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Original Article

Efficacy of deep brain stimulation for Tourette syndrome and its comorbidities: A meta-analysis

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ABSTRACT

Tourette Syndrome (TS) is a neurodevelopmental disorder characterized by multiple motor and vocal tics, often accompanied by comorbid disorders. Optional treatments for patients with TS include behavioral therapy, pharmacotherapy, and neurostimulation techniques. Deep brain stimulation (DBS) has been considered a therapeutic approach for refractory TS and its comorbid symptoms. However, systematic comparison is necessary to understand the therapeutic effect of DBS among patients with TS with various comorbid symptoms, demographic characteristics, or stimulation targets. Consequently, our research aimed to assess the clinical efficacy of DBS in alleviating the symptoms of TS and its comorbidities. A systematic literature search was conducted across five databases: PubMed, Web of Science, MEDLINE, Embase, and PsycINFO. The primary outcome was the mean change in the global score of the Yale Global Tic Severity Scale (YGTSS), which assesses the severity of tics. The secondary outcomes included mean improvement of comorbid symptoms, such as obsessive-compulsive behaviors (OCB), depression symptoms and anxiety symptoms. In total, 51 studies with 673 participants were included in this meta-analysis. Overall, the DBS led to a significant improvement in tic symptoms ($p < 0.001$), as well as the comorbid obsessive-compulsive, depression, and anxiety symptoms with effect sizes of 1.88, 0.88, 1.04, and 0.76 accordingly. In the subgroup analysis, we found that striatum stimulation led to a more significant improvement in OCB in patients with TS compared to that observed with thalamic stimulation ($p = 0.017$). The relationship between sex, age, and target with the improvement of tics, depression, and anxiety was not statistically significant ($p = 0.923$, 0.438, 0.591 for different male proportions; $p = 0.463$, 0.425, 0.105 for different age groups; $p = 0.619$, 0.113, 0.053 for different targets). In conclusion, DBS is an efficient treatment option for TS, as well as the comorbid OCB, depression symptoms, and anxiety symptoms. It is important to highlight that stimulating the striatum is more effective in managing obsessive-compulsive symptoms compared to stimulating the thalamus.

Introduction

Tourette syndrome (TS) is a neurodevelopmental disorder that usually starts in childhood and is characterized by multiple motor and vocal tics [1]. The estimated prevalence of TS is 0.3%–0.9% in school-age children and 0.002–0.08% in adults [2]. Current treatments for TS include behavioral therapies, pharmacotherapy, and brain stimulation. Deep brain stimulation (DBS) has been considered a therapeutic approach for patients with TS who are medically refractory [3]. This promising treatment has been available since 1999 [4]. Despite the fact that DBS is not approved by the US Food and Drug Administration (FDA) or regulatory agencies in other countries for treating TS, its effectiveness and safety profile are favorable [4]. A review of 163 studies suggested a greater improvement in patients with TS undergoing DBS than in those undergoing pharmacotherapy or psychotherapy [5]. Similarly, Lin et al. conducted another meta-analysis and reported that DBS was the most effective approach in reducing tics compared to repeat transcranial magnetic stimulation (rTMS) and behavioral therapy (BT) [6]. In a previous meta-analysis, authors described a 53% reduction in the Yale Global Tic Severity Scale (YGTSS) for patients who received DBS [4]. According to Coulombe et al., DBS in the pediatric population might also be an effective treatment for tic symptoms [7]. While existing evidence

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syntheses point to the potential utility of DBS for patients with TS, there is a notable gap in evidence regarding the impact of individual characteristics on the clinical outcome. The various clinical outcomes related to the stimulation targets on TS and comorbid symptoms are still under debate.

TS is frequently accompanied by various comorbid disorders, including obsessive-compulsive behavior (OCB), attention deficit hyperactivity disorders, and mood disorders. These comorbidities can often exacerbate the severity of the disease and have a negative impact on the patient's quality of life [8]. The presence of comorbidities might increase the need for timely treatment, and DBS may further improve the comorbid symptoms, including OCB, depression, aggression, and self-injurious behaviors [4]. Despite these promising observations, comprehensive evaluations and summaries of the therapeutic effects of DBS on mood disorders remain insufficient. Thus, it is crucial to ascertain the efficacy of DBS in improving both tics and comorbidities in patients with TS.

Dysfunction of cortico-striato-pallido-thalamo-cortical (CSTS) networks has emerged as a core mechanism for TS, which is partly targeted for stimulation in neurostimulation treatments for TS [6]. The most frequently targeted areas in this approach are the centromedian nucleus-parafascicular complex of the thalamus (CM-PFC) and the globus pallidus internus (GPi) [9]. These two regions are closely connected to subcortical and cortical motor and limbic areas, which are believed to be crucial in various dysfunctions in patients with TS, such as motor and sensory responses, and attention processing. Although many patients suffering from TS have experienced marked improvements with DBS, large inter-individual differences in clinical responses to DBS have been observed [10]. The target-specific benefits might play an important role in addressing the heterogeneity. Previous neuropathological studies have shown that the variability in target location within this network offers numerous target-specific benefits [11]. As described by Welter et al., patients receiving pallidal stimulation showed greater improvement in tics and OCB [12]. In addition, the outcomes reported in the randomized controlled clinical trials (RCTs) differ from those in open-label stimulations or uncontrolled studies. Results from RCTs appear less positive due to the limitations in sample size and follow-up period [13].

Indeed, DBS is a promising treatment for medically refractory TS. However, critical questions regarding its clinical effects remain unanswered. Therefore, it is critical to determine the reliable impact factors for clinical outcomes to enhance our understanding of how therapeutic responses to DBS vary among different participants [13]. In an effort to address these issues, we conducted a systematic review and meta-analysis on the clinical effects of DBS in patients with TS. In this meta-analysis, we aggregated data from several recent studies to provide an overview of the clinical outcomes of DBS for medically refractory TS and to investigate whether stimulation targets or other factors can predict clinical outcomes. In addition, we compared the beneficial effects of DBS on comorbid symptoms and identified the reliable impact factors in a similar manner.

Methods

This study was conducted according to the Preferred Reporting Items for Systematic Review and Meta-analysis [14] (Table S1). We performed an extensive and systematic search for eligible studies across PubMed, Web of Science, MEDLINE, Embase, and PsycINFO from their inception dates until March 2023. The search terms were “Tourette syndrome OR Gilles de la Tourette syndrome OR Tourette's disorder OR Tic disorder” AND “Deep Brain Stimulation OR DBS”.

After excluding duplicated papers, two authors independently screened the titles and abstracts, and read full texts to identify publications based on the eligibility criteria. Any conflicts in selection were resolved with the assistance of a third author. The reference lists of all eligible studies were also searched and evaluated for eligibility. Initially, we retrieved 4464 studies from the five databases. Out of these, we discarded 2183 duplicates. We further refined the list by excluding 1677 publications that were irrelevant and 495 that were not original research. After an in-depth text review, we removed an additional 32 records for the following reasons: 1) the primary outcome measurement was not available (n = 19); 2) tic reduction was not evaluated using YGTSS (n = 5); and 3) the study focused on the same or duplicated participants (n = 8) (Fig. 1).

Eligibility criteria

The meta-analysis included studies that met the following criteria: (1) the subjects were diagnosed with TS according to standardized diagnostic procedures; (2) the patients underwent DBS treatment; (3) the study involved comparisons, either pre- and post-surgery or between active and sham stimulation; (4) the study format was an RCT, open-label trial, or a case series. Additionally, we summarized the patient-level data extracted from single case reports because individual participant data meta-analyses are statistically and clinically different from aggregate data meta-analyses [15]; and (5) the efficacy outcomes were evaluated using YGTSS. Studies were excluded if they met the following criteria: (1) they were conference abstracts, poster presentations, commentaries, letters, or literature reviews; or (2) they contained duplicate participant data.

Data extraction and quality assessment

Data extraction was based on the PICO (Population: patients with TS, Intervention: DBS, Comparator: self-control, case-control, or sham stimulation control, and Outcome: improvement in tic symptoms, obsessive-compulsive symptoms, depression symptoms, and anxiety symptoms) format [16]. We extracted pre-specified data from the eligible studies onto a standardized sheet, including characteristics of studies (authors, year of publication, country, study design), demographic characteristics of participants (sample size, age, sex, duration of illness, age at surgery), primary or secondary outcome measurements (YGTSS changes evaluated tics, and other measurements evaluated comorbid symptoms such as obsessive behaviors, depression symptoms, anxiety symptoms), and the quality of studies. We evaluated the study quality using the eleven-item Agency for Healthcare Research and Quality, and categorized it as follows: 0–3 as low quality, 4–7 as moderate quality, and 8–11 as high quality [17].

Outcome measurements

Our primary outcome measurements focused on the mean change in rating scales assessing tic severity. An acceptable clinical scale for rating tic severity was the global score of the YGTSS [18]. For the secondary outcomes, the mean improvement in the severity of OCB, depression symptoms, or anxiety symptoms was measured using the standardized mean difference (SMD) [19]. All these outcomes evaluating the reduction of symptom severity were measured and pooled for the meta-analysis as SMD, as rating scales differed between the included studies.

Statistical analysis and meta-analytic procedures

The primary outcome was calculated using the SMD and 95% confidence intervals (CIs). Pre- and post-surgery global YGTSS scores were compared across the entire sample. The same effect size was used when analyzing the secondary outcomes: mean improvement of OCB (comparison of pre- and post-surgery Yale-Brown Obsessive-Compulsive Scale (Y_BOCS) scores), depression symptoms (comparison of pre- and post-surgery Beck Depression Index or Hamilton Depression Rating Scale scores), and anxiety symptoms (comparison of pre- and post-surgery Hamilton Anxiety Rating Scale or State-Trait Anxiety Inventory scores). We conducted a detailed examination of the sources of heterogeneity through meta-regression and subgroup analysis. Meta-regression was

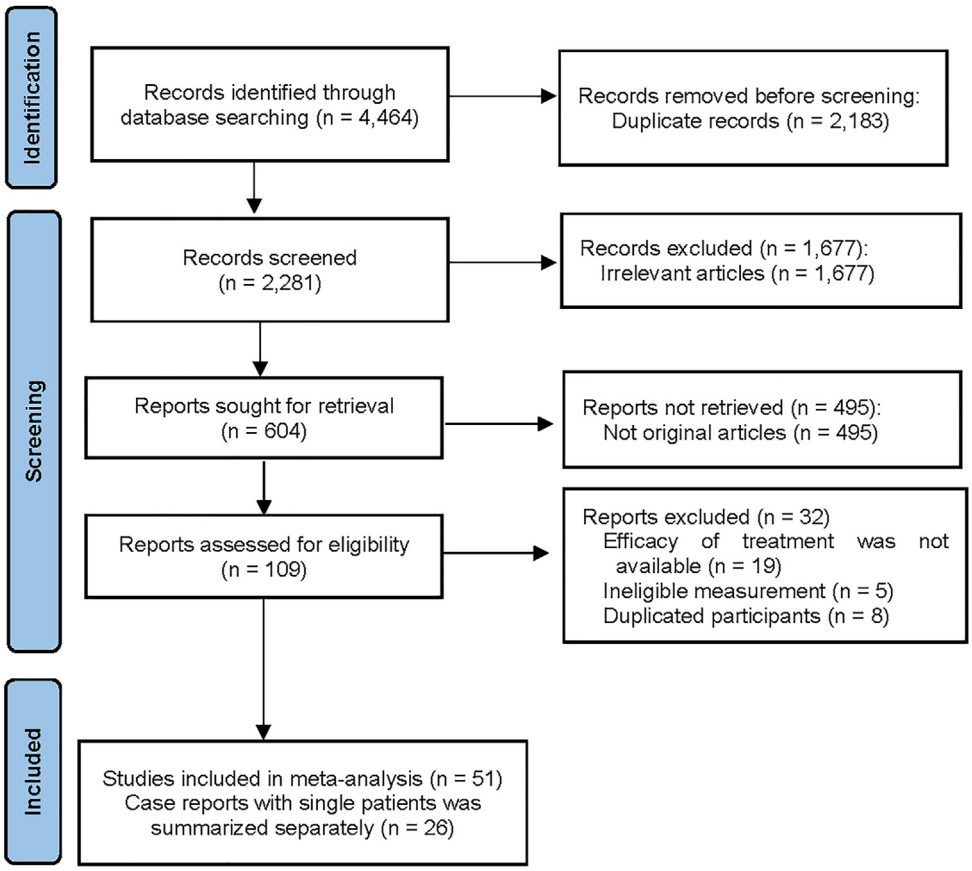

Fig. 1. Flow chart of study selection. A total 51 studies were eventually included in the meta-analysis, and data from 26 single case reports were summarized in the present study.

conducted based on the proportion of males, and subgroup analyses were performed based on two different individual characteristics: age strata, and surgical targets. We divided the studies into four subgroups based on age: ≤25 years old, 26–30 years old, 31–35 years old, and ≥36 years old [20]. We conducted the last subgroup analyses focusing on two different targets: the striatum and the thalamus. Additionally, the sensitivity analysis was conducted to identify any outlier studies.

Statistical analyses were conducted using Stata software (V15; StataCorp LP, College Station, TX). Heterogeneity was evaluated using the I^2 statistic, which was classified as follows: $I^2 \leq 25\%$ as low heterogeneity, ≤50% as moderate heterogeneity, and ≤75% as high heterogeneity. A two-tailed *p-value* of less than 0.05 was considered statistically significant.

Results

Included studies

For this meta-analysis, 51 eligible studies were included, enrolling a total of 673 participants with a mean age ranging from 20 to 41 years old. Single case reports (n = 26) were not included in the meta-analysis because they were statistically different from studies with aggregate data [15]. The detailed characteristics are summarized in Table S3. The most reported simulation targets included the GPi and the centromedian-parafascicular complex-ventral oral thalamic nuclei of the thalamus (CM-PFC Voi). Other detailed study characteristics are summarized in Tables S2–S3.

Clinical outcome

Fig. 2 shows the combined clinical outcomes of DBS on tics, as well as comorbid OCB, depression symptoms, and anxiety symptoms. Overall, the DBS led to a significant reduction in the Global YGTSS scale, showing a SMD of 1.88 (95% CI: 1.74 to 2.02, $p < 0.001$, $I^2 = 56.50\%$). Comparing the reduction of OCB severity in 314 participants, we observed a significant decrease in Y_BOCS scores (SMD = 0.88, 95% CI: 0.71 to 1.05, $p < 0.001$, $I^2 = 14.20\%$). A total of 19 studies were included in calculating the clinical effectiveness of DBS in improving depression symptoms in patients with TS, showing a reduction in depression symptoms after treatment (SMD = 1.04, 95% CI: 0.81 to 1.26, $p < 0.001$, $I^2 = 0.00\%$). In addition, a meta-analysis including 18 studies revealed a significant improvement in anxiety symptoms after treatment (SMD = 0.76, 95% CI: 0.46 to 1.07, $p < 0.001$, $I^2 = 2.00\%$). The detailed forest plots of each clinical outcome are presented in Supplementary Figs. S1–S4.

Subgroup analysis and sensitivity analysis

The data revealed a reduction in YGTSS scales in studies with varying male proportions (Fig. 3), while the meta-regression analysis reported no significant association between sex and changes in tic symptoms ($p = 0.923$). Regarding the improvement of OCB, depression symptoms, and anxiety symptoms, there was no significant difference of improvement in these three symptoms across studies with different male proportions as well.

In the subgroup analysis, improvements in tics, OCB, depression symptoms, and anxiety symptoms were significant across all age groups.

Outcomes	Combined effectiveness of DBS				
	Studies (n)	Participants (n)	SMD (95% CI)	I^2	*p* value
YGTSS	48	650	1.88 (1.74, 2.02)	56.50%	<0.001
Y_BOCS	23	314	0.88 (0.71, 1.05)	14.20%	<0.001
Depression symptoms	19	201	1.04 (0.81, 1.26)	0.00%	<0.001
Anxiety symptoms	18	131	0.76 (0.46, 1.07)	2.00%	<0.001

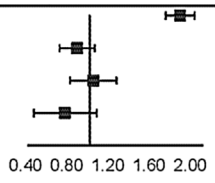

Fig. 2. Combined effectiveness of DBS in reducing tic symptoms, obsessive symptoms, depression symptoms, and anxiety symptoms. Tic symptoms were evaluated using the YGTSS, and they showed significant improvement after DBS treatment. We also found significant reductions in obsessive symptoms, depression symptoms, and anxiety symptoms. DBS: deep brain stimulation; SMD: standardized mean difference; YGTSS: Yale Global Tic Severity Scale; Y_BOCS: Yale-Brown Obsessive-Compulsive Scale.

Outcomes	Meta regression for effectiveness of DBS in studies with different male proportion				
	Studies (n)	Participants (n)	Mean male proportion (%)	SMD (95% CI)	*p* value of meta regression
Tic symptoms (YGTSS)	46	631	77%	0.10 (-1.98, 2.18)	0.923
Obsessive symptoms (Y_BOCS)	24	302	81%	1.18 (-0.47, 2.83)	0.152
Depression symptoms	17	176	79%	0.64 (-1.07, 2.36)	0.438
Anxiety symptoms	15	99	83%	0.74 (-2.17, 3.65)	0.591

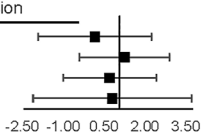

Fig. 3. Meta-regression for the effectiveness of DBS in studies with varying male proportions. Studies with varying male proportions reported improvements in tic symptoms, obsessive symptoms, depression symptoms, and anxiety symptoms. There were no significant differences between different sex proportion in the improvement of all symptoms. DBS: deep brain stimulation; SMD: standardized mean difference; YGTSS: Yale Global Tic Severity Scale; Y_BOCS: Yale-Brown Obsessive-Compulsive Scale.

However, higher age of patients was not significantly correlated with a greater reduction in these four symptoms ($p = 0.463$, 0.326, 0.425, and 0.105 respectively; see Fig. 4).

We proceeded to explore whether the different stimulation targets were associated with symptom improvement and found that the changes in the four symptoms were all significant across two different targets. Moreover, the stimulation of the striatum resulted in a more significant improvement of OCB in patients with TS compared to the thalamic stimulation ($p = 0.017$, Fig. 5). The meta-regression showed no association between the surgical target and changes in tic symptoms, depression symptoms, and anxiety symptoms ($p = 0.619$, 0.113, and 0.053, accordingly).

In addition, the detailed forest plot of subgroup analysis for the effectiveness of DBS in different symptoms in studies with various age groups or different target sites can be found in Figs. S5–S12 in the supplementary materials.

According to the sensitivity analysis (Fig. S13), there was no significant difference of symptom improvement after excluding each study evaluating the severity of tics, OCB, depression symptoms, and anxiety symptoms.

Discussion

Our findings revealed that DBS significantly improved tic symptoms in patients with TS while also reducing coexisting OCB, depression, and anxiety symptoms. Moreover, our meta-regression analysis suggested that stimulating the striatum was more effective in reducing the severity of OCB among patients with TS compared to thalamic stimulation.

In the past decades, several reviews have investigated the clinical effectiveness of DBS for TS. These reviews have compiled the results showing that DBS was associated with improvements in tics. However,

Outcomes	Combined effectiveness of DBS in sutides with different age group			
	Studies (n)	Participants (n)	Prevalence (95% CI)	*p* value of meta regression
Tic symptoms (YGTSS)				0.463
Age: ⩽25	13	93	1.91 (1.53, 2.28)	
Age: 26-30	14	307	1.90 (1.69, 2.10)	
Age: 31-35	13	149	1.69 (1.41, 1.97)	
Age: ⩾36	5	29	1.75 (1.02, 2.47)	
Obsessive symptoms (Y_BOCS)				0.326
Age: ⩽25	6	47	1.26 (0.81, 1.72)	
Age: 26-30	7	86	1.02 (0.70, 1.34)	
Age: 31-35	7	95	0.54 (0.25, 0.84)	
Age: ⩾36	3	13	0.97 (0.14, 1.80)	
Depression symptoms				0.425
Age: ⩽25	3	12	1.20 (0.26, 2.13)	
Age: 26-30	5	40	0.96 (0.49, 1.43)	
Age: 31-35	5	50	1.20 (0.76, 1.63)	
Age: ⩾36	3	13	0.42 (-0.38, 1.23)	
Anxiety symptoms				0.105
Age: ⩽25	3	11	1.14 (0.14, 2.14)	
Age: 26-30	6	41	0.85 (0.36, 1.34)	
Age: 31-35	4	36	0.75 (0.26, 1.23)	
Age: ⩾36	2	11	0.28 (-0.56, 1.12)	

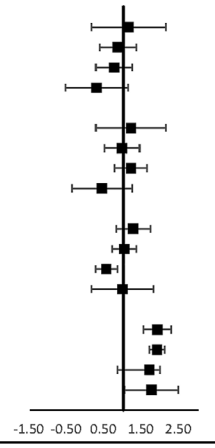

Fig. 4. Combined effectiveness of DBS in studies with different age groups. Studies were divided into four subgroups according to the mean age of participants: ≤25 years old, 26–30 years old, 31–35 years old, and ≥36 years old. The effectiveness of DBS did not show significant difference among the 4 age groups. DBS: deep brain stimulation; SMD: standardized mean difference; YGTSS: Yale Global Tic Severity Scale; Y_BOCS: Yale-Brown Obsessive-Compulsive Scale.

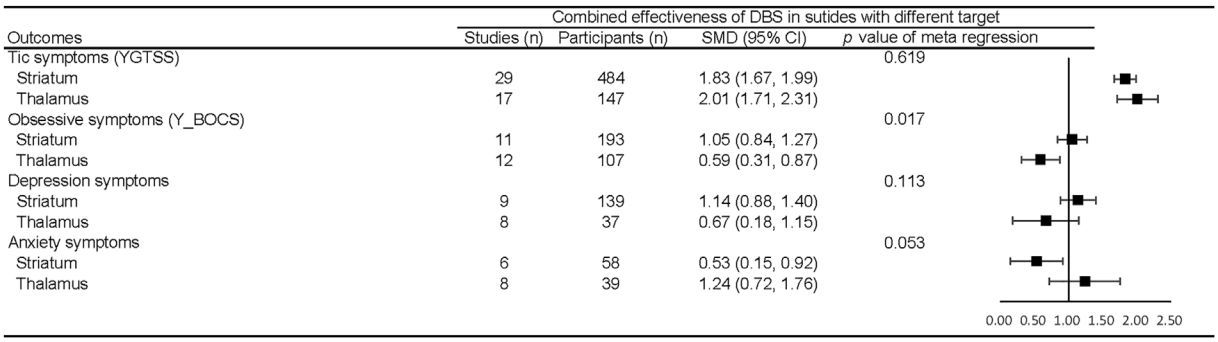

Fig. 5. Combined effectiveness of DBS in studies with different targets. Studies were divided into two subgroups based on different targets: the striatum and the thalamus. The stimulation of the striatum resulted in a significant improvement in OCB. There was no association between the surgical target and changes in tic symptoms, depression symptoms, and anxiety symptoms. DBS: deep brain stimulation; SMD: standardized mean difference; YGTSS: Yale Global Tic Severity Scale; Y_BOCS: Yale-Brown Obsessive-Compulsive Scale.

these studies have shortcomings, as described in our introduction, as many of them did not evaluate the improvement of various comorbidities. Moreover, the most appropriate brain targets for individual symptoms remain unclear. Our meta-analysis revealed a significant improvement in tics, along with a substantial impact on the OCB, depression symptoms, and anxiety symptoms. Meanwhile, we also found that for patients suffering from TS and OCB, striatal stimulation leads to higher treatment effectiveness.

Based on this up-to-date data, we suggest that DBS is an efficient treatment for patients with medicine-refractory TS, consistent with previous studies and data from the International TS DBS Database and Registry [4]. According to data from multiple centers, DBS may lead to improvement in about 5.6% of patients with severe TS [4]. The average improvement in YGTSS scores ranged from 45% to 90% in the previously reported results [13]. This wide range of clinical efficiency might be related to the different surgical techniques, treatment approaches, and poor patient compliance [21].

DBS was initially proposed to offer a safe and effective alternative to ablation and was applied to the management of movement disorders [22]. Among those disorders, the Food and Drug Administration (FDA) approved DBS as a treatment for Parkinson's disease, essential tremor, generalized/cervical dystonia, and obsessive-compulsive disorder (OCD) [23]. Although the underlying mechanisms for DBS in treating TS are still unclear, several theories have been proposed. The two most reported hypotheses are electrophysiological alterations and neurotransmitter modulation [23]. Non-invasive imaging techniques, such as electroencephalography (EEG), might provide relevant information on both local and systemic changes in electrophysiology [24]. Previous EEG studies have described neuronal inhibition of high frequent DBS, which might be caused by depolarization block resulting from increased potassium current and decreased activity of voltage-gated sodium channels [23,24]. Another proposed mechanism of DBS involves changes of various neurotransmitters, such as dopamine, adenosine, gamma-aminobutyric acid, glutamate, and serotonin [23,25–28]. Additional studies utilizing Positron Emission Tomography (PET) and functional Magnetic Resonance Imaging (fMRI) reported a decrease in cerebral blood flow and blood oxygen level dependent (BOLD) signals in supplementary motor areas and the anterior cingulate cortex during DBS stimulation [23,29]. This could further contribute to a reduction in the frequency of tics.

Furthermore, DBS might significantly improve the comorbid OCB and affective symptoms (depression symptoms and anxiety symptoms) in patients with TS. This finding is of great importance, as the prevalence of various comorbidities is relatively high and directly affects patients' quality of life [8]. Previously, the FDA approved DBS as an optional treatment for OCD. TS and OCD are both thought to arise from hyperactivity in the CSTC circuit, which connects the cortical region with the basal ganglia and thalamus [30]. GPi and CM-PFC are both important brain regions in the CSTC network [30]. It is possible that DBS might further inhibit or override the altered functional connectivity of key brain regions, leading to significant improvement in both tics and obsessive-compulsive symptoms [31]. This is in line with our study that DBS is an effective treatment for both tics and OCB.

Similarly, depression, although not officially approved for DBS treatment, has been treated by numerous research groups using DBS [32]. Usually, antidepressants and/or psychotherapy are the first-line treatments for depression, along with electroconvulsive therapy for major depressive disorder or treatment-resistant individuals [32]. In addition, an increasing number of studies have utilized DBS for those who do not respond to conventional interventions [32]. The regional brain stimulation of DBS might significantly alter the functional status of the limbic network, which could further lead to a remission of depressive symptoms [33]. There are some overlapping targets in treating depression and TS. The most commonly targeted areas in depressive patients include the ventral capsule/ventral striatum, subcallosal cingulate, the nucleus accumbens, and medial forebrain bundle, with response rates ranging from 41% to 92% [32].

Anxiety, another prevalent comorbidity in patients with TS, has also been studied in the context of DBS. Our research involved 131 participants across 18 studies to assess the reduction of anxiety symptoms through DBS. While the mechanistic understanding of DBS's impact on anxiety in patients with TS remains limited, earlier animal models demonstrated a rapid decrease in anxiety symptoms after DBS treatment [34]. Commonly reported stimulation targets for mood disorders and anxiety include the nucleus accumbens, subgenual cingulate cortex, and ventral capsule/ventral striatum. Studies reported complete symptom remission, and interestingly, some of these regions were also targeted for tic improvement [35]. In conclusion, these findings suggested that DBS may also be effective in managing comorbid OCB, depression symptoms, and anxiety symptoms in patients with TS.

Subgroup analysis identified that DBS was an effective treatment for tic symptoms across different age groups. According to the guidelines for DBS in patients with TS, the crucial factor is the age at which patients are included in the treatment. It is suggested that DBS should be applied to patients aged 18 years or older, based on the European guidelines [36]. Conversely, in the American guidelines, DBS is recommended as a treatment for TS in patients older than 25 years [36]. In our study, we observed greater improvement in younger patients (aged 20–24 years old), whereas the variation in tic reduction among different age groups was not statistically significant. This result was partly in line with previous reports [36,37]. Existing research supports the notion that the period between 15 and 25 years of age represents a critical transition phase from childhood to adulthood. Therefore, applying DBS treatment to patients with TS aged 15–25 could significantly improve their quality of life, considering potential educational, professional, and social impairments [36].

Thus far, two different brain regions are commonly used for DBS: CM-PFC and GPi [11,13]. Both targets have been considered core regions in the nonmotor basal ganglia circuitry [38]. Based on the subgroup analysis, we observed a higher mean change in the YGTSS total score when stimulating the GPi compared with other targets, although the difference was not statistically significant. This finding was in line with the clinical effectiveness of DBS for other movement disorders. It is worth noting that the GPi might be more important in reducing tics.

Considering the improvement of OCB, evidence from the subgroup analysis showed a promising reduction in symptoms among boys with TS and OCD, while sex did not show significance. It has been noted that sex was not related to the clinical efficacy and prognosis in a previous study [39]. Interestingly, we found that the stimulation of the GPi led to a greater reduction in obsessive-compulsive symptoms compared to CM-PFC stimulation. Previous studies have also shown that stimulating the GPi led to a significant reduction in OCB after DBS surgery. This target would be the preferred choice for DBS in patients with TS who also have obsessive-compulsive symptoms [11].

When treating affective symptoms in patients with TS, we found that stimulating the striatum and thalamus was effective in alleviating depression symptoms and anxiety symptoms in patients with TS. We also found that reductions of depression symptoms and anxiety symptoms were not statistically different across age groups. This phenomenon might be caused by different sample sizes. Similarly, there was no significant relationship between improvement of depression symptoms and anxiety symptoms with stimulation targets according to the subgroup analysis.

Our findings are indeed promising; however, it is worth noting that most of the eligible studies predominantly consist of case series, and thus represent a relatively lower level of evidence. There needs to be more rigorous evaluation of the clinical efficacy of DBS through double-blinded, randomized controlled trials with significantly larger sample sizes. Additionally, the high variance in follow-up duration, target selection, and participant enrollment across the different studies could potentially impact the results. Moreover, we were unable to conduct a more comprehensive subgroup analysis, which would include factors such as different disease courses and follow-up periods, due to a lack of sufficient data on these aspects.

Upon reviewing and analyzing data from 51 studies, we concluded that DBS is an effective clinical treatment option for TS, as well as co-existing OCB, depression symptoms, and anxiety symptoms. Additionally, our results indicated that stimulating the striatum leads to a higher rate of symptom reduction in OCD compared to thalamic stimulation. This suggested that the striatum may be an appropriate target for treatment in patients with TS who are simultaneously affected by OCD.

Author Contribution

Dr. Anyi Zhang conducted the literature search, and drafted the manuscript.

Dr. Anyi Zhang, conducted the analysis with the help from Dr. Tinghong Liu, Dr. Jinshan Xu, Dr. Qing Zhao, Dr. Xianbin Wang, and Zhongliang Jiang. All authors performed critical review of the manuscript and approved the final version of the manuscript.

Declaration of competing interest

All authors declare no conflict 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.neurot.2024.e00360.

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