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Deep Brain Stimulation of the bilateral anteromedial Globus Pallidus internus in an adolescent with refractory tourette syndrome and comorbid obsessive compulsive disorder– A case report

Deep Brain Stimulation (DBS) for treatment-refractory Tourette syndrome (TS) has been effective in adults for reduction in severity of tics and comorbidities such as Obsessive-Compulsive Disorder (OCD) and depression [1]. Concerns regarding potential risks, long-term outcomes, and ethical issues related to use of DBS in children and adolescents have been challenged by recent guidelines that now recommend age as only a relative contraindication, especially when tics are severely disabling [2,3]. There is meta-analytic evidence for effective use of DBS, with a moderate safety profile, in carefully selected children and youth (mean age at surgery 17.9 (2.7) years) [4]. Here, we describe 6-months outcome of DBS in the bilateral Antero-medial Globus Pallidus internus (AM-GPi) in a 14-years-old boy with treatment-refractory TS with multiple developmental and psychiatric comorbidities.

1. Case description

M, a 14-year-old boy presented with 3-years-history of TS, with a continuous course of fluctuating severity, with comorbid attention deficit hyperactivity disorder (ADHD) and OCD. The complex motor tics were characterized by sudden, repetitive shrugging of shoulders, vigorous slapping of face, poking into his eyes and posterior pharyngeal wall, triggered by strong urges to poke until he felt 'satisfied'. Tics were present throughout the day, occurring every 10–15 minutes, lasting up to 20–30 seconds at a time. They significantly interfered in his daily activities and interactions, and also resulted in facial and ocular injuries. Vocal tics presented as involuntary incomprehensible utterances and coprolalia. On a combination of pharmacological and Comprehensive Behavioural Interventions for Tics (CBIT), he had brief periods of partial remission, not lasting for more than 2 weeks at a time, with persistent self-injurious tics. M also had sexual and aggressive obsessions and 'need to know' with reassurance seeking compulsions, posing intrusive and inappropriate questions to his family members, later extending to unfamiliar people. There was a bidirectional worsening of OCD and tics, further resulting in severe emotional dysregulation, depressive cognitions, social difficulties, suicidal ideations and functional incapacitation.

There was poor response to multiple treatment strategies – pharmacotherapy, CBIT alongside family-focused work, and repetitive Transcranial Magnetic Stimulation (rTMS) (Supplement Table 1). He received intensive CBIT over 2 months of inpatient care, and booster sessions over 6 months. Family-focused interventions involved reducing criticality, strengthening the mother-child relationship, training mother as a co-therapist and ensuring a supportive home environment.

With a worsening course of TS, the child suffered irreversible loss of vision in his right eye, secondary to self-injurious tics, resulting in traumatic cataract, total retinal detachment and pre-phthisic status. The option of DBS was considered on humanitarian grounds, in view of potential high risk of mutilation of the other eye with persisting tics. Candidature for DBS was evaluated and recommended by an independent multi-disciplinary team with specialists from psychiatry, neurology, and neurosurgery, not primarily associated with the child's treatment and approved by the Institutional Mental Health Review Board [3].

The AM-GPi was targeted based on visual anatomy [5,6] (supplementary material). Postoperatively, the adolescent had scalp wound dehiscence, necessitating wound exploration and resuturing. A postoperative computed tomography (CT) scan was performed to check for the accuracy of the electrode position. The stimulation parameters were gradually optimised to 1.5 V at 60 μs and 130 Hz on both sides (C+,1- & C+,9-). No stimulation-related side effects were noted during the immediate post-operative period or follow-up.

Pre and post-operative clinical assessments are detailed in Fig. 1. Three months post-operatively, tics improved significantly, with minimal socio-adaptive dysfunction. Occasional self-injurious tics occurred under periods of stress. However, there was significant worsening of OCD with social dysfunction compelling the child to isolate himself from any social contact. Considering a failed trial of ongoing pharmacotherapy for OCD, Sertraline was cross-tapered with Fluoxetine, increasing up to 80mg/day. Also, Tetrabenazine was stopped in view of questionable benefit over more than 2 years. The DBS stimulation parameters were further optimised to 2 V on either side (C+,1- & C+,9-) at 60 μs and 130 Hz at 3-month follow-up.

At 6 months, child showed substantial improvement in OCD with maintenance of improvement in TS, and scored 25/100 on total YGTSS and 14 on CY-BOCS and significant improvement in functionality. No further complications or adverse effects from DBS were noted over 6 months follow-up.

2. Discussion

The effectiveness and tolerability of DBS for treatment-refractory TS in youth has been increasingly documented in the recent years [4]. The presented case report adds to the evidence for short-term (6 months) safety, tolerability and effectiveness of

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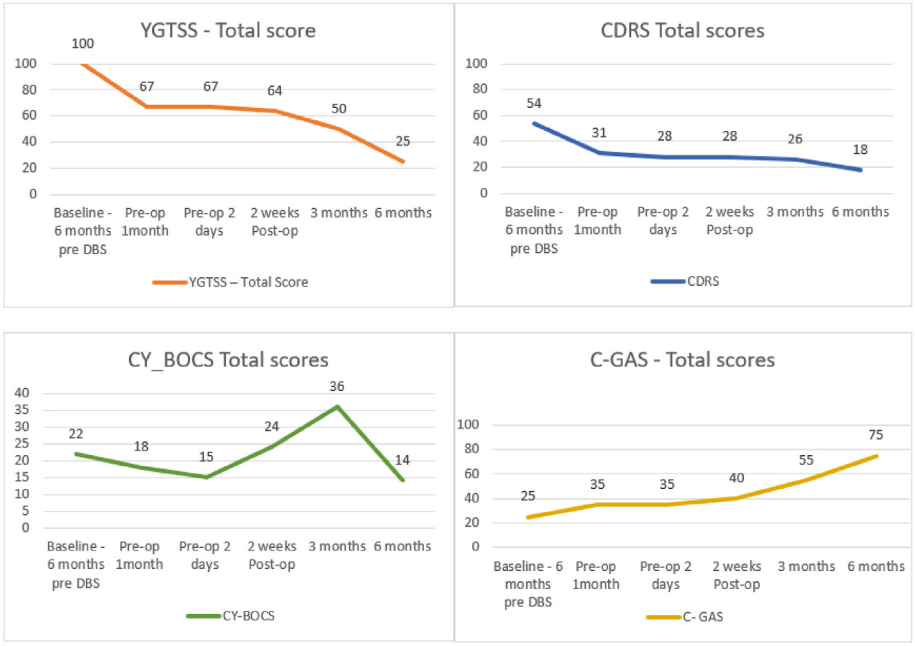

Fig. 1. Severity of tics and comorbid disorders
YGTSS _ Yale Global Tic Severity Scale [8], CDRS – Childhood Depression Rating Scale [9], CY-BOCS – Children's Yale Brown Obsessive Compulsive Scale [10], C-GAS – Children's Global Assessment Scale [11].. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

DBS for treatment-refractory TS in an early adolescent with self-injurious and incapacitating tics, at a younger age of 14 years.

Multiple targets have been identified for DBS in TS [5], among which, the AM-GPi is identified as an effective target for patients with TS and comorbid disorders, particularly OCD [7]. In this case, stimulation of bilateral AM-GPi is proven to be effective for reduction in the severity of self-injurious tics and OCD. An individual-participant meta-analysis of 58 young people reported an average improvement of 57.5% ± 24.6% on the YGTSS and 30.6% ± 44.7 improvement on the CY-BOCS at an average follow-up period of 34.2 ± 23.4 months [4]. The AM-GPi is a component of the limbic and associative cortico-striato-thalamo-cortical circuitry (CSTC), which is involved in the pathophysiology of both Tourette syndrome and OCD. In the above patient, an increase in amplitude of stimulation at 3 months follow-up, from 1.5 V to 2 V resulted in reduction in severity of OCD as well. The increase in volume of stimulation might have spread to OCD relevant CSTC pathways in the AM-GPi or neighbouring anterior limb of internal capsule, contributing to the anti-obsessive effects.

Beneficial effects of DBS appear up to and persist for at least 1 year [7]. There is a need for continued monitoring of tic severity and course of comorbid disorders over longitudinal follow-up. Further research to elucidate neurobiological mechanisms and post DBS trajectory of TS and comorbid psychiatric disorders among young people is warranted.

3. Previous presentation

This manuscript has not been previously published other than in form of abstracts and is not currently under consideration by any other journal.

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Author contributions

Dr. Dwarakanath Srinivas and Dr. Harshini Manohar have equal contributions to the conceptualization, management of the case and the manuscript drafting. Dr. Eesha Sharma, Dr. Lavanya Sharma and Dr. Sreyoshi Ghosh contributed to conceptualization, review and editing of the manuscript. Dr. Shyam Sundar Arumugham contributed to the conceptualization, methodology, review and editing of the manuscript.

Declaration of competing interest

The authors declare no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brs.2022.10.003.

References

[1] Porta M, Servello D, Zanaboni C, Anasetti F, Menghetti C, Sassi M, Robertson MM. Deep brain stimulation for treatment of refractory Tourette syndrome: long-term follow-up. Acta Neurochir 2012 Nov;154(11): 2029–41. https://doi.org/10.1007/s00701-012-1497-8.
[2] Schrock LE, Mink JW, Woods DW, Porta M, Servello D, Visser-Vandewalle V, Silburn PA, Foltynie T, Walker HC, Shahed-Jimenez J, Savica R. Tourette

syndrome deep brain stimulation: a review and updated recommendations. Mov Disord 2015 Apr;30(4):448–71. https://doi.org/10.1002/mds.26094.
[3] Martino D, Deeb W, Jimenez-Shahed J, Malaty I, Pringsheim TM, Fasano A, Ganos C, Wu W, Okun MS. The 5 pillars in tourette syndrome deep brain stimulation patient selection: present and future. Neurology 2021 Apr 6;96(14): 664–76. https://doi.org/10.1212/WNL.0000000000011704.
[4] Coulombe MA, Elkaim LM, Alotaibi NM, Gorman DA, Weil AG, Fallah A, Kalia SK, Lipsman N, Lozano AM, Ibrahim GM. Deep brain stimulation for Gilles de la Tourette syndrome in children and youth: a meta-analysis with individual participant data. J Neurosurg Pediatr 2018 Oct 26;23(2):236–46. https://doi.org/10.3171/2018.7.PEDS18300.
[5] Dwarakanath S, Hegde A, Ketan J, Chandrajit P, Yadav R, Keshav K, Sampath S, Pal PK, Reddy YC. "I swear, I can't stop it!"–A case of severe Tourette's syndrome treated with deep brain stimulation of anteromedial globus pallidus interna. Neurol India 2017 Jan 1;65(1):99. https://doi.org/10.4103/0028-3886.198188.
[6] Viswanathan A, Shahed JJ, Carvallo JF, Jankovic J. Deep brain stimulation for Tourette syndrome: target selection. Stereotact Funct Neurosurg 2012;90: 213–24. https://doi.org/10.1159/000337776.
[7] Wehmeyer L, Schüller T, Kiess J, Heiden P, Visser-Vandewalle V, Baldermann JC, Andrade P. Target-specific effects of deep brain stimulation for tourette syndrome: a systematic review and meta-analysis. Front Neurol 2021:1864.
[8] Leckman JF, Riddle MA, Hardin MT, Ort SI, Swartz KL, Stevenson JO, Cohen DJ. The Yale Global Tic Severity Scale: initial testing of a clinician-rated scale of tic severity. J Am Acad Child Adolesc Psychiatry 1989 Jul 1;28(4):566–73. https://doi.org/10.1097/00004583-198907000-00015.
[9] Poznanski EO, Mokros HB. Children's depression rating scale, [revised (CDRS-R)].
[10] Scahill L, Riddle MA, McSwiggin-Hardin M, Ort SI, King RA, Goodman WK, Cicchetti D, Leckman JF. Children's Yale-Brown obsessive compulsive scale: reliability and validity. J Am Acad Child Adolesc Psychiatry 1997 Jun 1;36(6):844–52. https://doi.org/10.1097/00004583-199706000-00023.
[11] Shaffer David, Gould MS, Brasic J, Ambrosini P, Fisher Prudence, Bird Hector, Aluwahlia S. A children's global assessment scale (CGAS). Arch Gen Psychiatr 1983;40(11):1228–31. https://doi.org/10.1001/archpsyc.1983.01790100074010.PMID6639293.

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