Bilateral Posteroventral GPi-DBS in a Patient with Tourette's Syndrome – A Rapidly Effective But Under-utilized Therapy

Dear Editor,

Tourette syndrome (TS) is defined as a childhood neurobehavioral disorder that is characterized by the presence of at least one vocal and two motor tics starting before the age of 18 years.[1] The symptoms generally exacerbate during puberty and resolve with early adulthood. However, in around one-fifth of the patients, the clinical course can be severe, leading to a substantial disturbance in quality of life.[1] Remarkably, in some of these patients with disabling refractory symptoms, deep brain stimulation (DBS) constitutes a crucial option for symptom improvement.[2] On the other hand, there are many challenges regarding the application of this therapy in TS.[3] For instance, the optimum stimulation parameters and the duration of the therapy required for the initiation of the efficacy remain to be elucidated.[3] Moreover, there is no consensus on the optimum target as various targets including the thalamus, GPi, nucleus accumbens, and anterior limb of the

internal capsule have been reported to improve symptoms.[2-5] Among these, the GPi is a promising DBS target whose efficacy has been shown in several recent reports.[2-4,6-9] However, the assessments of the therapy response were performed in the chronic period in most of these studies, and the initiation of the DBS effect in the early period is unclear. Besides, the recent European clinical guidelines still preferred to mention DBS in TS as an experimental treatment that should be used only in carefully selected.[8] In this regard, we sought to discuss these points via the detailed illustration of our patient with refractory TS who showed a dramatic improvement soon after the GPi-DBS therapy.

We present a 25-year-old female patient who received the diagnosis of TS at the age of 15 years. It was learned that her symptoms had initiated at the age of 13 years old with motor tics including sniffling, shrugging the shoulders, or jerking her arm. At the same period, vocal tics such as clearing the throat, yelling out a word, and coprolalia initiated, which disturbed her daily living activities markedly. Before admission to our clinic, various medications had been attempted for TS and depression, including haloperidol, risperidone, valproic acid, olanzapine, sertraline, and escitalopram, which did not provide a significant amelioration. At admission to our clinic, the patient was orientated and cooperative. The general appearance, behavior, and attentiveness were evaluated as normal. Her emotional expression, thinking, and perception were within normal limits. She suffered from depressive symptoms that were partially resolved with medications. On the other hand, during the interview, her speech was frequently interrupted due to recurring complex motor tics and accompanying vocal tics in the form of yelling out a word. The motor tics affecting the body frequently occurred, which were measured to occur 55 times for a 5-minute period. The other neurological exams including motor, sensory, and cerebellar functions were within normal limits. At baseline evaluation before surgery, she scored 89 out of 100 on the Total Yale Global Tic Severity Scale (TYGTSS) even after medication treatment. After inter-deparmental deliberations between neurosurgical, neurology, and psychiatry clinics, the DBS surgery targeting the bilateral posteroventral (PV)-GPi-DBS was decided based on the encouraging study results and our surgical experience in this target. The procedure was carried out under general anesthesia. The target was defined as 18 mm lateral to the midline, 4.5 mm posterior to the mid commissural point, and 1.5 mm superior to the anterior commissure–posterior commissure plane. The DBS was activated on the following day of the surgery. The DBS parameters were set to the following values: pulse voltage = 2.7 V (R), 3.5 V (L), frequency = 130 Hz, and duration = 120 μs using monopolar stimulation (bilateral most ventral). The stimulation provided a rapid resolution in her symptoms such that the assessment on the second day of the therapy revealed an improvement in the TYGTSS scores up to 19 points [Table 1]. The patient was discharged 1 week after the surgery with these settings. Remarkably, during the evaluations before discharge, the stimulation was de-activated, which resulted in the recurrence of the motor tics rapidly in a few minutes [Videos 1 and 2]. The follow-up 1 month later revealed persistence of the efficacy of the DBS therapy.

Discussion

Herein, we demonstrate the efficacy of GPi-DBS therapy in a patient with TS syndrome, which was dramatic and occurred rapidly. In addition to the illustrative images of our patient, the rapid resolution of the symptoms may also provide perspectives to be kept in mind in clinical practice.

Recently, Mahajan *et al*.[10] published a crucial paper evaluating the efficacy of DBS therapy on adult patients with refractory TS. In conclusion, they determined that those patients undergoing DBS experience greater symptomatic improvement with surprisingly low morbidity than can be obtained with pharmacotherapy or psychotherapy.[10] In this study, DBS targets included the GPi (94 patients), thalamus (70 patients), and ventral capsule/ventral striatum (1 patient). However, they did not find a difference in the effectiveness of DBS between targets. Nevertheless, several recent reports have drawn attention to the efficacy of the GPi-DBS in TS.[2-4,6,7] A meta-analysis in 2016 reported that the GPi-DBS improved the TYGTSS scores by an average of 58.03%.[11] Dehning *et al*.[12] showed a dramatic efficacy of the PV-DBS therapy in four of six patients with TS at the long-term follow-up. The efficacy of the GPi therapy has been confirmed in the other following studies including a limited number of cases.[3,4,6] Similarly, Azimi *et al*.[13] showed a marked improvement in tic severity in the evaluations 1 year after the GPi-DBS therapy in six patients with TS (reduction in the TYGTSS score from 75.6 to 28.3). On the other hand, in most of these studies, the assessments

Table 1: The temporal changes in the YGTSS sub-scores

Yale global tic severity scale	Sub-items	Baseline (raw scores)	First week assessments of the GPi therapy*	% change**	First month assessments of the therapy	% change**
YGTSS						
	Motor tic severity	21	6	71.4%	5	76.2%
	Phonic tic severity	18	3	83.3%	3	83.3%
	Impairment	50	10	83.3%	10	83.3%
	Total	89	19	78.6%	18	79.7%

*Third day after the surgery. ** Comparisons according to the baseline assessments

regarding the outcome were performed in the chronic period of the treatment, while the data about the effects in the early period were lacking.[2,3,11,13] Knowledge regarding the clinical application of the GPi is derived mostly from the dystonia clinical trials, and response to GPi stimulation is predicted to occur gradually in the chronic period in those patients with dystonia.[14] However, the response time to the stimulation in patients with TS is unclear, which may constitute a crucial handicap during the clinical evaluations. In a crucial study, the follow-up data of 11 patients with TS undergoing the anteromedial-GPi DBS were reported, which demonstrated a 48% reduction in motor tics and a 56.5% reduction in phonic tics at final follow-up [14 months after surgery (range = 4–30 months)].[6] Of note, the authors mentioned that 10 patients (91%) showed improvement in tic severity soon after the DBS therapy. In the other unique study by Sachdev *et al*.,[4] a positive response (50% reduction in the TYGTSS score) to the GPi-DBS therapy was reported in 12 out of 17 (70.6%) patients with TS. The graphical representation of the treatment response showed that the improvement occurred in a progressive manner within the first month after surgery; however, only slight improvement was observed in the following months.[4] Srinivas *et al*.[7] reported a detailed illustration of a TS subject undergoing GPi-DBS surgery who showed a significant improvement in motor tics. On the other hand, the improvement was slightly in the early period which had occurred gradually and progressively, which was found significant at the last follow-up 6 months after surgery.[7] Taken together, the dramatic response to GPi-DBS therapy that occurred rapidly in our patient with TS may be illustrative. Moreover, the acute and dynamic response to the stimulation was also observed clearly with the severe recurrence of the symptoms when the stimulation was de-activated before discharge.

In conclusion, we illustrate the impressive efficacy of the PV-GPi-DBS therapy in our patient with refractory TS. In light of limited literature data, the rapid response to the PV-GPi stimulation in our patient may provide useful perspectives for the clinical grounds.

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Ethical compliance statement

The authors confirm that the approval of an institutional review board was not required for this report. A written informed consent was obtained from the patient. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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