Pallidal stimulation for generalized dystonia

Report of three cases

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Pallidal stereotactic surgery is a well-accepted treatment alternative for Parkinson’s disease. Another indication for this procedure is medically refractory dystonia, especially generalized dystonia with abnormal axial and extremity movements and postures. Improvement of dystonia after pallidotomy has been reported in several recent papers. In this report the authors describe three patients with generalized dystonia (two primary, one secondary) and their improvement after bilateral pallidal stimulation at follow-up times of between 6 and 18 months.

Key Words • dystonia • deep brain stimulation • pallidal stimulation • pallidotomy • stereotaxis

Dystonia is a neurological syndrome characterized by involuntary, sustained, patterned, and often repetitive contractions of opposing muscles that causes twisting or spasmodic movements or abnormal postures. Primary dystonia is usually a hereditary disease, for which the gene locus has already been determined. In juvenile-onset primary dystonia, approximately 72% of patients have the tendency to develop generalized dystonia, in contrast with 5% of patients with adult-onset dystonia. Especially in the former patients, medical treatment is often disappointing. Botulinus toxin either cannot be injected or can be applied only to regional muscle groups, but many patients develop antibodies. Also, treatment with intrathecal baclofen is not very helpful, in our opinion, although contradictory reports exist. Chemopallidectomy was originally described as the stereotactic procedure of choice, but yielded beneficial results only in approximately 50% of patients. More recently the ventrolateral thalamus was chosen as the target (sometimes in combination with the medial pallidum) by many authors, with varying results. However, it was found that thalamotomy mainly improves distal limb dystonia without major effects on truncal or axial symptoms. Recent reports of pallidotomy describe a marked effect on all dystonic symptoms, including speech, writing ability, and gait. Bilateral pallidal stimulation is an attractive alternative to pallidotomy in Parkinson’s disease according to some authors, although others could not confirm these results and favor other targets such as the subthalamic nucleus. However, in generalized primary dystonia pallidal stimulation is a very effective procedure, as is shown in this report. The results in the first patient, who underwent the procedure 18 months ago, have already been published as an abstract.

Clinical Cases and Methods

Three patients underwent operation: two with primary dystonia musculorum deformans and one with secondary generalized dystonia after birth asphyxia. Patient characteristics are given in Table 1.

Pallidal stimulation was performed using the Zamora-Dujovny stereotactic system, guided by MR imaging. The surgical procedure was performed after the patient received a local anesthetic while in a state of stand-by anesthesia, with intravenous administration of conscious sedation and analgesic medication during application of the frame. No further medication was given during the imaging, microrecording, and stimulation phases of the operation. An MR-compatible frame was applied to the patient’s head to be as parallel as possible to the IC line according to external landmarks, and MR imaging was performed using a 1.5-tesla imager. A midsagittal image was obtained and the deviation of the frame to the IC line was determined. Axial slices were then obtained parallel to the IC plane. The primary pallidal target was chosen 3 mm anterior to the midcommissural point, 20 mm lateral to the midline, and 4 mm below the IC line. The target was corrected by using the angle deviation between the frame and IC line. Two precoronal burr holes were drilled 2.5 cm lateral to the midline, which created a trajectory between 4° and 12° with reference to the sagittal plane and 48 to 60° with reference to the anterior commissural-posterior
commissural line. Beginning 10 mm above the pallidal target, recordings were obtained with concentric bipolar tungsten microelectrodes (impedance 0.5–1 Mohm, tip 1–2 μm diameter) and a hydraulic microdrive. Spontaneous and evoked single-unit activity were recorded using conventional amplifiers with a bandwidth of 30 to 10,000 Hz and amplified 10,000 times. Analog data were displayed on an oscilloscope and stored on magnetic tape. Simultaneous recordings were collected with an analog/digital amplifier as digitized data and stored on analysis software for later review.

After determining the boundary of the GPi and the optic tract with microrecordings, macrostimulation was performed with a quadrapolar electrode. Sufficient microrecordings for later offline analysis were only obtained in the first two patients.

After temporary extension of the leads and connection to two external screening devices, a testing trial of 7 to 10 days was performed while the patients underwent antibiotic treatment. Subjective improvement of dystonia was reported by the first two patients and their physical therapist after 1 week of test stimulation. Therefore the impulse generators were implanted subcutaneously in a second operation. The third patient reported episodes of déjà vu with stimulator activation. A postoperative MR image revealed that the left-sided electrode was situated too far lateral and deep in the temporal lobe. Intraoperatively the patient had reported experiencing paresthesias with stimulation; therefore the left-sided electrode was placed 3 mm more lateral and 2 mm below the intended target, with its final position 23 mm lateral to the midline and 6 mm below the IC line. With the patient in a state of anesthesia, surgical revision with medial placement of the left-sided electrode was performed with stereotactic guidance. The episodes of déjà vu disappeared and the patient experienced marked benefit. Follow-up examinations were performed at 6 months in the second and third patients and at 12 and 18 months in the first patient.

**Sources of Equipment**

The stereotactic system was purchased from Howmedica-Leibinger, Freiburg, Germany. The MR imager (Edge) was acquired from Picker International, Cleveland, OH. The hydraulic microdrive was obtained from Trent-Wells, Coulterville, CA. The conventional amplifiers were pur-

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**Table 1**

Characteristics in three patients who underwent pallidal stimulation for generalized dystonia

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age Onset (yrs)</th>
<th>Previous Treatments</th>
<th>Burke &amp; Fahn Movement Scale*</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>27</td>
<td>anticholinergic &amp; neuroleptic agents, benzodiazepine, botulinum toxin, intrathecal baclofen</td>
<td>84 34.5</td>
<td>hereditary, DYT1 negative</td>
</tr>
<tr>
<td>2</td>
<td>28</td>
<td>dopamine agonists &amp; antagonists, baclofen, anticholinergic agents</td>
<td>70 60</td>
<td>secondary dystonia</td>
</tr>
<tr>
<td>3</td>
<td>18</td>
<td>anticholinergic agents, botulinum toxin, benzodiazepine</td>
<td>77 50.5</td>
<td>DYT1 positive</td>
</tr>
</tbody>
</table>

* Calculated according to the scale of Burke, et al.

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**Fig. 1.** Case 1. Photograph showing a 27-year-old patient with marked torsion dystonia before surgery.

**Fig. 2.** Case 1. Photograph of the same patient 12 weeks post-surgery. The truncal dystonia is markedly alleviated, although a laterocollis still exists. The patient’s laryngeal dystonia did not improve. After 6 months the patient passed his driver’s license examination.
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chased from Toennies, Würzburg, Germany. The digital storage oscilloscope (VC 6275) was acquired from Hitachi Denshi, Rodgau, Germany. The analog/digital amplifier was obtained from Brain Wave Systems Corp., Longmont, CO. The quadrapolar electrode (model 3387 DBS) was purchased from Medtronics, Inc., Minneapolis, MN.

Results

Our results are shown in Table 1 and Figs. 1 and 2. The patients with primary dystonia (Cases 1 and 3) experienced marked relief in axial and limb dystonia. The patient in Case 3 was able to walk for the first time in several years, and his speech was also improved. The patient in Case 1 still experienced major problems with laryngeal dystonia. The patient in Case 2, who had secondary dystonia, also experienced some benefit; however, the subjective improvement reported by this patient exceeded the objective measurements.

Discussion

The pathophysiological mechanism of dystonia is unknown. The observation that dystonia also occurs in Parkinson’s disease led to the hypothesis of a similar neuronal mechanism in these diseases. The fact that “off” dystonia was relieved by pallidotomy and the success of this procedure detailed in the earlier reports from the 1950s and 1960s led to a resurgence of pallidotomy as a treatment for dystonia. Compared with Parkinson’s disease and other movement disorders, high-frequency stimulation might also be considered as an alternative treatment option for dystonia. The advantages are as follows: 1) its reversibility; 2) the reduced risk compared with simultaneous bilateral operations; and 3) the ability to change stimulus parameters to enhance efficacy or reduce side effects. Only a few reports of single cases of bilateral pallidal stimulation for the treatment of generalized dystonia have been published so far, mainly in abstract form.7,14,23

Contrary to outcomes reported by other authors,15,26 we did not find a comparably slower neuronal activity in the medial globus pallidus in our patients compared with that in patients who have Parkinson’s disease. However, until now only small patient series from different hospitals that include microrecordings in patients with dystonia of different origins12,15,18,26 have been available to reach a conclusion. In addition, at several centers patients with dystonia underwent surgery in a state of general anesthesia, whereas in others conscious sedation was used throughout the procedure. This makes a comparison more difficult. We believe that microrecordings are very important in patients with dystonia because a clinical effect is rarely seen on intraoperative test stimulation. A slowly increasing clinical improvement within weeks after pallidotomy but no observable benefit intraoperatively has been reported by various authors. The same outcome holds true for pallidal stimulation. This is in contrast with the effects in patients with advanced Parkinson’s disease, leading us to postulate even more accurate microrecordings of spontaneous and driven neuronal activity in dystonic patients.

Another feature, which can only be observed in patients receiving stimulation is the effect of the return of dystonic movements after switching off the stimulating device. In our first patient with sufficient follow up, dystonia reoccurred 2 hours after the device was turned off at the 12-week follow-up examination. However, it took almost 2 days for recurrence of dystonic symptoms after switching the devices off at the 1-year follow-up examination. This outcome is also in strong contrast to the experience in patients with Parkinson’s disease. Whether this is due to plastic changes or reorganization of somatosensory input to the GPi neurons remains speculative. Interesting findings by Lenz, et al.,17 in the thalamus and GPi showed an enlarged receptive field with inclusion of the dystonic area. Therefore an overrepresentation of the dystonic area was hypothesized.

Conclusions

Pallidal stimulation is an effective and safe procedure for patients with generalized dystonia. Whether high-frequency stimulation will become an alternative treatment option for dystonia, as it is for other movement disorders, awaits confirmation in a larger series. A comparison of long-term results with patients who have undergone pallidotomy is desirable.

References


Addendum

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