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Tremor and Other Hyperkinetic Movements

Case Reports

# Development of Hyperkinesias after Long-term Pallidal Stimulation for Idiopathic Segmental Dystonia

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## Abstract

**Background:** Chronic deep brain stimulation (DBS) of the globus pallidus internus (GPi) has become an established treatment for dystonia. While bradykinetic symptoms may occur on chronic stimulation, the appearance of hyperkinetic movements has not been well characterized.

**Case Report:** We report on the development of hyperkinesias after more than 10 years of GPi DBS.

**Discussion:** Hyperkinesias may evolve upon long-term GPi DBS in dystonia. This might be related to a combined effect consisting of a reduced threshold for effective GPi stimulation for dystonia and spread of current to the globus pallidus externus.

**Keywords:** Deep brain stimulation, dystonia, globus pallidus, hyperkinesias, long term

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**Ethics Statement:** All patients that appear on video have provided written informed consent; authorization for the videotaping and for publication of the videotape was provided.

## Introduction

Chronic deep brain stimulation (DBS) of the posteroventral lateral globus pallidus internus (GPi) has become an established treatment for patients with idiopathic segmental dystonia, including Meige syndrome.[1–4] While stimulation is tolerated well, in general, and side effects are rare, recent reports have reported occurrence of bradykinetic symptoms in some patients upon chronic stimulation with high-energy delivery.[5,6]

Here, we report on the development of hyperkinesias after more than 10 years of bilateral GPi DBS and the complex effect of stimulation on both dystonia and hyperkinesias.

## Case report

A 62-year-old male was referred with a 5-year history of refractory idiopathic segmental dystonia diagnosed as Meige syndrome. He suffered mainly from phasic dystonic movements including blepharospasm, orofacial dystonia, aerophagia and mild cervical dystonia (Video 1, Segment 1). Treatment with botulinum toxin injections and trihexyphenidyl up to 30 mg daily had provided only limited improvement. The Burke-Fahn-Marsden (BFM) motor score was 26 (Table 1). His magnetic resonance scan was unremarkable, and there was no history of psychiatric comorbidity or previous neuroleptic medication.

The patient underwent computed tomography (CT) stereotactic awake implantation of bilateral DBS electrodes guided by microelectrode recording in the posteroventral lateral GPi (model 3387, Medtronic, Minneapolis). The preliminary target coordinates were x=20 mm lateral to, y=3 mm anterior to, and z=4 mm below the midpoint of the intercommissural line. Surgery was uneventful and there were no side effects. Postoperative stereotactic CT imaging confirmed appropriate placement of the DBS electrodes within the target, and the electrodes were connected to two implantable pacemakers (implantable pulse generator (IPG); Soletra, Medtronic). Further surgical details were reported previously (patient 5 in ref. 2). At the 6-month follow-up, dystonia improved with bipolar stimulation

(BFM motor 18, Table 1), and at 72 months there was further improvement after adjustment of chronic stimulation (BFM motor 16, Table 1; Video 1, Segment 2). The dosage of trihexyphenidyl was decreased. Temporarily the right DBS electrode was switched off because the patient noted a sensation of inner tension with bilateral stimulation that improved, however, with unilateral stimulation.

**Video 1. Development of hyperkinesias after long-term pallidal stimulation for idiopathic segmental dystonia. Segment 1.** At age 62 the patient suffers from segmental dystonia with blepharospasm, orofacial dystonia, aerophagia and mild cervical dystonia with the head tilted to the right. **Segment 2.** Six years after chronic pallidal deep brain stimulation (DBS), there is improvement of dystonia, in particular of blepharospasm and orofacial dystonia. **Segment 3.** More than 10 years after chronic DBS (10.5 years) dystonia recurs after stimulation has been switched off for 2 minutes, but there are also hyperkinesias now affecting the extremities and the trunk. **Segment 4.** Pallidal DBS improves both dystonia and the hyperkinetic movements, however, with much less energy delivered to the target than during the first years of stimulation.

At age 72, after about 10 years of chronic stimulation, he started to experience involuntary choreic movements of his arms and legs, but also of his trunk and face. The daily dosage of trihexiphenidyl was 25 mg at that time. The appearance of hyperkinesias was rather insidious with slow progression over the next few months. The impact of stimulation on the hyperkinetic movements remained unclear, and the suspicion of a psychogenic origin was raised. There were no other hints for comorbid somatization disorders. Hardware malfunction was excluded, and CT imaging confirmed that the electrodes were still in the same position as in the immediate postoperative imaging. Two months later, however, upon complete depletion of the IPGs both dystonia and hyperkinesias had worsened.

Five days after replacement of the IPGs (Activa PC, Medtronic), a detailed blinded assessment with various stimulation settings was performed (Table 1). In the DBS-off condition there was worsening of both dystonia and choreic hyperkinesias (Video 1, Segment 3). Higher voltage DBS resulted in improvement of dystonia but also in further deterioration of hyperkinesias, while lower voltage stimulation improved both dystonia and hyperkinesias (Video 1, Segment 4). DBS settings then were reprogrammed for chronic stimulation with remarkably lower voltage than during the first years of GPi DBS. With these settings, a satisfactory effect could be achieved on both dystonia and hyperkinesias at follow-up 132 months after DBS implantation (Table 1).

## Discussion

There is a plethora of movement disorders that might be caused by chronic DBS including both bradykinetic[5–7] and hyperkinetic symptoms.[3,7,8] It appears that at least some of these stimulation-related symptoms such as bradykinesia and freezing of gait may occur in the

Table 1. **BFM Motor Scores and Stimulation Settings in a Patient with Idiopathic Segmental Dystonia during Chronic Globus Pallidus Internus Deep Brain Stimulation**

| | | Preoperative | Follow-up 6 months | Follow-up 72 months | | Follow-up 126 months | | Follow-up 132 months |
|---|---|---|---|---|---|---|---|---|
| BFM motor | | 26 | 18 | 16 | 28 | 20 | 14 | 14 |
| Stimulation mode | R | – | 2+, 1– | 3+, 0– | Off | 1+, 0– | 1+, 0– | 2+,0– |
| | L | – | 2+, 1– | 3+, 0– | Off | 1+, 0– | 1+, 0– | 2+,0– |
| Amplitude | R | – | 2.1 | 2.4 | – | 3.0 | 0.4 | 0.4 |
| | L | – | 2.0 | 2.3 | – | 2.0 | 0.6 | 0.6 |
| Pulse width | R | – | 210 | 210 | – | 210 | 210 | 120 |
| | L | – | 210 | 210 | – | 210 | 210 | 120 |
| Frequency | R | – | 130 | 130 | – | 130 | 130 | 130 |
| | L | – | 145 | 130 | – | 130 | 130 | 130 |

Abbreviations: L, Left; R, Right.

presence of a satisfactory effect on the primary movement disorder that was the indication for surgery, and seemingly well-placed electrodes within the target structure. Thus far, it has been difficult to explain why such symptoms may occur and which are the pathophysiological mechanisms.[5,6]

While new dyskinesias were reported previously in patients with dystonia after the onset of pallidal stimulation these have been not well characterized and the impact of various stimulation settings thus far has not been investigated.[3,4] Chorea induced by pallidal stimulation has been observed in one patient with dystonia when dorsal contacts located in the globus pallidus externus (GPe) were activated.[8]

It remains unclear whether the occurrence of hyperkinesias in our patient upon long-term DBS was related to the effects of chronic stimulation or whether it was related to the natural course of the movement disorder itself. While the latter appears to be rather unlikely, a causal relationship between chronic GPi stimulation and the development of hyperkinesias would also be challenging to explain. Even more so, the complex effect of stimulation amplitude on hyperkinesias that reduce with low-amplitude stimulation but increase with higher-amplitude stimulation despite a stable effect on dystonia is puzzling.

One possible explanation would be that long-term stimulation might alter and ultimately reduce the threshold that is needed for effective stimulation of the GPi in single patients to abate dystonia, concurrently with suppression of hyperkinesias, but that spread of current to the adjacent GPe with electrodes placed relatively more lateral or deeper might have an effect on GPe neurons or their projections to the subthalamic nucleus, but only with higher stimulation amplitudes and a larger spread of current.

Other possible explanations for the delayed occurrence of choreic movements that, however, make it more difficult to explain the effects of stimulation at different intensities are secondary worsening of an undiagnosed tardive movement disorder, development of anticholinergic-induced chorea,[9,10] undetected mild concomitant dopaminergic denervation and altered sensitivity to spread of current to GPe,[11] and development of another neurodegenerative movement disorder. Finally, it might also be that a combination of such causes and effects might underlie the phenomena that were observed.

The observation that both dystonia and choreic hyperkinesias became acutely worse when stimulation was switched off completely may appear to be counterintuitive, as a stimulation-induced phenomenon should not worsen further when stimulation is switched off. It must be noted, however, that stimulation was switched off only for a short period and that we did not account for washout and rebound effects.

While there is no systematic study investigating the need for sustained stimulation with high-voltage settings after long-term chronic pallidal DBS in dystonia, it is remarkable that even sustained relief of dystonia has been observed despite prolonged cessation of stimulation in some patients.[12,13] This scenario does not only indicate that pallidal DBS might work as a disease-modifying treatment, but it might also provide support to our hypothesis that chronic stimulation might alter thresholds for both effective stimulation for dystonia in the GPi, and the occurrence of hyperkinesias via spread of current to the GPe in certain conditions.

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