



Bilateral GPI Deep Brain Stimulation for Tourette Syndrome

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ABSTRACT

OBJECTIVE: To describe the response of a medication-refractory, 16-year old male with severe Tourette syndrome (TS) and typical co-morbidities to bilateral deep brain stimulation (DBS) of the globus pallidus interna (GPI).

BACKGROUND: DBS for neurologic and psychiatric disorders has been gaining increasing attention. Case reports (and TV programs) suggest efficacy of DBS in treating severe TS. **METHODS:** Pre-surgical neuropsychological, psychiatric, and neurological evaluations were used to determine suitability for DBS including clinical interviews, Yale Global Tic Severity Scale (YGTSS), Tic Symptom Self Report (TSSR), Modified Rush Videotape Rating Scale (VRS), Behavior Assessment System – Child (BASC), and other behavioral and quality of life measures (SF-36). VRS, TSSR, and the clinician's global impression were used to determine need for stimulator adjustment every 2 weeks. Comprehensive clinical follow-up was performed 2 months after initial DBS programming. **RESULTS:** YGTSS: 97 pre-op, 36 at 2 months (63% improvement). TSSR: 94 pre-op, 14 at 2 months (85% improvement). VRS: 14 pre-op, no change at 2 months, but lower VRS scores (range 4-9) at subsequent visits. SF-36: 86.2 pre-op, 130 at 2 months (51% improvement). Psychosocial stressors influenced tic activity, but the patient felt well enough to consider returning to school at 6 weeks. **CONCLUSION:** Bilateral GPI DBS is safe and effective for severe TS, leading to dramatic improvement in tics (as measured by YGTSS and TSSR) and quality of life. Videotape rating scales may not be an adequate outcome measure, as uncontrollable factors may influence tic activity at any single clinic visit. Longitudinal follow-up is necessary to determine long-term outcomes and improvement in co-morbidities. Careful patient selection and screening, thorough pre- and post-op evaluation, an experienced surgeon, and frequent follow-up are critical for optimal management of severe TS patients with DBS.

INTRODUCTION

Tourette syndrome (TS) is characterized by vocal and motor tics, along with varying degrees of psychiatric co-morbidities including attention-deficit (+/- hyperactivity) disorder (ADHD), obsessive-compulsive disorder (OCD), anxiety, depression, and oppositional defiant disorder, amongst others (Jankovic, 2001). The majority of patients experience significant improvement in or remission of symptoms by the late teenage years (Lackman et al., 1996), although many will have milder, persistent tics and OCD even into adulthood (Pappert et al., 2003; Bloch et al., 2006). A subset experience a dramatic, debilitating worsening of symptoms that may persist into adulthood. Recent years have seen growing interest in the management of neuropsychiatric conditions with deep brain stimulation (DBS) (Kopell et al., 2004). Several cases of marked improvement of severe TS symptoms have been reported with DBS (Table 1).

Here, we describe our rationale for and experience with DBS of the bilateral globus pallidus interna (GPI) in a 16-year-old male with severe, medication refractory TS.

- The GPI was chosen as the target for the following reasons:
 - ◆ Increased paravulmin-staining neurons in the GPI of TS patients is associated with an increase in GPI volume (Kalanthri et al., 2005).
 - ◆ Irregular firing patterns in the GPI of TS patients have been observed.
 - ◆ The GPI has connections to the prefrontal cortex (PFC), an area that influences cognition and mood (Yoshida et al., 1993; Middleton and Strick, 2002).
 - ◆ Previous reports of success in treating severe TS with GPI DBS (van der Linden et al., 2002; Diederich et al., 2005; Houeto et al., 2005).

Table 1. Previous reports of deep brain stimulation in refractory Tourette syndrome

| Author/Center | N | Target | FUU | Outcomes | Adverse Events |
|--|---------------------------|---|---------------|---|--|
| Van der Linden et al.; Ghent, Belgium 2002 | 1 (tic only) | Medial thalamus and/or GPI (4 electrodes) | 6 mos | 80% tic reduction with high intensity MT stimulation; 95% tic reduction with low intensity GPi stimulation → chronic stim. with bilat. GPi. | None reported |
| Visser-Vandewalle et al.; Academic Hospital Maastricht, The Netherlands 2003 | 3 (tics) | Bilateral Thalamus (& CBs) | 8 mos - 5 yrs | Reduced tics (72%-90%); No comment on change in compulsive behaviors | Sexual dysfunction, "excessive energy" at higher stimulation settings |
| Maciunas et al.; Univ. Hospitals of Cleveland, [2004, unpublished] | 1 | Bilateral thalamus | 3 mos | Improved tics | None reported (**psychogenic) |
| Flaherty, et al.; Mass. Gen. Hosp 2005 | 1 (tic only) | Anterior limb of internal capsule | 18 mos | 45% reduction in tics; increased suppressibility of tics | Dysarthria, rhythmic teeth clenching at certain stim. settings; apathy, depression at settings near NAC; hypomania when in body of capsule |
| Diederich et al.; Vienna, Austria 2005 | 1 (tics, depr. anx & CBs) | Bilateral GPI | 14 mos | Improved tics (esp. vocal); depression, anxiety; no change in "mild" compulsive tendencies | Left hemiparkinsonism (hemorrhage around right electrode) |
| Houeto et al.; Saclay, Paris 2005 | 1 (tics, depr. anx & CBs) | Centro-median nucleus of the ans & thalamus and/or GPI (4 electrodes) | 11 mos | Improved tics, coprolalia and self-injurious behavior with either site; thalamic stim. w/ less depression and emotional instability | None reported |

CB: compulsive behaviors; depr - depression; anx - anxiety; post-op - postoperative disorder; stim - stimulation; NAC - nucleus accumbens

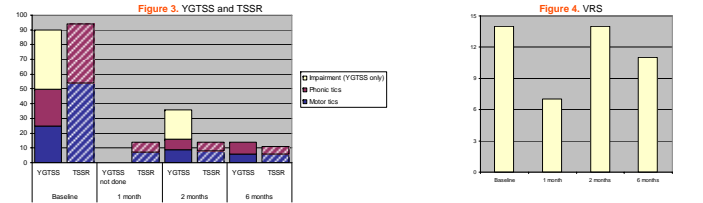
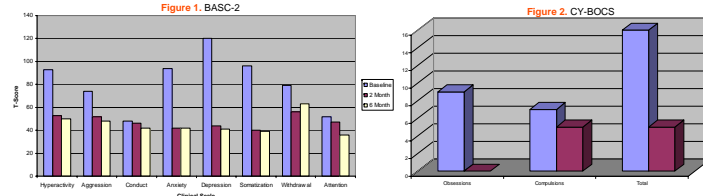
METHODS

- ◆ Pre-surgical neuropsychological, psychiatric, and neurologic evaluations were performed to determine the patient's suitability for the procedure, including:
 - Behavior Assessment System – Child (BASC) – to assess behavioral and psychiatric symptoms
 - Delis-Kaplan Executive Function System Verbal Fluency Subtest
 - Yale Global Tic Severity Scale (YGTSS)
 - Tic Symptom Self-Report (TSSR)
 - Modified Rush Video-Based Tic Rating Scale (VRS)
 - Child Yale-Brown Obsessive-Compulsive Scale
 - SF-36 to assess quality of life
- ◆ Staged, bilateral GPI DBS electrode and implantable pulse generator (IPG) implantation was performed. The two procedures were separated by 2 weeks.
- ◆ One month after electrode placement, the stimulators were turned "on" for the first time.
- ◆ The patient was followed at 2 week intervals. Tic rating scales and the clinician's global impressions were used to determine the need for adjustment of stimulation parameters.
- ◆ All rating scales were re-administered at 2 and 6 months (CY-BOCS and verbal fluency were only assessed at baseline and 6 months).
- ◆ Videotape assessments (VRS) were rated by a blinded, independent rater.

PATIENT HISTORY

- ◆ 16-year old, left handed male delivered at full-term via C-section for breech presentation.
- ◆ Normal birth history and development except for speech delay until the age of 3.
- ◆ Onset of simple motor and vocal tics at age 3.
- ◆ Obsessive-compulsive behaviors and ADHD by age 5.
- ◆ Coprolalia and copropraxia were present by the age of 7.
- ◆ Typical waxing and waning of tics, but overall progression in severity and frequency until presentation to our clinic in April, 2005.
- ◆ Multiple, severe, and complex motor and phonic tics and self-injurious behaviors (SIBs) were noted: screaming to the point of hoarseness; coprolalia and copropraxia; inappropriately approaching and attempting to touch or grab others; gagging himself until it "felt right" and he vomited (resulting in significant weight loss); exorcitations; pinching and picking at his skin; forceful left arm flexion and shoulder adduction, hitting the chest with his left arm, and screaming loudly (see Video).
- ◆ He and his family were no longer able to socialize or attend church. He failed classes, could not attend school, and would not go out in public.

RESULTS



- ◆ No changes were seen in tic severity in the one month between electrode implantation and the 1st programming session.
- ◆ Significant tics, anxiety, and OCD behaviors were noted, including pushing on the IPG site, which initially required the use of a body shield to protect the apparatus from damage and the patient from SIBs.
- ◆ There were no adverse effects except for mild dysarthria but verbal fluency was at baseline levels at 6 months.

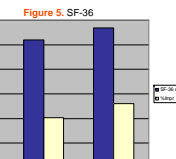


Table 2. DBS parameters

| | Baseline | | 2 weeks | | 4 weeks | | 6 weeks | | 8 weeks | | 24 weeks | |
|-------------|----------|------|---------|------|---------|------|---------|------|---------|------|----------|------|
| | R | L | R | L | R | L | R | L | R | L | R | L |
| Amplitude | 4 | 3.6 | 4.2 | 4.5 | 4.9 | 4.7 | 5 | 5 | 5 | 5 | 5 | 5 |
| Pulse Width | 90 | 90 | 90 | 90 | 90 | 90 | 90 | 90 | 90 | 90 | 90 | 90 |
| Frequency | 135 | 145 | 145 | 145 | 145 | 145 | 145 | 145 | 145 | 145 | 145 | 145 |
| Lead | C1x2 | C1x2 | C1x2 | C1x2 | C1x2 | C1x2 | C1x2 | C1x2 | C1x2 | C1x2 | C1x2 | C1x2 |

CONCLUSIONS

- ◆ Based on a single case, GPI DBS may be considered safe and effective in severe TS
- ◆ Marked improvement was demonstrated in tics and psychiatric co-morbidities, including hyperactivity, OCD, anxiety, and depression, and quality of life.
- ◆ No adverse effects of stimulation were noted except for mild dysarthria.
- ◆ Improvements were seen as early as 2 months following initial DBS programming, and were sustained at 6 months follow-up.
- ◆ Blinded ratings of videotaped recording do not necessarily parallel self-report measures or investigator's global impressions of tic activity.
- ◆ Guidelines are needed for appropriate patient selection and ongoing management of severe TS with DBS.
- ◆ Longitudinal follow-up is necessary to determine long-term outcomes and improvement in co-morbidities.

VIDEO LEGENDS

- ◆ **Segment 1.** The patient is shown at baseline exhibiting a severe screaming and clenching tic, along with copropraxia. The patient and his mother describe the impact of his tics on their quality of life.
- ◆ **Segment 2.** At 6 months follow-up, the patient and his mother describe a dramatic reduction in his severe motor and vocal tics, and a significant improvement in their quality of life. He has only minor motor tics on examination.

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