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Case report

Parallel improvement in anxiety and tics after DBS for medically intractable Tourette syndrome: A long-term follow-up

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1. Introduction

Tourette syndrome (TS) is a movement disorder characterized by repetitive vocal and motor tics that persist for more than one year. The onset is usually in childhood with alternating periods of improvement and deterioration in adolescence and a tendency to improve after age of 18 years [1]. In addition to the motor features, TS is commonly associated with neuropsychiatric comorbidities including obsessive-compulsive disorder (OCD) and attention-deficit/hyperactivity disorder (ADHD) with substantial anxiety symptoms. Although the severity and frequency of tics diminish considerably in adulthood, some patients remain very symptomatic despite behavioral and pharmacological therapies. Their quality of life is significantly impaired. The pathophysiology underlying TS remains unknown, but evidence supporting the role of basal ganglia-thalamocortical circuits in the generation of tics and obsessive-compulsive behaviors has led to stereotactic targeting of key-point structures in these circuits in refractory patients [2]. Here we describe a patient with refractory TS with an excellent long-term outcome following bilateral thalamic deep brain stimulation (DBS).

2. Case report

This 23-year-old, right-handed, otherwise healthy man had had severe, lifelong TS. He had a gradual onset of facial, neck, and vocal tics beginning at the age of six years. The facial tics entailed excessive blinking, sniffing, and grimacing. His vocal tics included grunting, loud noises, and occasionally cursing. His neck tics included head jerking towards the right side with both shoulders shrugging. At age 12, after regular use of clonidine and haloperidol, he experienced a small improvement in the tics. However, the symptoms worsened by the age of 20. Apart from increases in blinking and facial grimacing, he had frequent forceful, orchestrated arm swings, as if he were mimicking a chicken. He had bitten his teeth so violently that he often hurt himself. His frequent grunting and sniffing vocal tics severely disturbed his speech in a way sometimes associated with echolalia and coprolalia. At that time, he was single and unemployed. He was treated with clonidine, clonazepam and aripiprazole, yet with unsatisfactory effects. After being evaluated by several neurologists, psychiatrists, and clinical psychologists and having received an exhausting array of pharmacological treatment, he was referred for surgical evaluation when he was 23 years old.

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His Yale Global Tic Severity Scale (YGTSS) score was 95 (in a range of 0–100 and it is subdivided in Tic Severity [50] and Impairment in Quality of Life [50]) and his Hospital Anxiety Scale (HAS) was 17 (in range of 0–21). Psychiatrists agreed that he did not have obsessive-compulsive symptoms or depression and that he was mentally fit to consent to surgery. After extensive discussion regarding the potential benefits, risks, and complications of DBS, he was scheduled for surgery. The centromedian-parafascicular (CM-Pf) complex thalamic was targeted based on MRI landmarks and atlas coordinates.

Microelectrode recording mapping was performed from the ventral posterior medial nucleus of thalamus that responded to sensory stimuli on the face, to more medial target towards the CM-Pf. The DBS electrode (model 3387; Medtronic, Minneapolis, Minn., US) then replaced the microelectrode in the desired track and macrostimulation was performed with the patient awake. Curiously, when mild stimulation was initiated in the right thalamus, the patient described a significant sensation of well-being directly related to the stimulation, even in a blind fashion. This kind of response was only observed on the right side. However, when stimulation was applied at higher threshold intensities, paresthesias were elicited in the contralateral face. After 18 months of follow-up, a marked reduction of tics was observed (video 1). The YGTSS decreased from 95 to 28 (70.5% improvement) and the subscore 'Impairment' decreased from 50 to 20 (60% improvement). The HAS decreased from 17 to 8 (53% of improvement) after 18 months follow-up. The Patient Global Impression of Change, measured on a seven-point Likert scale, was 6 after the surgery ("much improved") (Fig. 1).

3. Discussion

The results of our case are in line with most previous reports showing that DBS is a safe treatment for patients with refractory TS [3]. Standard and validated outcome measures were used to gauge patient response. The YGTSS reports that the impact of tics on the patient's life including frequency, intensity, complexity and interference and can be used to compare the efficacy of other TS treatments. We observed positive effects on tic frequency and severity in the early postoperative period that continued for 18 months. Besides an improvement in tics, the patient showed good outcomes on anxiety scores, which have been little reported in previous studies [4].

DBS should be considered for patients with TS with severe functional impairment that cannot be managed medically. Patients should also have undergone psychiatric evaluation to determine whether cognitive behavioral therapy may be effective in controlling symptoms. Classically, the thalamus and the globus pallidus has been targeted in TS. The centromedian-parafascicular (CM-Pf) nucleus of the thalamus, along with ventro-oral internus (Voi), is thought to be situated in a unique position within the action-gating pathways of the basal ganglia. Diffusion tensor imaging studies in humans show structural connectivity between the CM-Pf nucleus and the putamen, pallidum, nucleus accumbens, amygdala, and hippocampus. The observed benefits of DBS for TS are apparently achieved through modulating the excitatory feedback loops between the CM-Pf/Voi and the motor and limbic striatum [5].

Findings on the psychiatric aspects of Parkinson's disease in patients who presented mirror symptoms of reduced anxiety following DBS suggest the possibility of co-treatment of different conditions. While it may be tempting to suggest that the reduction in anxiety is due to TS symptom relief, there is no consistent cause-effect correlation between them. One possible interpretation of the anxiety improvement after Cm-Pf bilateral DBS is that a positive effect on the theorized disrupted cortico-striato-thalamo-cortical circuit co-exists with underlying TS. However, adults with refractory TS treated with DBS may present neuropsychological deficits due to complications of thalamic DBS placement and/or chronic high-frequency electrical stimulation. While results to date are

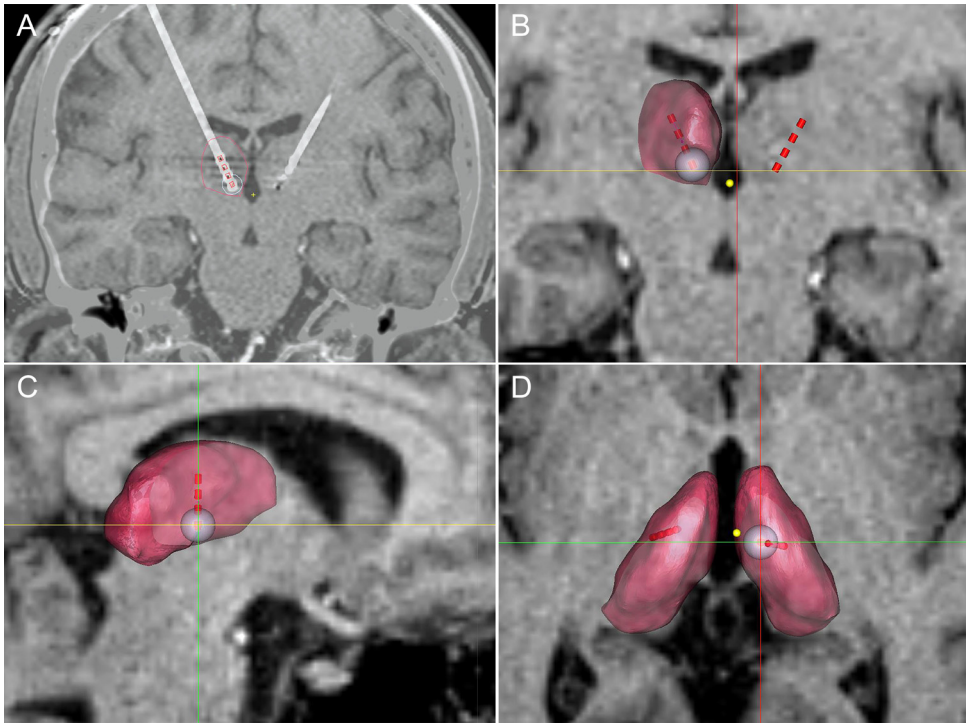

Fig. 1. Fusion images of pre-surgical MRI and post-surgical CT. A–D Fusion images show parafascicular thalamic nucleus bilateral DBS targeting using leads model 3387 (Medtronic Minneapolis, USA). (A) The figure shows the quadripolar right lead, it is easy to identify the four contacts 8, 9, 10, and 11, separated from each other 1.5 mm. (B) Coronal view of the parafascicular right thalamic nucleus, first contact (8) is being stimulated at 2.5 V, 90 μs and 130 Hz. The circle represents the power field of that stimulation on dark red the right thalamus. (C,D) sagital and axial 3-D view of the right thalamus and the position of the lead and stimulation of the most inferior contact (8).

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