

CASE REPORT

# Bilateral deep brain stimulation of the subthalamic nucleus effectively relieves dystonia secondary to Fahr's disease: a case report

Yu Ma,<sup>1</sup> Ming Ge,<sup>2</sup> Fangang Meng,<sup>1</sup> Kai Zhang,<sup>2</sup> and Jianguo Zhang<sup>1,2</sup>

<sup>1</sup>Department of Functional Neurosurgery, Beijing Neurosurgical Institute, Capital Medical University, Beijing, China;

<sup>2</sup>Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, Beijing, China

Fahr's disease (FD) is a rare movement disorder characterized by bilateral intracranial calcifications that is refractory to most treatments. We present the case of a 26-year-old male with FD who was unable to walk independently and could not eat solid food because of poor swallowing capability and severe cervical dystonia. Injections of botulin toxin into the neck muscles, as well as biperiden, tiapride, amantadine, L-dopa and clonazepam were ineffective. Deep brain stimulation (DBS) was performed with two permanent electrodes containing four contact sites implanted bilaterally into the subthalamic nucleus (STN). The antidystonic effect was evident immediately after STN stimulation, and it was sustained during a 24-month follow-up period. There was a marked reduction of cervical dystonia, and he could eat solid food and was able to walk independently. This case demonstrates that DBS of the STN can be effective for the treatment of dystonia associated with FD.

**KEYWORDS:** deep brain stimulation, dystonia, Fahr's disease, subthalamic nucleus

## Introduction

Fahr's disease (FD) is a rare neurological disorder characterized by abnormal deposits of calcium predominantly in the globus pallidus, although they can also occur in the basal ganglia, cerebral white matter, thalamus, internal capsule and/or cerebellum [1–3]. The disease usually includes motor symptoms, such as dystonia, dysarthria and spasticity, and the age of onset is typically between 30 and 60 years [1–3]. Both sporadic and familial cases with both autosomal dominant and recessive inheritance have been reported, and a susceptibility locus has been mapped to chromosome 14q [4]. The prevalence of FD is unknown, but an incidence of 0.68% was reported in an analysis of 3662 cranial computed tomography (CT) scans [5]. Although its gender and age predilections are different from those of dystonia, most investigators consider FD a variant of dystonia [3]. FD is refractory to most treatments.

Advances in neurosurgical techniques and the introduction of deep brain stimulation (DBS) have made it possible to modulate the activity of brain circuits, and DBS was first used to successfully treat dyskinesia in Parkinson's disease (PD) [6]. Since its success in the treatment of PD, DBS has been used to treat other movement disorders as well as depression and refractory epilepsy [7–13]. The globus pallidus interus (GPi) has been the primary target for the treatment of dystonias with DBS; however, reports have also shown that DBS of the subthalamic nucleus (STN-DBS) can also be effective [6,14,15]. There are, however, few reports of using DBS for the treatment of FD. Zorzi et al. [13] treated 12 patients with primary and secondary dystonia, including 1 patient with dystonia secondary to FD, with DBS of the GPi, and the patients with FD achieved a 73% improvement in symptoms.

Herein, we report the case of a male patient with FD refractory to treatment who achieved a significant improvement in symptoms with STN-DBS.

## Case presentation

The patient was a 26-year-old, right-handed male patient with a negative family history of neurological

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Correspondence: Jianguo Zhang, Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, No. 6 Beijing Tiantan Xili, Chongwen District, Beijing 100050, China. Tel: +86-1067057507. Fax: +86-010-67057507. E-mail: zjguo73@gmail.com

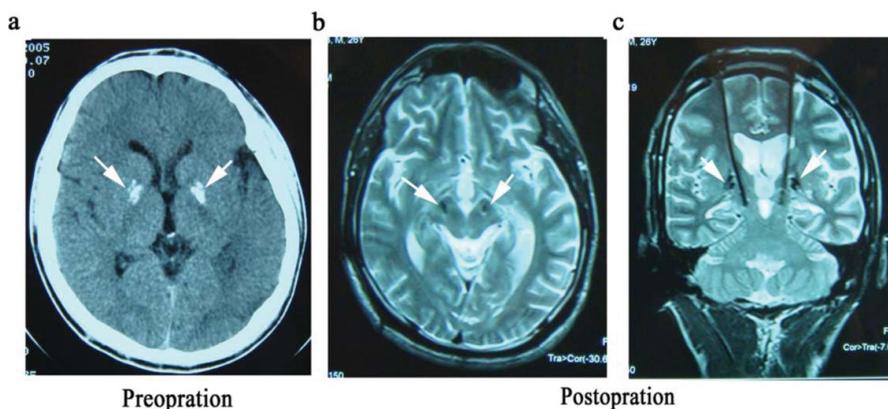


Figure 1. (a) Preoperative computed tomography. The white arrow shows calcification of the bilateral globus pallidus. (b, c) Postoperative magnetic resonance images demonstrating that the implanted electrodes were located in the subthalamic nucleus, not in the globus pallidus.

disease. His head and neck involuntarily twisted toward the right when he was 20 years old, and the symptoms gradually worsened until he was unable to eat solid food because of poor swallowing capability. Severe cervical dystonia rendered him unable to walk or speak (video segment 1, supplementary material available online), and extensive retrocollis hampered his respiration and forced him to sleep in a semirecumbent position. In addition, spasms of neck muscles kept his head forced to the right.

He had no history of convulsions or childhood developmental delay. Early-onset primary dystonia, pantothenate kinase-associated neurodegeneration and Wilson's disease were ruled out by clinical examination and genetic testing. CT scan of the brain revealed bilateral symmetric calcifications in the globus pallidus (Figure 1a), with other cortical and subcortical areas unaffected. Serum calcium, phosphate and parathyroid hormone levels were normal. Magnetic resonance imaging, electroencephalogram and other laboratory investigations did not reveal any abnormalities. Thus, he was diagnosed with FD on the basis of established criteria [15].

Local injections of botulin toxin with dosages from 100 to 250U into the neck muscles provided partial relief for a few months; however, his symptoms returned and his dysphagia worsened and thus the botulin toxin was discontinued. Biperiden, tiapride, amantadine, L-dopa and clonazepam were subsequently tried, but none provided any relief.

With a diagnosis of FD refractory to medical treatment, DBS was suggested as a potential treatment. The risks and benefits of the procedure were explained to the patient, and written informed consent was obtained. Preoperatively, he scored 8 on the Anxiety Scale and 9 on the Hamilton Depression Scale, demonstrat-

ing that he had mild anxiety and depression before surgery.

The STN was identified by a combination of neuroimaging, microelectrode recording and stimulation techniques. The surgical procedure was divided into two steps to evaluate whether the DBS worked before complete implantation. First, two permanent electrodes (Medtronic model 3387) containing four contact sites were bilaterally implanted into the STN (Figure 1b and 1c) under local anesthesia. Temporary stimulation was administered 3 days later, and an improvement in symptoms was noted after continuous stimulation for 3 days. Having shown definitive benefits for 2 weeks, the two implanted electrodes were connected to a pulse generator (Medtronic model 7424) that was implanted subcutaneously in the subclavicular area under general anesthesia.

Within 1 month of surgery, a programming session was performed during which the acute effects of increasing amplitudes of high-frequency neurostimulation were tested for each electrode contact (a trial of at least 30 seconds) in monopolar mode (frequency, 185 Hz; pulse width, 90  $\mu$ s) or bipolar mode. The contact for prolonged stimulation was selected on the basis of reduction in the dystonia and neuroimaging data. Adjustments could be performed at any time thereafter to maximize the clinical benefit or reduce adverse effects. After assessment of the effect of each stimulation mode, the best effect was noted when contact 3 was set as the anode and the case as the cathode. The stimulation effects of both sides improved with increasing voltage, and the voltage was gradually increased to 3.0 V for the left side and 3.2 V for the right side.

The antidystonic effect was evident immediately after STN stimulation, and it was sustained during the 12-month follow-up period. There was a marked reduction

Table 1. Results of Burke–Fahn–Marsden Dystonia Rating Scale (BFMDRS) and Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS).

Variable	Range	Score		Improvement (%)
		Baseline	12 months	
<b>BFMDRS (movement)</b>				
Total	0–120	48	4	91.7
Face (eyes and mouth)	0–16	8	0	100
Speech and swallowing	0–16	16	1	93.8
Axial (neck and trunk)	0–24	24	3	87.5
Arms and legs	0–64	0	0	0
<b>BFMDRS (disability)</b>				
Total	0–30	26	7	73.1
Speech	0–4	4	2	50
Writing	0–4	3	1	66.7
Feeding	0–4	4	0	100
Eating and swallowing	0–4	4	0	100
Hygiene	0–4	4	1	75
Dressing	0–4	3	1	66.7
Walking	0–4	4	2	66.7
<b>TWSTRS</b>				
Severity	0–35	28	8	71.4
Disability	0–30	24	6	75
Pain	0–20	7	0	100
Total	0–85	59	14	87.5

in the severity of cervical dystonia, and his swallowing improved such that he was able to eat solid food without difficulty. He was able to walk independently (video segment 2, supplementary material available online) and speak, although his speech was difficult to comprehend.

The Burke–Fahn–Marsden Dystonia Rating Scales for movement and disability (BFMDRS; scores ranging from 0 to 120 and 0 to 30, respectively, and higher scores indicating greater impairment), the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS; scores ranging from 0 to 85, and higher scores indicating greater impairment) were used before surgery and during the follow-up period. The BFMDRS movement score at baseline was 48 points and decreased to 4 points 12 months after stimulation (a reduction of 91.7%), and the BFMDRS disability score improved from 26 points to 7 points (a reduction of 73.1%). Likewise, the total TWSTRS score decreased from 59 points to 14 points (a reduction of 87.5%), with severity and disability improved by more than 70%, and his pain completely resolved (Table 1). At 24 months of follow-up, the patient is doing well, and no adverse effects have been noted.

## Discussion

We have reported a case of FD that was refractory to conventional treatments in which the patient's symptoms markedly improved with STN-DBS. Although DBS has been shown to have beneficial results in many

diseases, we found only one mention in the literature of FD treated with DBS.

The pathophysiological mechanism of FD has not been well elucidated, and for a diagnosis of FD, both calcification of certain brain areas and normal serum calcium and phosphate levels are required. In this case, calcifications were found bilaterally in the basal ganglia, and the patient's serum calcium and phosphate levels were normal. Although severity of symptoms is typically correlated with the amount of calcification, symptoms can also be related to the location of the calcifications [16].

The GPi has been shown to be an effective target for DBS in patients with dystonia [5], and among the many nucleus groups affected in patients with FD, the GPi is most frequently involved [17]. The severely calcified GPi in our patient obviated any clinical benefit of GPi-DBS, thus a different target had to be determined. The STN is important in muscle function, and lesions in the STN in experimental animals and humans are well known to produce dystonia [18]. In addition, the effectiveness of STN stimulation for the treatment of medication-induced dyskinesia in individuals with PD has renewed interest in the STN as a target for dystonia [7].

There have, however, been only a few studies evaluating STN stimulation in dystonia, and most are of PD-related dystonia. Detante et al. [14] reported that STN-DBS was ineffective in dystonia patients. In contrast, Sun et al. [15] studied 8 patients with generalized dystonia, and all the patients treated with STN

stimulation had an improvement in their dystonia, whereas a benefit was observed in only half of the patients who received GPi stimulation. In addition, the improvement after STN stimulation was seen soon after the initial programming session, whereas the beneficial effect of GPi stimulation was not observed for a few months. In a prospective study, Ostrem et al. [19] examined the effect of STN-DBS in 9 patients with medication-refractory cervical dystonia and reported the treatment was well tolerated with no serious adverse effects, a significant improvement in TWSTRS score from 53.1 preoperatively to 19.6 at 12-month postoperatively and improvement in quality-of-life measures. Similarly to the patients in the study by Sun et al. [15], our patient responded quickly to STN stimulation; an improvement in neck pain and resolution of the dystonic neck posture were observed 12 hours after STN stimulation. It is unclear why varying results to the STN stimulation have been noted; however, factors including differences in electrode placement, stimulation parameters or other technical factors may be partly responsible.

Although DBS is typically performed with the GPi as the target, there are two reasons we chose the STN in this case. First, the STN is a relative small nucleus and as such requires relatively lower stimulation amplitude. Second, in our practice, we have found that STN-DBS is very effective for patients with dystonias, and in this case because the primary clinical feature was dystonia, we believed the STN would be a suitable target. In addition, as mentioned above, we believed the marked calcifications in the GPi would decrease the effectiveness of GPi-DBS.

In summary, the remarkable effect of bilateral STN stimulation in our patient demonstrates that it can be an effective treatment for FD. This is the first report showing substantial improvement in an FD patient. Further studies and long-term follow-up are needed to clarify the mechanism by which DBS suppresses dystonia, and how the STN is involved in the pathophysiology of this condition.

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## Declaration of Interest

The authors report no conflict of interest. The authors alone are responsible for the content and writing of this paper.

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## Supplementary material available online

Video Segment 1. Marked cervical dystonia and inability to walk independently were seen before surgery.

Video Segment 2. After 3 months of STN stimulation, the patient could walk independently.