Long-term Neuropsychological Follow-up in Pallidal Stimulation for Medically Refractory Tourette Syndrome

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BACKGROUND

The optimal DBS target for medically-refractory TS is not established and limited long term neuropsychological (NPsy) follow-up data is available (1-5).

The posteroventral lateral globus pallidus interna (GPi) is the target of choice at our center for the following reasons:

1. Reports of successful pallidotomy and DBS in TS (1)
2. Altered firing patterns of GPi neurons during tics (6)
3. Altered migratory patterns of GABAergic neurons in GPi in TS (7)
4. Prefrontal connections from GPi that may be able to modulate psychiatric co-morbidities (8)
5. Success in treating dystonia, which has phenomenologic similarities to dystonic tics

We have previously described the 6-mo. improvement of tics and psychiatric co-morbidities in a 16yo M after bilateral GPi DBS (9).

METHODS

Criteria for placement of bilateral GPi DBS in TS:

1. Medication-refractory, severe, complex motor and vocal tics that have led to psychosocial distress or disability.
2. Co-morbidities such as OCD, ADHD, and mood disorders may be present, but are not the primary source of disability and are being addressed appropriately by alternate methods including medications and/or psychotherapy.
3. No neuropsychological or psychosocial contraindications to neurosurgery or conditions that would preclude appropriate follow-up for monitoring and DBS adjustment.
4. Age ≥14 (10).
5. Recommendation for surgery by consensus agreement from a group of Neurologists, Neurosurgeons and Neuropsychologists with expertise in the evaluation and management of patients undergoing DBS for Movement Disorders.

We have conducted a prospective, open-label NPsy follow-up of patients treated with bilateral GPi DBS for TS.

- NPsy testing was performed at baseline, 6mos, and periodically throughout DBS treatment to establish degree of benefit, presence of cognitive adverse effects, need for DBS or medication adjustment.
- We retrospectively reviewed NPsy data in 7 patients with ≥6mos NPsy follow-up.

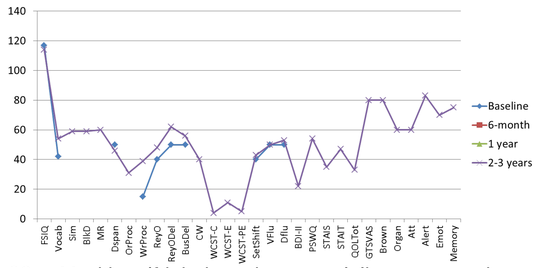
Individual follow-up scores were compared to baseline. Measures varied between patients based on age; batteries assessed general intellect, attention, information processing speed, verbal and visual learning/recall, visuospatial construction, executive functioning, mood, obsessive-compulsive symptoms (OCS), QOL, ADHD, and tics.

Measures administered: Vocabulary, Similarities, Block Design and Matrix Reasoning from the Wechsler Abbreviated Scale of Intelligence, Digit Span from the Wechsler Adult Intelligence Scale-Fourth edition, Symbol Digit Modalities Test (oral and written conditions), Rey-Osterrieth Complex Figure, Buschke Selective Reminding Test, STROOP Color Word Test, Wisconsin Card Sorting Test-64 card version, Trail making, Verbal and Design Fluency tests from the Delis Kaplan Executive Function System, Beck Depression Inventory-Second edition*^, Penn State Worry Questionnaire*^, State-Trait Anxiety Inventory*^, Obsessive Beliefs Questionaire-44*^, Obsessive Compulsive Inventory-Revised*^, Quality of Life for Gilles de la Tourette's syndrome* (QOLTot^ and QOLVAS+), Brown Attention Deficit Disorder Scales, Behavior Assessment System for Children second edition-Parent Form^, and Behavior Rating Inventory of Executive Function-Parent Form^.

*Data presented in raw scores. Neuropsychological data points are presented in T-scores with the exception of FSIQ which is a standard score.
^Higher scores evidence an increase in symptomatology.
+ Higher scores reveal improvement

RESULTS

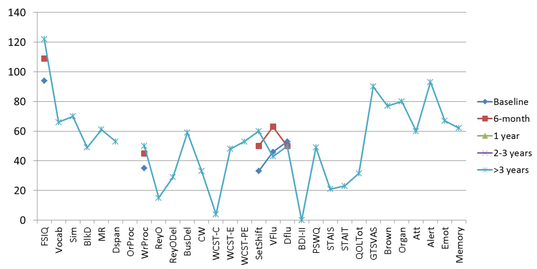
PATIENT 1:



36yo M with self-injurious tics, coprolalia, copropraxia, ADHD, OCD, depression, anxiety, panic attacks and past substance abuse.

- Baseline YGTSS 97, YBOCS 25.

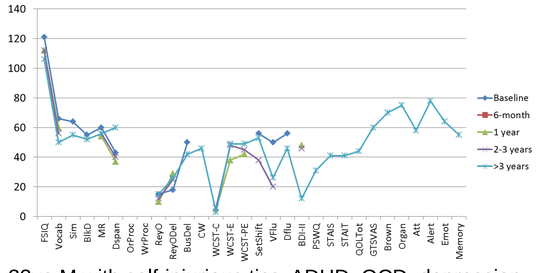
PATIENT 2:



16yo M with self-injurious tics, copropraxia, ADHD, OCD, and depression (9).

- Baseline YGTSS 100, YBOCS 16.

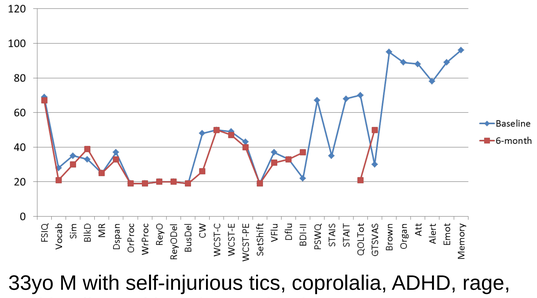
PATIENT 3:



33yo M with self-injurious tics, ADHD, OCD, depression, anxiety, depression and somatization.

- Baseline YGTSS 70, YBOCS 23.

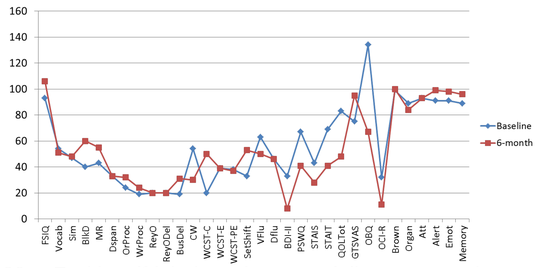
PATIENT 4:



33yo M with self-injurious tics, coprolalia, ADHD, rage, and intellectual impairment (MR).

- Baseline YGTSS 96.

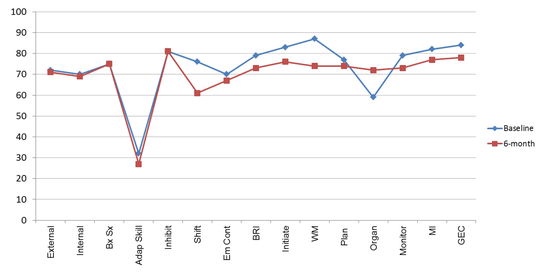
PATIENT 5:



20yo F with self-injurious tics, coprolalia, copropraxia, ADHD, OCD, depression, and anxiety.

- Baseline YGTSS 89, YBOCS 19.

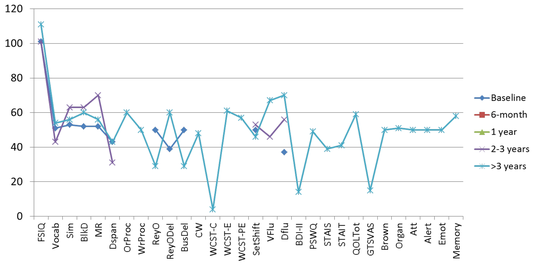
PATIENT 6:



16yo M with self-injurious tics, coprolalia, copropraxia, ADHD, OCD, depression, anxiety, and somatization.

- Baseline YGTSS 94, YBOCS 9 (compulsions only).

PATIENT 7:



14yo M with self-injurious tics, OCD, anxiety, and rage.

- Baseline YGTSS and YBOCS unavailable.

TABLE 1: SHORT AND LONG TERM YBOCS&YGTSS

	YGTSS – total tic score					YBOCS - total				
	B	6mo	1yr	2-3yrs	>3yrs	B	6mo	1yr	2-3yrs	>3yrs
Pt1	47	-38%	-46%	ND	-51%	25	-40%	-32%	ND	-40%
Pt2	50	-72%	-76%	ND	-46%	16	-69%	-69%	ND	-13%
Pt3	30	ND	10%	-23%	---	23	-13%	ND	-78%	---
Pt4	46	-45%	---	---	---	ND	---	---	---	---
Pt5	49	-55%	---	---	---	19	-32%	---	---	---
Pt6	44	-56%	---	---	---	9	11%	---	---	---
Pt7	ND	---	---	---	---	ND	---	---	---	---

YGTSS – Yale Global Tic Severity Scale
Y-BOCS – Yale-Brown Obsessive-Compulsive Scale
Pt 3 underwent cognitive behavioral therapy for OCD after DBS
ND – not done

CONCLUSIONS

7 patients (6M, age 14-37 at implantation) with bilateral GPi DBS for medically refractory TS were followed for 6mos (n=3) to 6yrs (n=1).

- Most neurocognitive domains (vocabulary, verbal abstract reasoning, visual pattern extrapolation through deductive reasoning, non-verbal concept formation/hypothesis testing and visuospatial planning/organizing) remained stable after DBS.
- Baseline deficiencies in visuoconstruction and visual memory in some patients, consistent with executive dysfunction associated with TS, remained stable or improved post surgically.
- Most patients experienced improved auditory attention, verbal long-term storage and set-shifting. However, variable neurocognitive performance was noted across patients; some experienced mild declines on timed tasks of verbal fluency and disinhibition. These mild declines in frontal lobe mediated processes are consistent with previous research (5&9) and warrant long-term assessment.
- Improvements in psychological distress including symptoms of depression and anxiety were noted with the exception of an increase in depressive symptomatology for Pt4, attributed to situational psychosocial factors.
- Additionally, improvements in QOL (QOLTot) and general satisfaction with current abilities (GTSVAS) were noted.
- ADHD (a common comorbidity) results in difficulties with attention/concentration, organization, alertness, emotional regulation and encoding of new material (Brown ADHD Scale); these skills continued to be impaired following GPi DBS.

Total tic severity improved 38-72% (6mos, n=5) and +10-76% (1yr, n=3), 23-51% (>2yrs, n=3) while OCD improved +11-69% (6mos, n=5), 32-69% (1yr, n=2), 13-78% (>2yrs, n=3); both fluctuated and one patient's OCD improved significantly after cognitive behavioral therapy.

In Pt 4 and 5, both administered the same NPsy at the same time points, preliminary findings reveal:

- Declines on timed tasks of verbal fluency and disinhibition.
- Attention, visuoconstruction, memory, and set-shifting improved.

Limitations of this prospective, unblinded series include:

- Age-dependent variability of assessments across patients.
- Examiner-dependent variability of assessments.
- Different follow-up periods.

Potential solutions include:

- New, more comprehensive TS DBS NPsy battery that can be compared across patients of different ages.
- Follow-up times determined and scheduled

Bilateral pallidal DBS in refractory TS results in tic improvement without adverse cognitive effects and with improvement in some frontal lobe mediated functions. Tics and OCS improved overall, but symptoms fluctuated throughout DBS treatment. Well-designed NPsy batteries and controlled trials of GPi DBS in TS are warranted.

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