Both thalamic and pallidal deep brain stimulation for myoclonic dystonia

Case report

JEAN Q. L. OROPILLA, M.D.,1 CID C. E. DIESTA, M.D.,1 PARUNUT ITHIMATHIN, M.D.,1 OKSANA SUCHOWERSKY, M.D., F.R.C.P.C.,1,2 AND ZELMA H. T. KISS, M.D., PH.D., F.R.C.S.C.1

Departments of 1Clinical Neurosciences and 2Medical Genetics, University of Calgary, Alberta, Canada

Myoclonic dystonia is poorly managed with medication and may be severe enough to warrant surgical intervention. Surgery has targeted either the globus pallidus pars interna (GPi) or the thalamus, but there is no accepted target for this condition. The authors present the case of a 23-year-old man treated with unilateral deep brain stimulation in both the thalamus and GPi. His movement disorder improved dramatically with stimulation. Two years postoperatively, the authors performed a double-blind assessment of the effects of each stimulator together, separately, and off stimulation. Videotape assessment, using tremor, dystonia, and myoclonus rating scales, showed that most of the benefit could be attributed to pallidal stimulation, although there was some advantage to stimulation at both sites. These results suggest that while GPi stimulation may be the better target for this condition, thalamic stimulation may be added in cases in which the benefit is insufficient. (DOI: 10.3171/2009.10.JNS091062)

Key Words • dystonia • deep brain stimulation • surgery • globus pallidus • thalamus • tremor • myoclonus • torticollis

Myoclonus–dystonia syndrome, a movement disorder with onset in childhood or adolescence, is characterized by both myoclonic jerks and dystonia, usually with myoclonus as the predominant and most disabling symptom.18 In some cases, the myoclonus appears intermittently rhythmic, and it has been viewed as a form of tremor. Medical options are limited and a small number of patients have undergone either thalamic20 or pallidal surgical procedures.2,16 We report on the case of a patient who underwent DBS of both thalamic and pallidal targets unilaterally.

Case Report

History and Examination. This 23-year-old right-handed man presented with a 10-year history of involuntary movements. Born of a normal pregnancy and delivery, the patient began experiencing intermittent involuntary jerking of the neck, and occasionally his right arm, at the age of 12 years. The patient denied an urge to move and could not suppress the movements. His mother described that he was slightly slower in attaining gross motor milestones than other children, but he did become a good athlete. The movements gradually progressed, such that by age 18 years he had a prominent tremor of his neck and right upper limb, which was reduced by alcohol. His speech had always been slurred and this affected his confidence and academic progress. Although he completed high school, he was working as a laborer. There was no history of similar conditions in the immediate family. Investigations (brain MR imaging, DYT1 gene, serum copper, and ceruloplasmin) failed to identify an abnormality. He had received clonazepam, valproic acid, metoprolol, and primidone therapies without benefit. Because the disability was not due to neck movements, but due to his proximal arm tremor, he had not tried botulinum toxin injections and instead was referred to the functional/sterotactic neurosurgical service.

On examination he had both a postural and action nonrhythmic irregular tremor of the right upper limb (Video 1).

Video 1. Video assessments before surgery and 6, 12, and 24 months after surgery. Click here to view with Windows Media Player.

In addition, he demonstrated occasional arm and neck myoclonic jerks, and a side-to-side tremor of his head. Dystonia of the right upper limb appeared when the patient attempted to use his right hand for specific tasks.

Abbreviations used in this paper: CRST = Clinical Rating Scale for Tremor; DBS = deep brain stimulation; GPi = globus pallidus pars interna; TWSTRS = Toronto Western Spasmodic Torticollis Rating Scale; UMRS = Unified Myoclonus Rating Scale; Vim = ventrointermedius nucleus of thalamus.
(that is, during writing and drinking from a glass). No abnormal movements were seen in his left upper and lower limbs. Motor examination revealed normal strength, tone, and deep tendon reflexes. Mental status, cranial nerve, and sensory examinations demonstrated normal results aside from slurred speech.

Surgery and Postoperative Course

Operation. In February 2006, 2 DBS electrodes (Medtronic 3387) were implanted in the left side of the patient’s brain, targeting the GPi and thalamus (Vim nucleus). Correct placement was determined using intraoperative microelectrode recording and stimulation. Coordinates for the most ventral contacts of the GPi and thalamic quadripolar electrodes were 20 mm lateral to midline, 2 mm anterior to the midcommissural point, 4.5 mm ventral to the intercommissural line and 14 mm lateral, 3 mm anterior to posterior commissure, and 1.5 mm ventral to the intercommissural line, respectively. The thalamic DBS lead was placed in the physiologically recorded Vim, where kinesthetic and deep responding neurons were encountered and microstimulation reduced tremor. Due to the acute angle of the lead placement in thalamus, the electrodes spanned from the ventrooralis anterior anterodorsally to the anterior margin of ventrocaudal nucleus. The leads were externalized and tested during the immediate postoperative period. Because some benefit was obtained from both electrodes in the 2 targets, we decided to connect both leads to a dual-channel pulse generator after verification of correct electrode placement with MR imaging (Fig. 1). The leads were internalized and connected to the pulse generator (Kinetra, Medtronic) implanted subcutaneously in the subclavicular region.

Assessments. To evaluate clinical outcome, our patient was assessed by a trained movement disorders nurse before surgery, and 6, 12, and 24 months after surgery; the Fahn-Tolosa-Marin CRST5 and the TWSTRS were used.3 At the 2-year time point, a detailed double-blind randomized assessment was performed using the aforementioned scales and the UMRS7 by an independent neurologist. Programming was performed by a neurosurgeon who randomly changed the programming settings. Four states were examined (off/off, off thalamic/on GPi, on thalamic/off GPi, and on/on). Video recordings were made at least 1 hour after a change in stimulation settings, and both the patient and evaluating physician were unaware of which settings were programmed.

Double-Blinded Assessment of Long-Term Outcome. Two years postoperatively, stimulation parameters were 140-Hz, 0.12-msec pulse width, 2.3-V, monopolar (2-) stimulation through the GPi lead and 140-Hz, 0.09-msec pulse width, 2.1-V, monopolar (2-) stimulation through the thalamic electrode (likely in the ventrooralis posterior nucleus). With both channels on, the total improvement in CRST was 62% and total TWSTRS improvement was 81% compared with baseline (Table 1). In the stimulation off state 2 years after DBS surgery, the patient’s dystonic symptoms were similar but his tremor scores were lower than his preoperative scores (Video 1).

During testing of each electrode separately, the patient had most improvement in dystonic symptoms with both stimulators on (Video 2). Video 2. Videos comparing simultaneous pallidal and thalamic stimulation, pallidal stimulation alone, thalamic stimulation alone, and no stimulation at 2 years after surgery. Click here to view with Windows Media Player.

His tremor scores were better with pallidal than thalamic stimulation at 2 years, but this difference was less obvious at 6 and 12 months. Dystonia and myoclonus scores were better with pallidal stimulation alone than thalamic stimulation alone, although either was better than no stimulation (Table 2). With tremor severity, myoclonus at rest, and functional tests of myoclonus, the benefit could be attributed entirely to pallidal stimulation. Simultaneous pallidal and thalamic stimulation was better than GPi-DBS alone in functional tests of tremor, cervical dystonia severity, and myoclonus during action.

Discussion

This report is, to the best of our knowledge, the first to document the long-term results of both pallidal and thalamic stimulation together and independently for myoclonic dystonia, assessed in a blinded fashion using standardized rating scales.
Deep brain stimulation for myoclonic dystonia

Our patient had a complex unilateral tremor with some features of both essential tremor and myoclonic jerks, but with additional mild cervical dystonia. The most accepted diagnosis for this constellation of symptoms is myoclonic dystonia. Although essential tremor is primarily treated with Vim thalamic stimulation, myoclonic dystonia can be treated with either thalamic\(^{14,20}\) or pallidal stimulation.\(^{2,15}\) However, Vim stimulation addresses tremor and myoclonus but rarely dystonic symptoms\(^{14,20}\) unless it is a secondary form\(^{13}\) or specifically directed at pallidal-receiving nuclei.\(^{8}\)

We planned to implant both thalamus and GPi with DBS leads and postoperatively test each electrode separately to determine which provided better results. Because both provided some immediate improvement, we connected both to a dual-channel pulse generator. On long-term follow-up these effects persisted. Using combined pallidal and thalamic stimulation, this patient had an 80% improvement in TWSTRS-measured severity, better than the average reported in the literature.\(^{12}\) This may be attributed to possible synergism between pallidal and thalamic stimulation because of the angle of the thalamic electrode (Fig. 1). Because the GPi electrode was implanted first in this patient, the thalamic DBS lead trajectory was somewhat unorthodox based on bur hole location in the calvaria. The more acute angle of insertion and the use of the Lead 2 may have affected the pallidal-receiving thalamus (ventrooralis anterior–ventrooralis posterior) rather than cerebellar thalamus.\(^{30}\) Also, this patient’s tremor did not achieve the same severity postoperatively as it had at baseline. This may be due to a temporary residual benefit from stimulation, even though we left a minimum of 1 hour between changing stimulation settings and testing. An alternative explanation may be a long-lasting effect of stimulation, as has been suggested with other forms of dystonia.\(^{9,22}\) Improvement in tremor scores may also be related to a change in the manifestation of the disease unrelated to stimulation.\(^{19}\)

Palilal stimulation for myoclonic dystonia has been reported previously. In a 28-year-old man with familial myoclonic dystonia, bilateral pallidal stimulation abolished neck dystonia, and myoclonus was significantly reduced in frequency and magnitude at 8-week follow-up.\(^{15}\) An 8-year-old boy with inherited myoclonus dystonia syndrome had an 81% improvement in his UMRS scores 20 months postoperatively.\(^{2}\) In a 26-year-old with childhood onset of the disease, the patient experienced a 48 and 79% improvement in Burke-Fahn-Marsden severity and disability scores, respectively.\(^{16}\)

Bilateral thalamic stimulation has also been advocated and was performed in a 60-year-old man symptomatic since age 6 years. While stimulation improved his myoclonic symptoms by 80% using a modified score, dystonic symptoms did not improve.\(^{20}\) Thalamic stimulation was also used in a 36-year-old man with myoclonic dystonia and disabling involuntary jerking movements since his teenage years; clinical scales were not used but the patient was reported to have regained much of his independence.\(^{6}\)

There are 2 case reports of simultaneous implantation of pallidal and thalamic stimulators. Trottenberg et al.\(^{21}\)

<table>
<thead>
<tr>
<th>TABLE 1: Summary of CRST and TWSTRS scores*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scale</td>
</tr>
<tr>
<td>CRST</td>
</tr>
<tr>
<td>A (location/severity)</td>
</tr>
<tr>
<td>B (specific motor tasks)</td>
</tr>
<tr>
<td>C (functional disability)</td>
</tr>
<tr>
<td>total</td>
</tr>
<tr>
<td>TWSTRS</td>
</tr>
<tr>
<td>A (severity)</td>
</tr>
<tr>
<td>B (disability)</td>
</tr>
<tr>
<td>C (pain)</td>
</tr>
<tr>
<td>total</td>
</tr>
</tbody>
</table>

* Thal = thalamus.
† Double-blind assessments only performed at 2 years.

<table>
<thead>
<tr>
<th>TABLE 2: Summary of UMRS scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>UMRS Category</td>
</tr>
<tr>
<td>patient questionnaire</td>
</tr>
<tr>
<td>myoclonus at rest</td>
</tr>
<tr>
<td>stimulus sensitivity</td>
</tr>
<tr>
<td>myoclonus w/ action</td>
</tr>
<tr>
<td>functional tests</td>
</tr>
<tr>
<td>global disability</td>
</tr>
<tr>
<td>negative myoclonus</td>
</tr>
<tr>
<td>severity of negative myoclonus</td>
</tr>
</tbody>
</table>

* Scores are based on function over time and cannot be assessed during a few hours of testing.
placed bilateral pallidal and bilateral thalamic electrodes in a 70-year-old woman with severe tardive dystonia. The patient’s dystonic symptoms improved on pallidal stimulation and she showed no additional benefit from the thalamic stimulation. In a patient with nonfamilial generalized dystonia and tremor, bilateral pallidal and thalamic stimulators were implanted, but clinical outcome was not provided.\textsuperscript{1,11} Goto et al.\textsuperscript{1,11} reported that a patient with focal hand dystonia in whom good benefit was obtained with either GPI or ventrothalamic DBS. Interestingly this patient received unilateral stimulation. In fact, there have been only a few cases of unilateral stimulation helping cervical dystonia.\textsuperscript{1,11}

In conclusion, pallidal stimulation appears to be sufficient to manage myoclonic dystonia; however, in our patient, simultaneous pallidal and thalamic stimulation provided some moderate advantage over pallidal stimulation alone.

Disclosure

Drs. Kiss and Oropilla have received research and educational funding from Medtronic for work unrelated to this report. Dr. Kiss is a Clinician-Scientist of the Canadian Institutes for Health Research and a Clinical Scholar of the Alberta Heritage Foundation for Medical Research. Dr. Oropilla received the 2007 Kenichiro Sugita International Fellowship from the Congress of Neurological Surgery.

Acknowledgments

The authors thank Drs. Scott Kraft and Kristina Doig-Beyaert for videotaping, programming, and patient management.

References


Portions of this work were presented in abstract/poster form at the American Society for Stereotactic and Functional Neurosurgery meeting in Vancouver, June 2008. Please include this information when citing this paper: published online November 20, 2009; DOI: 10.3171/2009.10.JNS091062.

Supplemental online information:


Address correspondence to: Zelma H. T. Kiss, M.D., Ph.D., F.R.C.S.C., Room 1AC58 HRIC, 3280 Hospital Drive NW, Calgary, Alberta, Canada T2N 4N1. email: zkiss@ucalgary.ca.