

CASE REPORT

Deep brain stimulation of anteromedial globus pallidus internus improved OCD rather than tics in a Gilles de la Tourette syndrome patient

Zahra Aminzade^{1,2}  | Sepand Tehrani Fateh^{1,2}  | Reza Jalili Khoshnoud¹ | Farzad Ashrafi¹  | Mehri Salari¹ 

¹Functional Neurosurgery Research Center, Shohada Tajrish Comprehensive Neurosurgical Center of Excellence, Shahid Beheshti University of Medical Sciences, Tehran, Iran

²School of Medicine, Shahid Beheshti University of Medical Science, Tehran, Iran

Correspondence

Mehri Salari, Functional Neurosurgery Research Center, Shohada Tajrish Comprehensive Neurosurgical Center of Excellence, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Email: mehri.salari@gmail.com

Funding information

None of the authors have received any funding of any kind for either this project or other projects

Abstract

A 32-year-old gentleman with refractory Gilles de la Tourette syndrome went on a DBS procedure on anteromedial globus pallidus internus. At the most suitable adjustment, the OCD component of his disease improved almost completely while his tics remained unchanged which was in contrast with other previous studies. Moreover, variations in symptoms were seen in response to different adjustments. We discuss that these variations and fluctuations in the therapeutic outcomes may be due to differences in physiological conditions of tic- or OCD-specified pathways and areas including distinct stimulation threshold and occurrence of neuroplasticity in neural circuits which may determine the responsiveness of each pathway or circuit to a specific stimulus. At last, we suggest that pathways and circuits should be targeted for DBS rather than single components; as these components may be involved in multiple pathways, related to different pathophysiological states.

KEYWORDS

deep brain stimulation, Gilles de la Tourette Syndrome, movement disorders, neuromodulation

1 | INTRODUCTION

Gilles de la Tourette syndrome (TS) is a chronic developmental neuropsychiatric disorder with an onset in early childhood, affected by both genetic and environmental factors. TS is characterized by multiple complex motor and vocal tics, in addition to some other psychological disorders such as attention deficit hyperactivity disorder (ADHD) and obsessive-compulsive disorder (OCD). The exact pathophysiology of TS is unclear but recent studies suggest that there may be a

defect in the cortico-striato-thalamo-cortical (CSTC) circuit. Besides self-limited cases, some TS patients with mild symptoms may need conventional treatments such as psycho-behavioral therapy, educational therapy, and pharmacotherapy while refractory cases are potential candidates for deep brain stimulation (DBS) procedure which leads to an improvement in both tic component and other comorbidities of TS, but with different extents.¹ Herein, we report a patient with TS whose OCD improved after DBS without his tic being improved.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2021 The Authors. *Clinical Case Reports* published by John Wiley & Sons Ltd.

2 | CASE PRESENTATION

A 32-year-old right-handed gentleman was diagnosed with TS at the age of 5 with a progression through adolescence, presented by fluctuating complex motor tics including shoulder elevation, repetitive movement in the thumbs, and eye blinking, which was accompanied by severe disabling OCD, beginning at the age of 8, sleep disorder for 15 years, adult-onset ADHD, and anxiety disorder during his illness. He reported social impairment during school and at work. He had several unsuccessful behavioral- and pharmaco-therapies (Table 1) since he was diagnosed. He had a positive family history of TS in his father accompanied by OCD and simple motor tic in his sister. Due to severe symptoms, lack of response to multiple drugs unsuccessful psycho-behavioral therapy, and the patient's functional impairment, he was known as a refractory case of TS and became a candidate for DBS surgery.

Consent was obtained from the patient, and DBS surgery was carried out under local anesthesia. Targets were determined and calculated via Medtronic S8 planning station software and approved via an MRI and microelectrode recording. Electrodes (3389/ Medtronic) were administered through the coronal suture site, parallel to the midline, and implanted symmetrically on the anteromedial globus pallidus internal (GPI) (Right: $x = 15.22$, $y = 6.40$, $z = -7.74$, and Left: $x = -14.32$, $y = 7.29$, $z = -9.37$). Stimulation test results during surgery demonstrated proper response with no immediate side effects. A post-operative computed tomography scan demonstrated the appropriate position of electrodes. No complications were observed after the surgery. An IPG (Active PC/Medtronic) became connected to the leads and implanted subcutaneously in the right chest wall.

One month after surgery the IPG was turned on, during the assessment, right side stimulation showed no side effects while at the left side dyspnea related to ventral electrodes and paresthesia and vertigo related to dorsal electrodes were detected. The parameters were set on, Amplitude: 1, Pulse width: 80, frequency: 85, Bipolar on the left (3^+ , 0^-), and unipolar on the right (Case $^+$, 8^-).

During follow-up sessions, the patient's condition was fluctuating in response to alterations in stimulation parameters as is shown in Table 1. At the optimum parameters which were obtained after 8 months, OCD decreased dramatically; on the other hand, however, tics frequency and intensity did not change significantly and ultimately worsen over time. The patient's improvement in OCD also caused his medications to be reduced (Table 1).

3 | DISCUSSION

Different studies have revealed the circuits involved in tics, OCD, and also TS, which are generally known as CSTC circuits.¹⁻³ CSTC components, including the thalamus, posterolateral GPI, and anteromedial GPI, are among the most used targets for DBS procedures in TS. Other targets, including the subthalamic nucleus (STN), globus pallidus externus (GPe), anterior internal capsule (ALIC), and nucleus accumbens (NA), are also considered helpful in some studies.² It has been shown that stimulation of each target would improve specific aspects of the disease (e.g., tics, OCD) while it varies in different cases.² Anteromedial GPI is mainly known as an effective target for the improvement of the tic component of TS, while some studies have stated its ineffectiveness.^{2,3} Previous reports demonstrated that the stimulation of anteromedial GPI could also be an effective target in the treatment of isolated OCD,^{4,5} whereas the studies with the purpose of TS treatment have mentioned no significant improvement in the OCD component of TS.² Consequently, there is no consensus yet on how stimulation of anteromedial GPI affects different components of TS (either tic or OCD).³

In the current case, fluctuations and variations in the therapeutic outcome of TS components have been observed, which are dependent on the stimulation parameters. The optimal setup was achieved based on alterations in symptoms and patient compliance. With this setup, stimulation of anteromedial GPI led to significant improvement in OCD, but the tics still existed and progressively worsened. To the best of our knowledge, stimulation of GPI with similar therapeutic outcomes has not yet been reported.

Despite many studies on how the CSTC circuit may play an essential role in Tic, OCD, and TS, our observation and many others still need to be explained in terms of variations in therapeutic outcomes. Many neural pathways connect different and specific parts of the cerebral cortex, striatum, and thalamus together, making multiple parallels and integrated circuits,⁶⁻⁸ some of them are involved in both OCD and tic or either of them.^{1,9,10} Anteromedial GPI is related to the pathways involved in tic or OCD, commonly or specifically. DBS studies have also demonstrated that anteromedial GPI is a beneficial target for both tic and OCD,¹¹ indicating its involvement in both tic and OCD generating pathways and areas. In this case, neural impulses and the stimuli of the DBS procedure affecting anteromedial GPI would be directed toward both tic- and OCD-specified or common pathways and areas, leading to specific clinical outcomes. However, due to these pathways and areas' unknown physiological conditions, predicting clinical outcomes through stimulating a single target with an association to these pathways would

TABLE 1 Pre-operation and follow-up sessions data

Session / Evaluation	Pre-operation	#1 After 4 weeks	#2 After 6 weeks	#3 After 8 weeks	#4 After 11 months	#5 After 3 months
Stimulation Parameters	N/A	Amplitude: 1V Pulse width: 80 Frequency: 85	Amplitude: 1.2V Pulse width: 80 Frequency: 85	Amplitude: 1.3V Pulse width: 90 Frequency: 90	Amplitude: 1.4V Pulse width: 90 Frequency: 90	Amplitude: 1.5V Pulse width: 90 Frequency: 90
Description	Refractory TS	Tic improved	Tic was the same, but OCD improved	He was satisfied with OCD improvement, but tic was the same as before	Tic got worsened, OCD improved dramatically	Improvement in OCD but newly emerged tic in his eyebrows
Medications	Sertraline/200 mg Aripiprazole/7.5 mg Pimozide/12 mg Clomipramine/300 mg Mirtazapine/15 mg Buspirone/10 mg Venlafaxine/150 mg Citalopram/10 Desmopressin/60 µg	The same as pre-operation	Sertraline/100 mg Aripiprazole/7.5 mg Pimozide/12 mg Clomipramine/300 mg Mirtazapine/15 mg Buspirone/10mg Venlafaxine/150 mg Citalopram/10 Desmopressin/60 µg	Sertraline/200 mg Aripiprazole/7.5 mg Pimozide/12mg Clomipramine/300 mg Mirtazapine/15mg Buspirone/10 mg Venlafaxine/150 mg Desmopressin/60 µg	Sertraline/200 mg Aripiprazole/7.5 mg Pimozide/12mg Mirtazapine/15 mg Desmopressin/60 µg	Venlafaxine/75 mg Aripiprazole/35 mg Fluvoxamine/250 mg Orap/4 mg
Y-BOCS	38	9				
PUTS	28	23				

Abbreviations: Y-BOCS, Yale-Brown obsessive-compulsive scale; PUTS, Premonitory Urge for Tics Scale.

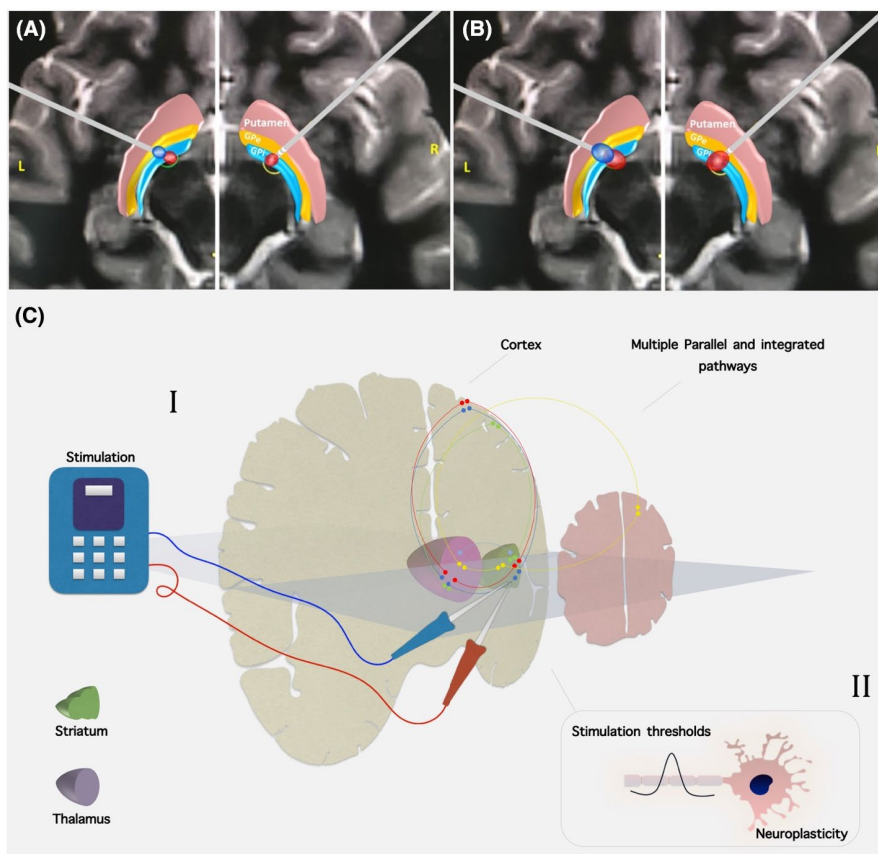


FIGURE 1 Schematic illustration of the hypothesis. (A, B) Bilateral GPI lead location, globus pallidus internus (light blue), globus pallidus externus (orange), and putamen (pink), Volume of tissue activated (VTA) (red for negative and blue for positive) are shown for reference; (A) Volume of tissue activated (VTA) in the initial programming setting, L-GPi (3+;0-), R-GPi (C+;8-), 90 pulse width, 90 Hz frequency, and 1.3 amplitude; (B) VTA in the second programming setting: L-GPi L-GPi (3+;0-), R-GPi (C+;8-), 90 μ s pulse width, 90 Hz frequency, and 2.5 amplitude. (CI) Multiple parallel pathways connect different parts of the cortex, striatum, and thalamus. Stimulation of a target (e.g., anteromedial GPI) as a member of these multiple parallel pathways, would spread through all different pathways related to anteromedial GPI, and subsequently, these pathways would respond to the stimuli in a term of resynchronization as an embodiment. (CII) The response can be varied in respect to pathways physiological condition including different stimulation thresholds and occurrence of neuroplasticity

be challenging. In other words, physiological conditions of stimulated pathways and their subsequent cumulative response to the specific stimulus adjustments would determine the therapeutic outcome variations (Figure 1). In our case, firstly, we observed fluctuations in symptoms, and eventually, at the best adjustment, OCD improved significantly while tic remained unchanged.

In conclusion, we suggest that the anteromedial GPI can be described as a portal to the pathways involved in both tic and OCD, and stimulation of this target would possibly make an impact on all these pathways but with different extents. Hence, anteromedial GPI itself is not probably the single determining factor in improving OCD or tic components of TS and the condition of involved pathways on the downstream is also playing an important role. This hypothesis perhaps would explain variations in therapeutic outcomes of DBS for TS patients in other studies.

ACKNOWLEDGMENT

We would like to acknowledge our patient who cooperated with us kindly.

CONFLICT OF INTEREST

The authors of this article declare no conflict of interest.

AUTHOR CONTRIBUTIONS

The authors declare that they have an equal role in writing the article. The specific role of each author is listed below: MS: Conceptualization, study design, and supervision. MS, ZA, and RJK: Data collecting. ZA and ST: Writing Manuscript. MS, ST, and FA: Editing.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

DATA AVAILABILITY STATEMENT

All data will be available through a request from the corresponding author.

ORCID

Zahra Aminzade  <https://orcid.org/0000-0002-2018-3436>

[org/0000-0002-2018-3436](https://orcid.org/0000-0002-2018-3436)

Sepand Tehrani Fateh  <https://orcid.org/0000-0003-2842-0480>

[org/0000-0003-2842-0480](https://orcid.org/0000-0003-2842-0480)

Farzad Ashrafi  <https://orcid.org/0000-0002-5959-5462>

Mehri Salari  <https://orcid.org/0000-0001-7102-821X>

REFERENCES

1. Robertson MM, Eapen V, Singer HS, et al. Gilles de la Tourette syndrome. *Nat Rev Dis Primers*. 2017;3(1):1-20.
2. Casagrande SCB, Cury RG, Alho EJJ, Fonoff ET. Deep brain stimulation in Tourette's syndrome: evidence to date. *Neuropsychiatr Dis Treat*. 2019;15:1061.
3. Martinez-Ramirez D, Jimenez-Shahed J, Leckman JF, et al. Efficacy and safety of deep brain stimulation in Tourette syndrome: the international Tourette syndrome deep brain stimulation public database and registry. *JAMA Neurol*. 2018;75(3):353-359.
4. Azriel A, Farrand S, Di Biase M, et al. Tractography-Guided deep brain stimulation of the anteromedial globus pallidus internus for refractory obsessive-compulsive disorder: case report. *Neurosurgery*. 2020;86(6):E558-E563.
5. Escalona PR, Adair JC, Roberts BB, Graeber DA. Obsessive-compulsive disorder following bilateral globus pallidus infarction. *Biol Psychiatry*. 1997;42(5):410-412.
6. Gilani IA, Oguz KK, Boyaci H, Doerschner K. Assessing topographic structural connectivity of the human basal Ganglia and Thalamus. *bioRxiv*, 2020. doi:10.1101/2020.03.06.981142
7. Cacciola A, Milardi D, Bertino S, et al. Structural connectivity-based topography of the human globus pallidus: implications for therapeutic targeting in movement disorders. *Mov Disord*. 2019;34(7):987-996.
8. Yuan R, Di X, Taylor PA, Gohel S, Tsai Y-H, Biswal BB. Functional topography of the thalamocortical system in human. *Brain Struct Funct*. 2016;221(4):1971-1984.
9. Wang Z, Maia TV, Marsh R, Colibazzi T, Gerber A, Peterson BS. The neural circuits that generate tics in Tourette's syndrome. *Am J Psychiatry*. 2011;168(12):1326-1337.
10. Milad MR, Rauch SL. Obsessive-compulsive disorder: beyond segregated cortico-striatal pathways. *Trends Cogn Sci*. 2012;16(1):43-51.
11. Nair G, Evans A, Bear RE, Velakoulis D, Bittar RG. The anteromedial GPI as a new target for deep brain stimulation in obsessive compulsive disorder. *J Clin Neurosci*. 2014;21(5):815-821.

How to cite this article: Aminzade Z, Tehrani Fateh S, Jalili Khoshnoud R, Ashrafi F, Salari M. Deep brain stimulation of anteromedial globus pallidus internus improved OCD rather than tics in a Gilles de la Tourette syndrome patient. *Clin Case Rep*. 2021;9:e05204. doi:[10.1002/ccr3.5204](https://doi.org/10.1002/ccr3.5204)