Efficacy of Deep Brain Stimulation for Tourette Syndrome

The first description of the “Maladie des Tics” in 1885 by the French neuropsychiatrist Georges Gilles de la Tourette has developed into a well-known syndrome bearing his name. It has historically been difficult to arrive at an accurate diagnostic criteria or devise optimal medical and pharmacological strategies for the treatment of Tourette Syndrome (TS). The first neurosurgical procedures for TS were ablative, whereby Baker reported selective bifrontal transection of white matter in 1962. Stereotactic procedures were also reported in subsequent years, but their results were inconsistent. Deep brain stimulation (DBS) of the thalamus for TS was introduced in 1999 by Vandewalle et al. Since then, multiple case reports and series have demonstrated the viability of DBS as a potential surgical option for select cases of refractory TS. However, the small number of patients and the heterogeneity of the methodologies used by the various authors have not been enough to provide strong recommendations about its clinical utility and generalizability.

The International Tourette Syndrome Deep Brain Stimulation Public Database and Registry is a multinational collaborative effort designed to share data and improve the quality of outcomes research in the treatment of TS with DBS, which was utilized by Martinez-Ramirez et al in a recent publication of the Journal of the American Medical Association Neurology. Data was collected from 171 patients between January 2012 and December 2016 across 31 institutions from 10 different countries. There was a greater prevalence of male gender (78.4%) and the mean (SD) age of symptom onset was 7.8 (3.5) years. The mean age (SD) at time of DBS surgery was 29.1 (10.8) years. The most common comorbidities were obsessive-compulsive disorder (64.2%) and depression (47.3%). Moreover, the brain targets reported were the centromedian thalamic region (57.1%), anterior globus pallidus internus (25.2%), posterior globus pallidus internus (15.3%), and anterior limb of internal capsule (2.5%), although the latter was excluded from analysis due to small sample size.

The authors utilized the Yale Global Tic Severity Score (YGTSS) to compare symptoms between three time points (baseline prior to surgery, 6-month and 12-month post-operative follow ups) and between the three anatomical DBS targets described. There was a significant difference (p<0.001) when comparing the baseline mean (SD) YGTSS total score with the 6-month and 12-month follow up, with an improvement of 40.1% (from 75.01 [18.36] to 44.92 [19.01]) and 45.1% (to 41.19 [20.00]) respectively. This difference (p<0.001) was also present when the motor and phonic components of the YGTSS were analyzed separately. Additionally, there was a significant difference at 12-month follow up of all the total YGTSS components (motor and phonic) when compared to baseline and the three anatomical targets were analyzed separately, as shown in Figure 1. However, no statistical difference was observed for YGTSS scores between the three targets (p=0.57). The most common adverse events seen with DBS were stimulation-related symptoms (30.4%), such as transient dysarthria and paresthesias.

In 2016, a systematic review and meta-analysis was published about DBS for TS. A pooled analysis of 156 patients from 57 different studies met the inclusion criteria. There was a significant median improvement of 52.66% (IQR = 40.83; p<0.001) for the global YGTSS, declining from a median score of 83 to 35 at last available follow-up. The anatomical DBS targets analyzed in this meta-analysis were the same used in the International TS DBS Public Database and Registry, and no difference was observed between targets (p=0.496).

Movement disorder groups should be encouraged to treat refractory TS with DBS with increasing confidence due to the results of these recent studies. Standardized surgical criteria are being developed, which may translate in a decreased time lapse between symptom onset and surgical intervention. The current neuroanatomical DBS targets include the centromedian thalamic region, anterior globus pallidus internus, posterior globus pallidus internus, and anterior limb of internal capsule. Stimulation of different deep brain areas can significantly improve the symptoms of TS with minimal risk of complication. Future prospective clinical trials will further evaluate the utility of DBS in treating TS and other neuropsychiatric disorders.

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References


Figure 1. Yale Global Tic Severity Scale (YGTSS) Scores by Time and Brain Target

A, YGTSS motor tic scores at baseline, 6 months, and 1 year. B, YGTSS phonic tic scores at baseline, 6 months, and 1 year. C, Total YGTSS scores at baseline, 6 months, and 1 year. CM indicates centromedian; GPI, globus pallidus internus.