Deep Brain Stimulation Results in Greater Symptomatic Improvement in Tourette Syndrome than Medication or Behavioral Therapy: a Meta-Analysis

David Arnold Purger MD, PhD; Uma Mahajan; Alessandra Mantovani MD; Nolan Williams; Flint Martin Espil; Sherman C. Stein MD; Casey H. Halpern MD

Stanford University School of Medicine, Departments of Neurosurgery and Psychiatry

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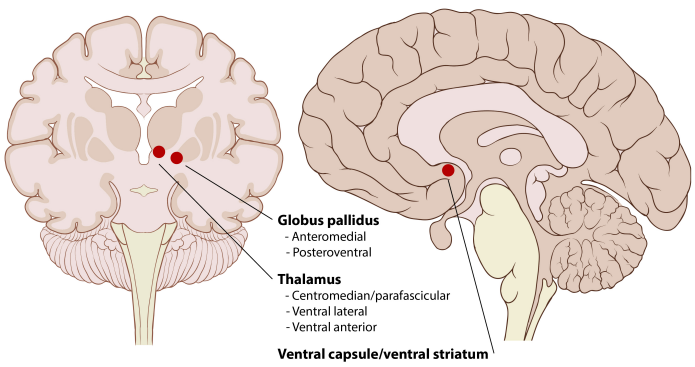
Introduction

Deep brain stimulation (DBS) has emerged as a safe and effective therapy for severe, treatment-refractory Tourette syndrome (TS), a potentially debilitating disorder affecting approximately 1:2000 adults in the US. Recent studies have demonstrated that DBS is effective in reducing TS symptoms as measured by the Yale Global Tic Severity Scale (YGTSS), but no studies, to our knowledge, have compared the effectiveness of DBS with conservative therapy.

Deep brain stimulation targets



Deep brain stimulation targets included in meta-analysis were globus pallidus (94 patients), thalamus (76), and ventral capsule/ventral striatum (1).

Methods

We performed a meta-analysis of studies investigating patient outcomes reported as YGTSS scores after DBS surgery, pharmacotherapy, and behavioral therapy. Single case reports and studies with participant mean age <16 years or without YGTSS data were excluded. Data were pooled using a random effects model of inverse-variance weighted meta-analysis (n=171 for DBS, 133 for medications, 201 for behavioral therapy). There was no significant difference in age between participants in studies in each treatment group, and symptom duration was similar between DBS and behavioral groups (no information available for medication studies). All DBS targets, all medications, and all psychotherapeutic modalities were pooled for analysis.

Baseline and percent improvement in total YGTSS score by treatment modality

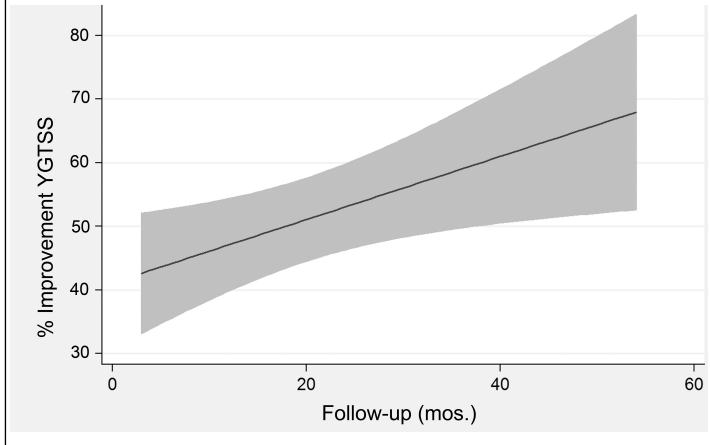
Treatment	DBS		Meds		Behavioral	
	Mean	SD	Mean	SD	Mean	SD
Baseline	80.0	9.8	54.1	9.8	48.2	2.3
% Improvement	49.9%	17.5%	22.5%	15.2%	20.0%	11.3%

Treatment with DBS significantly decreased total YGTSS score more than medication (P=0.001) or behavioral therapy (P<0.001). There was no significant difference between medication and behavioral therapy (P=0.692).

Results

DBS resulted in a significantly larger reduction in YGTSS total score than pharmacotherapy (P=0.001) or behavioral therapy (P<0.001). The complication/adverse effect rate was 0.15/case for DBS (including 0.04 major complications such as infection and lead migration per case) versus 1.13/case for medications and 0.60/case for psychotherapy. Groups were demographically similar, though baseline YGTSS total score for DBS patients was 80.0 ± 9.8 (mean ± SD; total 100), significantly greater than the baseline score for participants in medication (54.1 ± 9.8) or behavioral (48.2 ± 2.3) trials (P<0.001). There was no difference in effectiveness of DBS between targets (P=0.792).

Meta-regression of effectiveness of DBS over time



% Improvement in YGTSS does not significantly change over time with medication (P=0.390) or behavioral therapy (P=0.643), but approaches significance with DBS (P=0.094). Black line=fitted mean; shading=95% CI.

Incidence of treatment-related events (%)

Treatments/Complications	DBS		Meds		Behavioral	
	Mean	SD	Mean	SD	Mean	SD
Device-related						
lead infection	5.2	1.7	0	0	0	0
wound infection	0.6	0.6	0	0	0	0
surgical site pain	1.1	0.8	0	0	0	0
misplaced/migrated electrode	1.1	0.8	0	0	0	0
Neurological						
tics worse	0.6	0.6	0	0	6.6	2.2
dyskinesia	0	0	11.9	3.1	0	0
visual*	6.3	1.8	2.4	1.5	0	0
coordination**	3.4	1.4	2.9	1.6	0	0
seizures	0.6	0.6	0	0	0	0
Neurobehavioral* **	4	1.5	68.7	4.5	36.9	4.4
Autonomic** **	1.7	1	50.7	4.9	23	3.8
Pain						
headache	1.7	1	10.7	3	22.1	3.8
somatic pain	0	0	2.8	1.6	32	4.2
Total complications	26.4	3.3	150.1†	34.7	120.5†	29.5

*: blurriness, diplopia. **: dizziness, vertigo, unsteady gait, dysarthria. ***: apathy, fatigue, lethargy, psychosis, sleep disorders, anxiety, depression, aggressiveness, phobias. ****: nausea, vomiting, eating disorder, weight change, sexual dysfunction, gastrointestinal disturbance, postural hypotension, rhinitis. †: incidence >100% indicates some participants had >1 adverse event

Conclusions

Our data suggest that, despite greater baseline symptom severity, TS patients undergoing DBS experience greater symptomatic improvement with surprisingly low morbidity as compared with pharmacotherapy and behavioral therapy. Randomized controlled trials are warranted to pursue regulatory approval of DBS as a mainstream therapeutic option for patients with severe TS.

Abridged References

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(full references available on request)