Long-term follow-up of Huntington disease treated by bilateral deep brain stimulation of the internal globus pallidus

Case report

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Deep brain stimulation is now accepted as a safe and efficient treatment for movement disorders including selected types of dystonia and dyskinesia. Very little, however, is known about its effect on other movement disorders, particularly for “choreic” movements. Huntington disease is a fatal autosomal-dominant neurodegenerative disorder characterized by movement disorders, progressive cognitive impairment, and psychiatric symptoms. Bilateral chronic stimulation of the internal globus pallidus was performed to control choreic movements in a 60-year-old man with a 10-year history of Huntington disease. Chronic deep brain stimulation resulted in remarkable improvement of choreic movements. Postoperative improvement was sustained after 4 years of follow-up with a marked improvement in daily quality of life. (DOI: 10.3171/JNS/2008/109/70130)

**KEY WORDS** • deep brain stimulation • globus pallidus • Huntington disease

Huntington disease is a fatal autosomal-dominant neurodegenerative disorder, characterized by progressive cognitive impairment, movement disorders, and psychiatric symptoms. Treatment consisting of neuroleptics is tailored toward symptoms, and the clinical efficacy of pharmacological treatment for choreic movement remains poor. Furthermore, adverse effects are commonly dose limiting. Bilateral implantation of human fetal striatum has produced variable clinical results and is of limited access.

Deep brain stimulation has proven to be an effective treatment for medically refractory Parkinson disease and ameliorates not only parkinsonism but also choreic dyskinesia induced by levodopa. Chronic stimulation of the GPi alleviates, in particular, levodopa-induced dyskinesia.

We performed bilateral chronic stimulation of the GPi in a patient with severe choreic movements but no marked cognitive impairment. After a long-term follow-up of 4 years, we confirm the benefits of DBS for treating the symptoms of chorea in HD.

**Case Report**

*History and Examination.* This 60-year-old man was referred to our institution in 2002 to undergo assessment for DBS treatment to control choreic movements associated with HD. In 1993 the patient (at the age of 50 years) developed late motor symptoms, and in 1997 HD was genetically confirmed (44 repetitions of the IT15 gene) by a neurologist. There was no family history of HD. He had undergone treatment during multiple drug trials (haloperidol and tetrabenazine), which offered no alleviation of progressive and debilitating choreic movement despite high doses (haloperidol up to 10 mg and tetrabenazine up to 75 mg).

The patient suffered from continuous severe choreic movement in the face, neck, trunk, and upper and lower extremities, as well as oromandibular hyperkinesias. He was able to walk unaided. Examination of the extremities revealed hypotonia, although we observed no bradykinesia or dystonia. We found no evidence of either dysphagia or dysarthria. The patient showed tender limb reflexes and silent plantar responses. Sensory examination revealed normal findings. Neuropsychological assessment (Mattis Dementia Rating Scale, Mini-Mental State Examination, and Trail Making Test) indicated moderate subcortical cognitive dysfunction with no impact on daily activities. Magnetic resonance imaging showed caudate atrophy.

*Operation.* In 2003 it was decided that the patient would undergo surgery, following a 10-year history of HD, based on the absence of marked neuropsychological deficits and mood disorder as well as the marked impact of movement...
disorder on daily life. An established long-term efficacy of continuous electrical stimulation of the GPi in the treatment of many dystonodyskinetic syndromes sometimes associated with choreiform rapid dyskinesias allowed us to propose this technique to selected patients with HD.

After general anesthesia was induced, electrodes were placed stereotactically. Magnetic resonance imaging and the Leksell stereotactic frame were used to localize the posteroventral part of the GPi. Target coordinates were calculated using dedicated software. A quadripolar MR imaging–compatible electrode was implanted with the aid of radioscopic control (Medtronic Ruel-Malmaison). No electrophysiological recordings were taken. Control MR images were obtained immediately postoperatively with the stereotactic frame in place to verify electrode position and detect any complications (Fig. 1). The entire procedure was performed on the same day. Five days later, the electrodes were connected to 2 internal pulse generators implanted subcutaneously in the abdomen (Soletra, Medtronic).

All examinations and stimulation parameter adjustments were performed before surgery and at monthly intervals during the 1st year and every 3 months thereafter by the same physician.

Assessments. We used the UHDRS to assess 4 domains of clinical performance and capacity in HD (motor and functional assessments, and cognitive function and behavioral abnormalities). The motor section of the UHDRS assesses motor features of HD with standardized ratings of oculomotor function, dysarthria, chorea, dystonia, gait, and postural stability (maximum score 125). Choreic movement is assessed in upper and lower extremities, trunk, face, and mouth (maximum score 28). The functional assessments included the HD functional capacity scale, the independence scale, and a checklist of common daily tasks. The patient was assessed by 2 physicians preoperatively and 4 years postoperatively in stimulation-on and -off conditions with video recording. Intermediate consultations did not include video recording. We carried out functional assessments preoperatively and 4 years postoperatively in the stimulation-on condition. To assess neuropsychological performances, we used the Mattis Dementia Rating Scale, Mini-Mental State Examination, and Trail Making Test preoperatively and 4 years postoperatively in the stimulation-on condition.

Postoperative Course. The postoperative MR images showed that the centers of Contacts 1 and 2 were respectively 1 mm under and above the target in the posteroventral part of the GPi. On postoperative Day 1 we adjusted the stimulator to monopolar stimulation by using Contact 1 as the negative and the internal pulse generator case as the positive pole, with an amplitude of 1 V, a frequency of 130 Hz, and a pulse width of 450 μsec. We observed a reduction in choreic movement disorders of the limbs and trunk 10 days after surgery.

We started seeing bradykinesia in the lower extremities 2–3 weeks after introducing DBS, which improved following treatment with levodopa (187.5 mg). For the next 3 months we further adjusted the stimulator to bipolar stimulation (Contacts 1 and 2) with an amplitude of 1.9 V. At the follow-up review 3 months after surgery we observed a continued suppression of chorea of the upper and lower extremities, trunk, face, and mouth with the same stimulation parameters (Contact 1: negative pole, and Contact 2: positive pole; amplitude 1.9 V, frequency 130 Hz, and pulse width 450 μsec).

Four years after surgery the improvement of chorea remained stable. Motor assessments preoperatively and 4 years postoperatively are presented in Table 1. We observed a clear improvement in motor control when comparing stimulation-on and -off conditions at 4 years. Neuropsychological assessment again found a moderate subcortical cognitive dysfunction with no evolution.

Discussion

The benefits of DBS in treating many movement disorders including syndromes associated with dystonia and/or dyskinesia (particularly primary generalized dystonia) have previously been documented. The most significant improvements were attained in patients with DYT1-positive dystonia, with mixed results reported in patients with secondary dystonia. Very little data exist, however, regarding DBS treatment of other movement disorders, especially choreic syndromes. The abnormal movements associated with HD severely impair daily life, and treatment remains aimed at symptoms and relies on neuroleptics that provide little relief of choreic movements. In addition, the adverse effects associated with these pharmacological drugs are a dose-limiting factor. Recent reports have shown the efficiency of bilateral globus pallidus stimulation in treating symptoms of HD with a very short follow-up (< 1 year).

In this study we have demonstrated the long-term efficacy of GPi stimulation in controlling choreic movements (face, mouth, trunk, and extremities) after a 4-year follow-up.

By performing a “blind off-test” unknown to the patient or the family, we can check the actual improvement offered by DBS. Indeed when switching off the internal pulse generators we observed an immediate and severe worsening of chorea in the extremities, trunk, and face. Furthermore, autonomous standing and gait became impossible, speech mostly incomprehensible, and hand usage impossible in the stimulation-off condition. This clearly signifies a control of DBS on motor symptoms despite evolution of the illness as shown by a worsening of the chorea score with time (stimulation-off condition). For individuals who develop HD, members of the immediate family commonly take on a caring role. After 14 years of disease evolution (4 years postoperatively) experienced by our patient, unaided daily tasks including eating, dressing, and bathing became possible, resulting in an increase in the quality of life of the patient and also the spouse. Furthermore, the patient was able to keep hobbies including philately (involving the complicated usage of the stamp tong), as well as fishing (involving complicated motor tasks like fixing the hooks).

The overall tolerance of the procedure was good in our patient with no complications after a 4-year follow-up. Chorea remained suppressed with the same stimulation parameters (low current) as during the follow-up review 3 months after surgery. The device’s batteries were recently replaced (October 2006).

Cognitive impairment and psychiatric symptoms in HD must be carefully screened at the time of patient selection, but further studies are needed before defining precise selection criteria. In this case, we proposed DBS because the patient essentially presented with motor symptoms and moderate cognitive impairment in the absence of psychiatric symptoms.

**Conclusions**

In light of this study, we can confirm that in the patient who suffers from HD, chronic GPi stimulation is a valuable treatment option. Long-term and sustained control of motor symptoms has been achieved resulting in an improvement in the quality of life.

**References**


**TABLE 1**

Long-term assessment based on the UHDRS

<table>
<thead>
<tr>
<th>Category</th>
<th>Preop</th>
<th>Postop 4 Yrs (stimulation on)</th>
<th>Postop 4 Yrs (stimulation off)</th>
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</thead>
<tbody>
<tr>
<td>motor assessment</td>
<td>37/125</td>
<td>35/125</td>
<td>52/125</td>
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<td>chorea</td>
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<td>25/28</td>
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<td>checklist of common daily tasks</td>
<td>50/100</td>
<td>70/100</td>
<td>25/100</td>
</tr>
<tr>
<td>independence scale</td>
<td>11/13</td>
<td>10/13</td>
<td>1/13</td>
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**References**