The tracing shows a 1-second epoch. RATIB, Right anterior tibialis (muscle).

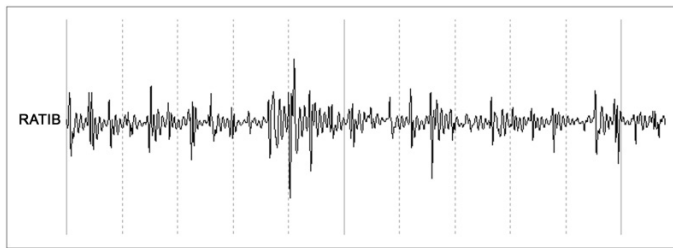


Figure 4. Intraoperative surface EMG recordings of the right anterior tibialis during macrostimulation with the patient supine in the operating table shows no definite tremor bursts while pushing down on the leg against resistance. The tracing shows a 1-second epoch. RATIB, Right anterior tibialis (muscle).

demonstrating continued improvement. At last follow-up 30 months following DBS, he continued to experience a good response to stimulation alone (with no anti-tremor medications). He was able to stand in place at least 7 minutes or more before needing to sit or lean on something. The left IPG settings on last follow-up were: contacts 4 and 5(-); contact 6(+); amplitude 2.2 volts; pulse width 90 milliseconds; and frequency 185 Hz. The right IPG settings were: contact 0(-); contact 1(+); amplitude 2.7 volts; pulse width 90 milliseconds; and frequency 185 Hz.

Discussion

Our case further supports the efficacy of thalamic Vim DBS in treating medically refractory OT. Electrophysiological mapping intraoperatively helps localize the leg area in the Vim subnucleus. Although OT is a tremor disorder that appears on standing, we have demonstrated that the tremor can also be detected on surface EMG with the patient lying on the operating table by asking the patient to put pressure on the legs against resistance or by stepping down on a footboard. This technique allows monitoring of response of the leg tremor to microstimulation and macrostimulation. On surface EMG with the patient supine with macrostimulation, and post-operatively in our movement disorders laboratory while standing with the stimulators on, the leg tremor still persists though is less continuous, less rhythmic and of lower frequency. Thus, thalamic Vim DBS does not completely eradicate the tremor but rather modifies its consistency, rhythmicity and frequency characteristics.

OT is considered to be a rare disorder and the incidence and prevalence are unknown.⁷ The pathophysiology is unclear. Gerschlagler and colleagues⁷ studied 41 patients with OT, noting that, while in most cases the symptoms remained unchanged over years, approximately 15% of patients developed progressive symptoms. Medications have been generally ineffective. There have been three reported case of OT treated with DBS. Espay and co-workers¹¹ reported two patients who underwent thalamic DBS for refractory OT. Both patients, as in our case, had progressive symptoms for nearly three decades. One patient underwent bilateral thalamic Vim DBS with sustained improvement at last follow-up 18 months after surgery. The second patient underwent unilateral thalamic Vim DBS, but relapsed 3 months after surgery.¹¹ Although the patient undergoing

bilateral DBS noted significant improvement in unsteadiness and quality of life, the 15 Hz oscillatory activity and posturographic measures were unchanged. They postulated that the absence of reduction in postural stability, in the absence of visual or proprioceptive inputs, argues against the attenuation of tremor disruption of the proprioceptive afferent pathways as the pathophysiologic mechanism underlying OT.^{11,13}

Guridi et al.¹² described a case of a patient with severe medically refractory OT successfully treated with thalamic Vim DBS. They noted that the minimally effective current was 1.3 volts. Interestingly, during the 4-year follow-up period there were three occasions where the tremor worsened, which coincided with spontaneous disruption of unilateral stimulation. This finding is consistent with our case and the observation by Espay and colleagues¹¹ that bilateral DBS may be necessary for efficacy of DBS in OT. Krauss et al.¹⁴ reported a single case of successful treatment of OT with spinal cord stimulation. The subjective improvement, however, was only noted with stimulation in the 50–150 Hz range and required stimulation induced paresthesias. Espay has postulated that since thalamic and spinal stimulation produce similar results in OT, perhaps a common modulatory role of the “cerebello-thalamo-cortico-spinal system” is being affected at different levels of the neural axis.¹¹ Our case is consistent with the few reported cases in the literature. Sustained long-term improvement in OT, as noted in our case, suggests that thalamic Vim DBS may be an option for these patients. Although unilateral thalamic Vim DBS may benefit OT, bilateral stimulation appears to have more consistent and enduring effects.

The major limitation of this report is that it is a single case. The paucity of these cases makes any conclusions regarding the efficacy of DBS for medically refractory OT premature. However, this disease can be extremely disabling to those patients afflicted. Thalamic DBS is a safe procedure and the clinical application of DBS to OT is intriguing. Bilateral thalamic DBS may be a viable option for medically refractory OT. Monitoring of surface EMG intraoperatively may help locate the optimal lead position to achieve tremor control. Deep brain stimulation does not eradicate the tremor completely, but tends to modulate the tremor making it slower in frequency, consistency and rhythmicity. This can lead to functional improvement of the patient’s ability to stand despite persistence of the tremor. Controlled clinical trials are needed and long term responses need to be monitored and observed.

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