

## Pallidal deep brain stimulation for the treatment of DYT6 dystonia: a case report and review of literature

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### Abstract

Little is known about the results of pallidal deep brain stimulation (DBS) in DYT6 dystonia. This will be the first report of DYT6 dystonia treated with pallidal DBS from Iran. A 21 years old male patient with DYT6 dystonia underwent bilateral deep brain stimulation. The target of DBS was the sensorimotor region of the posteroventral globus pallidus internus (GPi). DBS parameters included an amplitude of 2.7 V, frequency of 160 Hz, and pulse width of 90  $\mu$ s which were adjusted according to the patient's response 12 months after surgery. Treatment outcome was measured by the patient's Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) score. Before surgery, the patient's BFMDRS score was 32. However, BFMDRS score reduced to 7 at one year follow up after surgery (78% improvement of total score). Dystonic symptoms of extremities and mouth completely resolved. Also speech and swallowing function significantly improved. Although previous observations reported a poor to moderate response in speech, we found DBS as an effective treatment not only for dystonic features, but also for speech improvement of DYT6 dystonia.

**Keywords:** Deep brain stimulation, DYT6 dystonia, Globus pallidus internus.

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### Introduction

Dystonias are a heterogeneous group of movement disorders defined by involuntary muscle contractions causing repetitive and twisting movements or abnormal postures (1,2). Depending on etiology, dystonia can be primary (without a known cause) or secondary to acquired brain lesions (3). Primary or hereditary dystonias are classified by their heterogeneous genetic background into 20 different genetic forms (DYT1 to DYT20) (4). However, a few genes (TOR1A/ DYT1, GTPCH/ DYT5, THAP1/ DYT6,  $\epsilon$ Sarcoglycan/ DYT11, Na/K ATPase  $\alpha$ 3 subunit/ DYT12) for primary dystonia have been identified so far (5).

The pharmacologic treatment for primary generalized dystonia including a combination of anticholinergics, dopamine agonists

and antagonists, and benzodiazepines, are usually unsatisfactory with transient effects (3). Therefore, surgical interventions have been suggested to relieve symptoms of patients with medically refractory disease (6,7). In recent years, pallidal deep brain stimulation (DBS) has been used as a safe and effective method to treat advanced, disabling primary dystonia, especially DYT1 form and secondary dystonia such as tardive dystonia (3,8). However, due to existence of clinically and genetically diverse forms of primary dystonia, little is known about the results of bilateral pallidal stimulation in other types such as DYT6 dystonia (7). DYT6 gene has been recently identified and there have been few studies exploring its treatment results with DBS (9).

In this study, we present a case of primary

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DYT6 dystonia and describe his clinical features, in addition to his initial response to bilateral DBS. This would be the first report of DYT6 dystonia treated with pallidal DBS in Iran.

**Case report**

A 21 years old boy presented to our clinic with dystonic movements in his right hand since the age of 8, gradually had progressed to other body regions. At the time of our first visit (11 years after the disease onset), his most important complaint was cervical involvement. Also dystonia was apparent in his face and oromandibular dystonia was also detectable. He had retrocollis, in addition to dystonic movements in his upper extremities. No sign of rigidity, hypokinesia or bradykinesia was detected. The patient’s BFMDRS (Burke-Fahn-Marsden Dystonia Rating Scale) score was 32 (Table 1). Genetic assessment for the patient using DNA from peripheral blood leukocytes and PCR amplification revealed mutation in THAP1 by sequence analysis.

The patient had used trihexyphenidyl 10-15mg and clonazepam 2-3 mg daily. He had a positive history of febrile seizure when he was 5 years old. The patient had two healthy brothers and negative family

history for dystonia.

The patient underwent bilateral deep brain stimulation in the sensorimotor region of the posteroventral GPi. DBS parameters set on amplitude of 2.5 V, frequency 145 Hz, pulse duration 90 µs after surgery. According to clinical effects, after one year follow-up the parameters were adjusted to an amplitude of 2.7 V, frequency of 160 Hz, and pulse width of 90 µs.

BFMDRS score of the patient reduced to 7 one year after surgery (total 78% improvement). Dystonic symptoms of extremities and mouth completely resolved. Also speech and swallowing function significantly improved (Table 1). No complication was observed in the patient during one year of follow up.

**Discussion**

DYT6 dystonia is associated with mutation of the gene encoding thanatos-associated protein (THAP1) (10) and first has been described by Almasy et al. in 1997 (2). The disease mainly involves upper limbs, cervical or cranial muscles and it may be characterized by early onset cervico-laryngeal dystonia (2,4,11). Medically refractory cases of DYT1 dystonia are considered for surgical treatments such as DBS (8). However, there is little experience with

Table 1. Changes in BFMDRS sub scores of the studied patient with DYT6 dystonia one year after DBS.

BFM	Provoking factor		Severity factor		Weight		Product	
	Before	After	Before	After	Before	After	Before	After
Mouth	4	0	3	0	0.5		6	0
Speech and swallowing	3	2	4	1	0.5	0.5	6	1
Neck	4	4	4	2	0.5	0.5	8	4
Rt arm	2	0	2	0	1		4	0
Lt arm	2	0	2	0	1		4	0
Rt leg	2	2	2	1	1	1	4	2
Total score							32	7

Table 2. Review of literature for the results of DBS in patients with DYT6 dystonia

Study No.	Year	First author	Reference No.	No. patients	Follow up	Motor score improvement	Speech improvement
1	2010	Groen et al.	1	4	6 months	33%	Little/ no
2	2010	Zittle et al.	4	2	2-7 years	Moderate	No
3	2011	Jech et al.	10	1	32 months	85%	Fair
4	2012	Panov et al.	9	3	3 years	48%	Little/no
5	2012	Franca et al.	12	1	2 months	59%	Not mentioned
6	2012	Miyamoto et al.	13	1	Years	Moderate, needed second surgery	Not mentioned

DBS in the treatment of DYT6 dystonia. To date, only 6 studies (including 12 patients) have been presented in the literature to demonstrate result of DBS in this specific group of dystonia patients (Table 2).

Zittel et al. reported two DYT6 dystonia patients who treated with bilateral pallidal deep brain stimulation. These patients experienced moderate symptoms improvement and also no improvement in their oromandibular or laryngeal dystonia was observed even seven years after surgery (4). Groen et al. reported four other patients with early onset DYT6 dystonia who underwent bilateral GPi DBS. They observed 33% motor improvement on BFMDRS 6 months after surgery. However, they found no improvement on patient's speech (1).

Excellent effects of GPi-DBS in DYT6 dystonia was only reported by Jeck et al. Their patient had 98% improvement in 1 month and 85% improvement 32 months postoperatively. They argue that this favorable result from DBS is due to a specific THAP1 mutation in their patient (10). In another report by Franca et al., satisfactory results were obtained from DBS of a Portuguese DYT6 patient 2 months after surgery (59% improvement of BFMDRS score) and cervical and oromandibular dystonia improvement was remarkable (12).

Finally, in a recent study on three patients with DYT6 dystonia, pallidal DBS had a modest effect on symptoms improvement during the first two years after surgery and even some symptom regression have been observed (9).

Our case also illustrates a successful application of DBS for DYT6 patients. He experienced near significant resolution of dystonic movements on extremities and mouth during a 12-month follow up after surgery. A near complete improvement in speech and swallowing function was also observed. We suggest GPi DBS as a useful and effective treatment for DYT6 positive patients.

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