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Editorial

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Deep Brain Stimulation for Tourette Syndrome

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Tourette syndrome (TS) is a chronic neurodevelopmental disorder characterised by motor and vocal tics. Tics often present early in childhood at 6-8 years old, commonly following a waxing and waning course before reaching a peak in severity at around 12 years of age [1]. Although symptoms can subside by early adulthood, a significant number of patients continue to experience severe tics across the lifespan [2].

It has been shown that tics often affect health-related quality of life and require active treatment intervention [3,4]. First line recommended treatment includes both pharmacotherapy, usually in the form of neuroleptics or atypical antipsychotics [5], and behavioural interventions, such as habit reversal therapy and exposure with response prevention [6].

In a proportion of patients, these interventions fail to provide adequate control over tic symptoms. This may be due to lack of efficacy or intolerable adverse effects, or a combination of both [7,8]. Surgical interventions may therefore be considered, in order to improve the quality of life of patients with severe and refractory tics that impact on their daily functioning and well-being [2].

Traditional forms of ablative surgery were invasive procedures, usually involving the frontal cortex, limbic system, thalamus and cerebellum, and sometimes associated with permanent disabling adverse effects, such as dystonia and paralysis [8-10]. However over the last decades, deep brain stimulation (DBS) with stereotactically-guided electrode implantation at selected targets has been identified as a safe, effective and potentially reversible alternative intervention for movement disorders such as Parkinson disease, tremor and dystonia [2,7,11]. More recently, DBS has also been implemented in the treatment of other severe neuropsychiatric disorders, such as refractory depression and obsessive-compulsive disorder (OCD) [12].

In 1999, DBS of the thalamus was trialled as a therapeutic option for severe cases of TS [13] since then; there have been several reports of successful tic reduction following DBS of the thalamus and other brain regions. In total, seven areas have been the target of DBS in the treatment of patients with TS over the last decade [14]. These include the centromedian parafascicular (CM-Pf) and ventralis oralis internus (Voi) nuclei of the thalamus, postero-ventrolateral and antero-medial portions of the globus pallidus – pars interna (GPi), nucleus accumbens (NAc), anterior limb of the internal capsule (AIC) and subthalamic nucleus (STN) [2].

A recent review [2] reported that 97% of cases in published studies have exhibited improvements in patients' tics, with additional improvements in common co-morbidities such as OCD and self-injurious behaviours. Furthermore, serious or chronic adverse effects from this procedure have rarely been reported. However, it is acknowledged that there is the potential for such events to occur, through the direct effects of both surgery (e.g. bleeding and infection) and brain stimulation (e.g. sedation, altered mood, anxiety and changes in sexual function) [1]. With regard to cognitive functioning, a recent study [15] suggested that DBS is unlikely to produce neuropsychological adverse effects in patients with TS, thus providing further evidence for the safety of this procedure.

Although encouraging, the current literature on DBS in TS is mostly made up of isolated case reports, with only three small double-blind randomised controlled studies ever published [16-18]. Additionally, the exact number of patients with TS who have undergone DBS is still disputed, with variations in the figures reported in different publications [1,2,7]. Moreover, it is likely that DBS has been carried out on a greater number of patients than has been reported due to publication bias in favour of cases where DBS had a positive effect [2].

The recently published European clinical guidelines for TS and other tic disorders state that while there are recommendations for the use of DBS, it is also acknowledged that there are a number of debatable issues [1]. Only patients who fulfil specific diagnostic criteria for TS (e.g. DSM-IV-TR criteria) should be considered eligible for DBS therapy [2]. In addition, patients must have experienced severe functional impairment, with a Yale Global Tic Severity Score of 35/55 or above, for at least 12 months prior to surgery, with unlikely spontaneous symptom improvement [1,2]. Importantly, tics must cause significant impairment in quality of life, including effects on the patient's relationships, home environment, employment or studies [1].

Another critical factor for DBS eligibility is treatment resistance [2]. This will be assumed for patients who fail to respond to or encounter intolerable adverse effects from three different pharmacological interventions, including both an antidopaminergic and an α2-adrenergic drug, in adequate doses and over a suitable time period [1,2,7]. In addition, behavioural techniques should also have been performed for at least 12 sessions without substantial benefit [1,2].

With regard to age, there is agreement among most experts that DBS should only be performed on adults, with some suggesting a minimum age of 25, while others recommending an age threshold of 18 to be eligible for DBS [1], as it has been shown that nearly half of patients with TS can experience spontaneous remission of their symptoms by the age of 18 [2,16]. However, it could be argued that DBS could be beneficial for younger patients with extremely severe tics who are unlikely to improve spontaneously. In fact, DBS

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procedures have occasionally been carried out on younger patients due to the severity of their symptoms, yielding good results. For this reason, it has been suggested that age should not be a limiting factor for DBS eligibility [7].

Experts have tried to identify which area of the brain is the most effective target region for DBS. Thalamic stimulation has been performed most frequently, with GPi the second most popular target area [1]. The European guidelines state that no recommendation for the optimal target can be given at present, due to the lack of evidence in the current literature [1]. Difficulties determining the exact location for the electrode within the thalamus have been experienced, while Ackermans et al. [17] reported the potential for side effects such as vertical-gaze palsy. The GPi can be easily visualised on MRI, which allows for more accurate confirmation of the electrode location compared to other brain areas [2]. Finally, there is preliminary evidence that simultaneous stimulation of two target areas bilaterally - for example the thalamus and the GPi using four electrodes - is more effective than bilateral stimulation at one target area in the brain [16-21].

In conclusion, DBS is a promising therapeutic option for treatment-resistant patients with TS, whose tics cause them to have severe functional impairment and a poor quality of life. Large, multicentre trials are required in order to validate previous results from small case series and to build upon the current evidence base for DBS in TS. This will allow formulating clear recommendations for the use of DBS in clinical practice, with focus on the selection of suitable patients and the identification of the most appropriate target areas for each candidate.

References

1. Müller-Vahl KR, Cath DC, Cavanna AE, Dehning S, Porta M, et al. (2011) European clinical guidelines for Tourette syndrome and other tic disorders. Part IV: Deep brain stimulation. Eur Child Adolesc Psychiatry 20: 209-17.
2. Cavanna AE, Eddy CM, Mitchell R, Pall H, Mitchell I, et al. (2011) An approach to deep brain stimulation for severe treatment-refractory Tourette syndrome: The UK perspective. Br J Neurosurg 25: 38-44.
3. Eddy CM, Rizzo R, Gulisano M, Agodi A, Barchitta M, et al. (2011) Quality of life in young people with Tourette syndrome: A controlled study. J Neurol 258: 291-301.
4. Cavanna AE, Schraq A, Morley D, Orth M, Robertson MM, et al. (2008) The Gilles de la Tourette syndrome-quality of life scale (GTS-QOL): Development and validation. Neurology 71: 1410-6.
5. Roessner V, Plessen KJ, Rothenberger A, Ludolph AG, Rizzo R, et al. (2011) European clinical guidelines for Tourette syndrome and other tic disorders. Part II: Pharmacological treatment. Eur Child Adolesc Psychiatry 20: 173-96.
6. Verdellen C, van de Griendt J, Hartmann A, Murphy T, the ESSTS Guidelines Group (2011) European clinical guidelines for Tourette syndrome and other tic disorders. Part III: Behavioural and psychosocial interventions. Eur Child Adolesc Psychiatry 20: 197-207.
7. Pansaon Piedad JC, Rickards HE, Cavanna AE (2012) What patients with Gilles de la Tourette syndrome should be treated with deep brain stimulation and what is the best target? Neurosurgery 71: 173-92.
8. Temel Y, Visser-Vandewalle V (2004) Surgery in Tourette syndrome. Mov Disord 19: 3-14.
9. Mukhida K, Bishop M, Hong M, Mendez I (2008) Neurosurgical strategies for Gilles de la Tourette's syndrome. Neuropsychiatr Dis Treat 4: 1111-28.
10. Ackermans L, Temel Y, Visser-Vandewalle V (2008) Deep brain stimulation in Tourette's syndrome. Neurotherapeutics 5: 339-44.
11. Gross RE, Lozano AM (2000) Advances in neurostimulation for movement disorders. Neurol Res 22: 247-58.
12. Lujan JL, Chaturvedi A, McIntyre CC (2008) Tracking the mechanisms of deep brain stimulation for neuropsychiatric disorders. Front Biosci 13: 5892-5904.
13. Vandewalle V, van der Linden C, Groenewegen HJ, Caemaert J. (1999) Stereotactic treatment of Gilles de la Tourette syndrome by high frequency stimulation of thalamus. Lancet 353: 724.
14. Neuner I, Podoll K, Janouschek H, Michel TM, Sheldrick AJ, et al. (2009) From psychosurgery to neuromodulation: deep brain stimulation for intractable Tourette syndrome. World J Biol Psychiatry 10: 366-376.
15. Porta M, Brambilla A, Cavanna AE, Servello D, Sassi M, et al. (2009) Thalamic deep brain stimulation for treatment-refractory Tourette syndrome: Two-year outcome. Neurology 73: 1375-1380.
16. Leckman JF, Zhang H, Vitale A, Lahnin F, Lynch K, et al. (1998) Course of tic severity in Tourette syndrome: The first two decades. Pediatrics 102: 14-19.
17. Ackermans L, Temel Y, Bauer NJ, Visser-Vandewalle V, Dutch-Flemish Tourette Surgery Study Group (2007) Vertical gaze palsy after thalamic stimulation for Tourette syndrome: Case report. Neurosurgery 61: E1100.
18. Welter ML, Mallet L, Houeto JL, Karachi C, Czernecki V, et al. (2008) Internal pallidal and thalamic stimulation in patients with Tourette syndrome. Arch Neurol 65: 952-957.
19. Maciunas RJ, Maddux BN, Riley DE, Whitney CM, Schoenberg MR, et al. (2007) Prospective randomized double-blind trial of bilateral thalamic deep brain stimulation in adults with Tourette syndrome. J Neurosurg 107: 1004-1014.
20. Houeto JL, Karachi C, Mallet L, Pillon B, Yelnik J, et al. (2005) Tourette's syndrome and deep brain stimulation. J Neurol Neurosurg Psychiatry 76: 992-995.
21. Servello D, Sassi M, Brambilla A, Porta M, Haq I, et al. (2009) De novo and rescue DBS leads for refractory Tourette syndrome patients with severe comorbid OCD: A multiple case report. J Neurol 256: 1533-1539.

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