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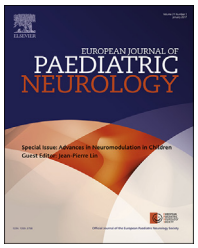

Case study

Long-term follow-up of pallidal Deep Brain Stimulation in teenagers with refractory Tourette syndrome and comorbid psychiatric disorders: About three cases

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ABSTRACT

Objectives: Tourette syndrome (TS) is a complex neuropsychiatric disorder associated with comorbid psychiatric disorders. Peak of tic severity typically occurs in early adolescence and impacts quality of life. Since 1999, promising therapeutic effects of Deep Brain Stimulation (DBS) have been reported in tic reduction for adults with refractory TS. The aim of the study was to assess the long-term risk-benefit ratio of pallidal DBS for young patients with refractory TS and severe comorbid psychiatric disorders.

Methods: We retrospectively assessed the long-term clinical outcomes of three adolescents who underwent pallidal DBS for the treatment of refractory TS.

Results: The mean duration of follow-up was 52 months in our case series. We observed that motor tics decreased with posteroventral GPi DBS in all patients, without reaching a continuous significance over the long-term follow-up. Self-reported social inclusion was globally improved, despite lack of efficacy of DBS on comorbid conditions.

Conclusions: These findings suggest a long-term therapeutic benefit of early DBS intervention for highly socially impaired young patients suffering from intractable TS with severe comorbid psychiatric conditions. Further studies are needed to determine the most effective targets of DBS on both tics and comorbid psychiatric profile of TS.

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1. Introduction

Tourette syndrome (TS) is a complex neuropsychiatric disorder characterized by motor and phonic tics beginning in childhood. About 90% of children with TS have comorbid psychiatric disorders, such as obsessive-compulsive disorder (OCD), attention-deficit hyperactivity disorder (ADHD), depression, anxiety, or impulse control disorder (ICD). Comorbid psychiatric conditions are key determinants of quality of life in children and adolescents with TS. There is typically a peak of tic severity in early adolescence. Besides, tic severity is one of the predictors during childhood of a poorer quality of life in adults with TS.[1] In 1999, high frequency Deep Brain Stimulation (DBS) was introduced as a new treatment of TS resistant to psychological and medical care. Since then, therapeutic effects of DBS have been assessed for different brain targets belonging to the cortico-basal ganglia (CBG) loops involved in TS pathophysiology. Multiple networks modulation including sensorimotor and limbic-associative relays of the CBG loops is now receiving a growing body of evidence in TS with psychiatric conditions.[2] Promising tic improvements with DBS have specially been reported in adult cohort studies on the centromedian-parafascicular thalamic complex (CM-Pf) and the globus pallidus internus (GPi). Furthermore, interest of DBS on psychiatric comorbid conditions remains unknown. Therefore, our objective was to explore the long-term outcomes of TS, psychiatric symptom severity, and quality of life in a small cohort of three teenagers treated with pallidal DBS for refractory TS with severe comorbid psychiatric disorders.

2. Case study

We retrospectively assessed the long-term clinical outcomes of three adolescents with refractory TS and comorbid psychiatric disorders who underwent surgery for DBS treatment in the Functional Neurosurgery Unit at Gui de Chauliac University Hospital (Montpellier, France). Stereotactic surgery with Leksell frame was performed under general anesthesia, by direct targeting. Bilateral implantation of quadripolar electrodes (Model 3389, Medtronic) on brain targets was MRI-guided and electrode position was checked by a post-operative MRI. Both MRI acquisitions were done with a 1.5-T scanner. The patients initially underwent multi-target DBS of both motor (posteroventral GPi) and limbic (anteromedial GPi) or associative (GPe) networks. Secondly, bilateral implantable pulse-generators (IPG) Kinetra or Activa PC were positioned abdominally. Thereafter, progressive adjustments of stimulation settings and selective off-stimulation tests were programmed during the postoperative follow-up. For each electrode, amplitude has been adjusted according to efficacy and safety of DBS, at constant frequency (130 Hz) and pulse width (450 μs). Baseline and postoperative tic severity was assessed using the total score of the Yale Global Tic Severity Scale (YGTSS).[3] Most of psychiatric assessments were collected from observations in medical records. At final assessment in July 2015, The Gilles de la Tourette-Quality of Life scale (GTS-QOL) was rated. Informed written consent was obtained for all patients.

Demographics, clinical characteristics and stimulation parameters are detailed in Table 1 for each of the three patients.

2.1. *Patient 1*

This young man was 18 years old at the time of surgery. He underwent bilateral posteroventral GPi and globus pallidus externus (GPe) DBS in February 2010 for medication-resistant TS associated with severe OCD (symmetry obsessions and counting mental compulsions), ADHD, anxiety-depressive disorder, and ICD. Despite reduction of motor tics after DBS of posteroventral GPi and GPe, the patient subsequently suffered from worsening of anxiety-depressive and impulsive (acute drug self-induced overdoses) disorders. These mood fluctuations were empirically imputed to GPe DBS. Reimplantation of bilateral posteroventral GPi and anteromedial GPi was performed in May 2013 because of persistent axial motor tics and vocal tics with coprolalia and OCD. Only posteroventral GPi DBS was activated. Then, a stabilization of motor tics and OCD was observed. The patient lately suffered from exacerbation of phonic tics and OCD. Nevertheless, he has reported a global improvement of motor tics and greater quality of life since DBS. GTS-QOL score was moderate (47).

2.2. *Patient 2*

This adolescent was 12 years old at the time of the DBS surgery. He was addressed to the Department of Neurosurgery by pediatric neurologists for DBS treatment of refractory TS (with history of familial provisional tics in his older brother) with ADHD and ICD. Before surgery, the patient was bedridden because of violent motor tics involving cervical region that were at risk of cervical myelopathy. He underwent bilateral posteroventral GPi and anteromedial GPi DBS in October 2011. The initial anteromedial GPi DBS was stopped because of behavioral disinhibition, without efficacy on tics. Then, a great improvement of tics was observed during the first year of posteroventral GPi DBS, despite dysarthria. Thus, he was able to return to school. Thereafter, severity of tics was fluctuating: motor tics tended to decrease whereas phonic tics remained. Persistence of comorbid ADHD impacted his school learning. Surgical replacement of bilateral IPG was performed in November 2014. Recently, dysfunction of a contact of the left posteroventral GPi electrode led to asymmetric DBS that could have induced recurrence of severe phonic tics. He has now integrated a high school and wants to become a child care worker. GTS-QOL score was moderate (52).

2.3. *Patient 3*

This teenager was 17 years old at the time of neurosurgery. Previously, tic disorders were resistant to electroconvulsive therapy that was performed to treat a major depressive episode. He underwent bilateral posteroventral GPi and centromedian-parafascicular thalamic complex (CM-Pf) DBS in May 2012 for treatment of severe TS with OCD (contamination obsessions with cleaning compulsions) and ICD.