Illustration of the Dramatic and Dynamic Efficacy of Chronic GPi-DBS Therapy in a Patient with Tardive Dyskinesia/Dystonia

Dear Editor,

Tardive dystonia/dyskinesia (TD) occurs as a side effect of anti-dopaminergic drugs, most commonly neuroleptics and metoclopramide, and is often refractory to medication. The Deep brain stimulation (DBS) of the sensorimotor part of the GPi is efficient for the treatment of severe TD.[1-3] In a recent review investigating the efficacy of globus pallidus internus deep brain stimulation (GPi-DBS) in TD, the improvement rate of the abnormal involuntary movement scale (AIMS) score after DBS surgery was 62% ± 15% across the 51 cases.[3] The improvement of the BFM motor score after DBS surgery was reported to be 76% ± 21% across the 67 cases.[3] However, the period required for the initiation of the DBS efficacy and the alterations of the clinic in association with the stimulation

is under-clarified in TD.[3] Herein, we aimed to present a rare and interesting observation of the rapid recurrence of TD in a patient under chronic GPi-DBS therapy after deactivation of the DBS.

A 40-year-old male patient who had undergone GPi-DBS therapy for refractory TD applied for routine polyclinic follow-up. It was learned that the patient had initially presented with dystonic/dyskinetic involuntary movements of orofacial muscles, tongue, and cervical muscles which had emerged 6 years before. The symptoms had progressed gradually in a few months and also involved the upper limbs, scalp, and trunk. Medical history revealed previous use of sertraline, paroxetine, valproic acid, and haloperidol for the treatment of bipolar affective disorder. Remarkably, these involuntary movements had started after months of chronic use of haloperidol therapy (5-mg tablet daily). The cessation of haloperidol and attempts of various other medications[1] could not provide a worthwhile amelioration of the spasms. As such, the Burke–Fahn–Marsden dystonia rating scale (BFM) motor score was evaluated as 30 points. Due to the refractory symptoms and severe disruption in daily living activities, the patient had undergone bilateral GPi-DBS (Medtronic 3387) 4 years ago, which provided a dramatic improvement. The final evaluation at admission to our clinic revealed that the patient was symptom-free without taking any medication (BFM motor score: 0) [Video 1]. The DBS settings were as follows; bilateral most-ventral monopolar active contacts; 3.4 V (right), 3.4 V (left); 240 us (bilateral); 130 Hz (bilateral). To evaluate the dynamic impact of DBS, the DBS was turned off. However, due to the rapid clinical deterioration [Video 2], we had to reactivate the DBS 10 min later. The BFM motor score was 28 points, and the AIMS score was 29 points. During the assessments, the stimulation was turned off [Video 1]. His symptoms resolved completely in a few minutes after the DBS was reactivated.

Herein, we illustrate the rapid relapse of TD soon after the deactivation of GPi-DBS, which is an interesting observation and may provide crucial perspectives related to responsible mechanisms. The improvement of the motor features in TD occurs gradually over months after surgery and persists for a long time.[3] However, many issues related to DBS in TD, including its indications, the response rate of the clinic, stimulation parameters, and implanted targets, are still being studied by many authors.[3] Concerning the unknown points in this regard, the most striking one may be temporal evolution of the clinical response in association with the stimulation. We know that different symptoms characteristically respond to DBS with different time courses.[4] In addition, it has been proposed that the time course of the reemergence of the symptoms when DBS is stopped mirrors the time course of symptom relief when stimulation is initiated.[4,5] However, there may be some debates regarding this view. For instance, contrasting with the gradual course of initiation of efficacy after GPi-DBS, the worsening of dystonia occurs in a more rapid manner, leading to dystonic storm even over a few days after the stimulation is interrupted.[6,7] In contrast, some authors also reported maintained clinical efficacy despite DBS interruption in primary or cervical dystonia subjects, which was explained in the context of a possible disease-modifying effect of DBS.[8-10] Finally, the time course required for the efficacy of DBS certainly varies among distinct diseases due to differing underlying pathomechanisms. For instance, whereas abnormal synaptic plasticity and elevated low-frequency band power in GPi may be responsible for primary dystonia, postsynaptic dopamine receptor hypersensitivity developing due to chronic blockade of dopamine receptors is considered to lead to TD.

Data on DBS in patients with TD are limited. A recent group also reported excellent motor improvement rates[2] at the second follow-up 6 months after surgery in 10 TD subjects.[2] In this report, they mentioned that relapses of the TD symptoms were observed with the DBS off, and immediately improved when the DBS was reinitiated at the second follow-up visit.[2] However, no details about these observations were included in the report. To the best of our knowledge, in only a unique previous case report, the reoccurrence of TD after interruption of chronic GPi DBS therapy was illustrated in detail.[10] The authors interpreted this presentation as a finding against the view of disease-modifying effect of DBS in TD.[10] Moreover, they recommended to ensure a long observation period to decide that symptoms will not reoccur.[10] The symptoms in that patient[10] had recurred a few months after cessation of therapy; however, we observed the reemergence of symptoms soon after the deactivation of the stimulation, which was a more striking finding compared to the previous illustration.[10] Taken together, rather than the concept of neuroplastic reorganization, our observation may support the sustained dynamic effects of GPi stimulation, which is reversible and might be responsible for most portion of the mechanisms underlying the persistent efficacy of DBS in TD. The demonstration of temporal evaluation of the clinical efficacy of DBS therapy in association with the stimulation status in distinct phenomenologies and etiologies separately may contribute critically to our understanding of the specific mechanisms underlying these entities and DBS-related mechanisms of action, which probably differ according to the underlying causes.

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

1 Neuroleptics (Risperidone, clozapine, and olanzapine), benzodiazepines (clonazepam and clobazam), and tetrabenazine (3 × 25 mg) were the drugs that had been tried for the medical treatment of TD.

2 BFM motor score improvement by 87.3 ± 17.0%, AIMS score improvement by 88.4 ± 16.1%.

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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