Review

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Deep brain stimulation (DBS) in movement disorders management: exploring therapeutic efficacy, neurobiological mechanisms, and clinical implications

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Introduction: Deep brain stimulation (DBS) has emerged as a promising therapeutic approach, offering targeted neuromodulation for movement disorders refractory to medical management or stereotactic surgery. However, assessing its benefits against potential risks is essential. This meta-analysis aims to evaluate the efficacy and safety of DBS in movement disorders, shedding light on its role as an alternative therapeutic option.

Methods: A comprehensive search of databases after systemic review yielded studies published in English from 2000 to the present. Data selection, screening, extraction, and risk of bias assessment were performed meticulously. Statistical analysis was conducted using RevMan 2.0, with significant heterogeneity addressed through appropriate methods.

Results: Our meta-analysis included 40 studies assessing the Unified Parkinson's Disease Rating Scale Part III, revealing a significant improvement in motor symptoms (mean difference [MD]: −18.05, 95% confidence interval [CI] [−20.17, −15.93], $P < 0.00001$). Hoehn and Yahr Stage analysis demonstrated a reduction in disease severity (MD: −0.58, 95% CI [−1.05, −0.12], $P = 0.01$). Tremor severity (MD: −8.22, 95% CI [−12.30, −4.15], $P < 0.0001$), overall tremor (MD: −2.68, 95% CI [−4.59, −0.77], $P = 0.006$), gait velocity (MD: 0.13, 95% CI [0.08, 0.18], $P < 0.00001$), and Yale Global Tic Severity Scale score (MD: −9.75, 95% CI [−14.55, −4.96], $P < 0.0001$) also showed significant improvements with DBS.

Conclusion: DBS demonstrates efficacy in improving motor symptoms, disease severity, tremor, gait, and tic severity in movement disorders. However, further research is needed to elucidate long-term efficacy and safety outcomes.

Keywords: deep brain stimulation, meta-analysis, movement disorders, Parkinson's disease, parkinsonism, PD

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HIGHLIGHTS

- We evaluated the efficacy and safety of deep brain stimulation (DBS) in movement disorders, shedding light on its role as an alternative therapeutic option.
- Our meta-analysis included 40 studies assessing the Unified Parkinson's Disease Rating Scale Part III, revealing a significant improvement in motor symptoms, reduction in disease severity, tremor severity and gait velocity.
- The final results demonstrated efficacy in improving motor symptoms, disease severity, tremor, gait, and tic severity in movement disorders in DBS.

Introduction

Movement disorders is an umbrella term that includes an array of different neurological disorders affecting different regions in the brain especially the cerebellum leading to an increase or a decrease in the duration and rate of a particular action along with defects in the planning, control, and execution of different movements.[1,2]

Movement disorders were once originally termed as extrapyramidal disorders by Wilson for most of the 20th century when the first formal attempt to classify these disorders was made in

1963 by Jorg Baumann based on these disorders' pathology and anatomical location. However due to the inaccuracy of the term, on 1968 Stanley Fahn at the University of Pennsylvania changed the term from extrapyramidal to movement disorders[2,3].

The complex nature of movement disorders has made it difficult to come up with a comprehensive classification due to their genetic, pathological and clinical variability. However, they are generally classified as hyperkinetic and hypokinetic disorders. The hyperkinetic disorders include dystonia, chorea, athetosis, tics, tremor, myoclonus, stereotypy and startle syndromes. Hypokinetic disorders include Parkinson's disease (PD), rigidity, and other parkinsonian disorders. Gait disorders such as ataxia and spasticity in addition to disorders of psychogenic or functional etiology are also included.[2–4]

Symptomatic treatment through pharmacological medications varies widely and is tailored to the needs of the patient, underlying pathology and the clinical manifestations of these disorders.[5] These treatments may include deutetrabenazine and tetrabenazine for Huntington's disease chorea.[6] monoamine-depleting drug, new formulations of botulinum toxin are also being used in the treatment of hyperkinetic disorders.[7] Immunotherapies such as glucocorticoids, plasma immunoglobulins, cyclophosphamide for immune-mediated movement disorders.[8] Propranolol, primidone, and topiramate (>200 mg/day) for the treatment of essential tremor.[9] Nonergot dopamine agonists, levodopa, and rasagiline for the treatment of Parkinson's motor fluctuations[10]. Lastly, physiotherapy has been considered a cornerstone in the multidisciplinary treatment of functional movement disorders.[11] Targeted gene-specific therapy through striatal cAMP turnover modulation has also been suggested in cases of genetic based paroxysmal movement disorders such as episodic ataxia and paroxysmal dyskinesia.[12] Stereotactic surgery is considered in cases where medical therapy fails.[5]

Deep brain stimulation (DBS) is a neurosurgical procedure that allows targeted circuit-based neuromodulation and promises to give novel solutions to many psychiatric and movement disorders. It works through modulating neuronal activity by the implantation of electrodes into the brain parenchyma. In general, high frequency stimulation appears to have an inhibitory effect on nearby neurons while low frequency stimulation showed an excitatory effect. However, the exact physiological mechanisms by which DBS work are still not fully understood.[13,14]

DBS basic frame existed since the 19th century and was advanced forward in 1947 when x-ray pneumoencephalography was introduced which enabled accurate target localization by the surgeons. In 1963, high frequency DBS was reported to alleviate parkinson's tremor substantially for the first time. In 1993, DBS was presented as an alternative for pallidial ablative surgery in the treatment of Parkinson disorder motor symptoms. Currently DBS is used in the standard treatment of dystopia, essential tremor, and PD and is now considered as an option for treatment-resistant conditions like Alzheimer disease, Tourette syndrome (TS), and schizophrenia.[13,14]

DBS is a subject of current interest in the treatment of a wide array of movement disorders especially when pharmacological therapies fail to control the condition or are poorly tolerated by patients due to their side effects.

It is now considered a gold standard treatment to many of the common movement diseases due to its higher efficacy, fewer complications, and minimal invasiveness in comparison to its lesioning and stereotactic surgical counterparts. However DBS like any other foreign body has its setbacks represented in a higher rate of infection, hemorrhage, malfunction and frequent need of follow-up; hence, a review concerning DBS potential benefits against its potential risks is deemed necessary.[15] The primary importance lies in consolidating evidence from multiple studies to achieve a higher level of statistical power and precision. By synthesizing findings on the efficacy, safety, and outcomes of deep brain stimulation (DBS) across diverse populations and study designs, our meta-analysis identifies trends, quantifies effect sizes, and addresses inconsistencies in the literature. This approach enables us to provide robust, evidence-based insights to guide clinicians in optimizing the use of DBS for the effective management of movement disorders. The primary importance of this study is to conduct a meta-analysis of randomized controlled trials (RCTs) on DBS for movement disorders, with a specific focus on PD. While previous reviews have largely concentrated on specific aspects such as motor symptoms, dyskinesias, and quality of life, this meta-analysis broadens the scope by including a more extensive set of outcomes. These include the clinical effects of DBS on tremor, gait, Unified Parkinson's Disease Rating Scale (UPDRS) scores, and tic scales. Additionally, this review examines advancements in DBS technology, its indications, and its applications in the management of movement disorders as an effective alternative to medical therapy and lesioning surgeries. It also evaluates the efficacy, safety, and potential risks associated with DBS therapy, offering a comprehensive perspective on its role in improving patient outcomes.

Methods

According to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist and the Cochrane Handbook for Systematic Reviews of Interventions, this study was conducted[16,17].

Search strategy

Three databases (PubMed, Cochrane Library, and Science Direct) were searched using the following terms: ("deep brain stimulation" [MeSH Terms] OR "deep brain stimulation "[Text Word] AND "movement disorders" [MeSH Terms] OR "movement disorders"[Text Word]). The search was limited to studies published in the English language without any restrictions on time.

Data selection and screening

We included peer-reviewed research articles, clinical trials (both randomized and non-randomized), observational studies, focusing on clinical outcomes, complications, and efficacy of DBS in the treatment of movement disorders. The search encompassed studies published in English between 2000 and the present date.

Exclusion criteria comprised studies not directly related to DBS and its clinical outcomes, systematic reviews, meta-analyses, commentaries, and editorial articles, as well as studies conducted solely on animal subjects or lacking sufficient data to evaluate DBS efficacy or clinical outcomes. Additionally, we excluded studies published before 2000 or in languages other than English, and those with sample sizes smaller than ten.

Further exclusions encompassed case reports, case series, conference abstracts, and editorial articles, as well as studies displaying obvious bias or inadequate data. These criteria were

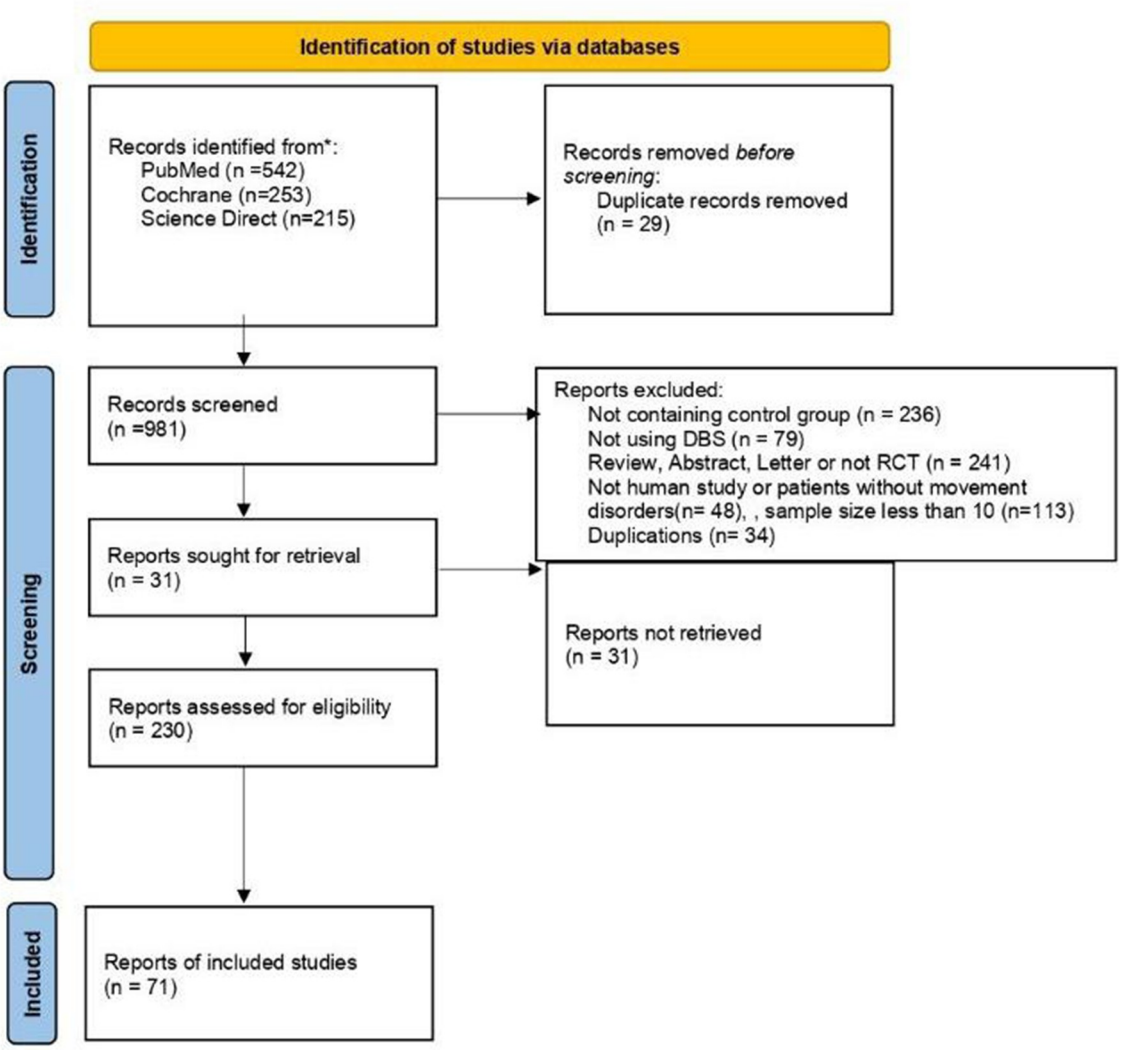

Figure 1. Flow diagram of included studies.

meticulously applied to ensure the selection of studies meeting the specified research focus and quality standards.

Screening was done through two steps: title/abstract screening and then full-text screening. Screening was done by two investigators, and the disagreements between them were resolved by a third one, as illustrated in Fig. 1. The summary of characteristics of included studies is illustrated in Table 1.

Data extraction

The data extraction step was done by two independent authors, and any disagreement was resolved by a third one. Relevant data extracted included study characteristics (author, year of publication, study design, countries, duration, places, sample size), participant demographics (age, sex, type of movement disorder, used medications, and disease duration), and outcomes (UPDRS III, Hoehn & Yahr, tremor severity, tremor, gait velocity, and Yale Global Tic Severity Scale [YGTSS]).

Risk of bias assessment

The quality of the data was assessed by two independent authors using risk of bias in non-randomized studies (of interventions) tool[18] for non-randomized studies and Cochrane Risk of Bias Tool 2 (RoB 2)[19] for randomized studies.

ROBINS-l tool consists of seven domains which are confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes, and selection of the reported result.

The risk of bias for each domain in this tool is rated as low, moderate, serious, critical, or no information but the RoB 2 tool consists of five domains which are randomization process, deviations from intended interventions, missing outcome data, measurement of outcomes, and selection of the reported result. The risk of bias for each domain in this tool is rated from low to high and any disagreement was resolved by a third author.

Table 1

Summary of characteristics of included studies

Study ID	Year of publication	Study design	Countries	Duration	Sample size	Age (y)	Type of movement disorders	Deep brain stimulation treatment	UPDRS III
Herzog *et al*	2006	Randomized controlled trial	Germany		11	57.7 ± 10.9	Parkinson's disease	STN-DBS	16.5 ± 9.8 44.4 ± 9.6
Hilker *et al*	2008	Randomized controlled trial	Germany	6 months	12 10	65 ± 8 67 ± 4	Parkinson's disease	STN-DBS	22 ± 8 46 ± 11
Hyam *et al*	2015	Randomized controlled trial	UK	3 years	13	68 (48–79)	Essential tremors	Thalamic or zona incerta stimulation	
Israeli-Korn *et al*	2013	Randomized controlled trial	Israel	At least 3 months	12	61.8 ± 7.7 61.8 ± 7.7	Parkinson's disease	Bilateral STN-DBS	
Jech *et al*	2012	Randomized controlled trial	Czech	1 month	12	55.9 ± 6.8	Parkinson's disease	STN-DBS	15.8 ± 4.8 35.8 ± 7.0
Jech *et al*	2006	Randomized controlled trial	Czech		12	57.3 ± 6.3	Parkinson's disease	STN-DBS	23.3 ± 12 43.8 ± 15
Johansson *et al*	2014	Nonrandomized study	Sweden	1 year	10	60.4 ± 8.7	Parkinson's disease	STN-DBS	
Johnsen *et al*	2009	Nonrandomized study	Denmark	12 hours	12 12	60.1 ± 8.1	Parkinson's disease	STN-DBS	16.8 ± 8 37.6 ± 13.1
Jones *et al*	2010	Randomized controlled trial	USA	6 hours	12	61.3 ± 2.39	Parkinson's disease	STN or GPi DBS	
Karimi *et al*	2008	Randomized controlled trial	USA	1 year	31	61 ± 10	Parkinson's disease	STN-DBS	19.6 ± 9.1 42.1 ± 13.7
Kefalopoulou *et al*	2015	Randomized crossover trial	UK	3 months	15	34·7 ± 10	Tourette's syndrome	GPi DBS	
Koller *et al*	1999	Randomized controlled trial	USA	1 year	20	72.3 ± 5.5	Essential head tremor	Unilateral DBS of the VIM nucleus of the thalamus	
Kronenbuerger *et al*	2009	Randomized controlled trial	Germany		12 25	64.2 (10.6) 46.3 (21.1)	Essential tremor	DBS	
Kupsch *et al*	2006	Randomized controlled trial	Germany	6 months	20 20	40.5 ± 13.5 38.4 ± 13.8	Generalized or segmental dystonia	GPi DBS	
Jeune *et al*	2010	Randomized controlled trial	France	3 months	20 13	57.9 (±9.7) 53.23 (±11.2)	Parkinson's disease	STN DBS	
Lee *et al*	2013	Randomized controlled trial	USA		12	68 ± 7.5	Parkinson's disease	STN-DBS	35.7 ± 5.1 48.2 ± 6.5
Li *et al*	2017	Randomized controlled trial	China	3 months	32 32	55.47 ± 9.13 56.88 ± 9.89	Parkinson's disease	STN-DBS	–26.03 ± 14.02 (change from baseline) –4.44 ± 10.44 (change from baseline)
				1 year	61				18.07 ± 9.04 40.87 ± 15.40
Lilleeng *et al*	2014	Randomized controlled trial	Norway	9 years	12 12	61 (8.0) 61 (8.3)	Parkinson's disease	STN-DBS	17 (6.4) 16 (8.4)
Liu *et al*	2013	Randomized controlled trial	China	2 years	40	56.32 (7.96)	Parkinson's disease	STN-DBS	4.8 ± 7.3 12.1 ± 10.9
Liu *et al*	2005	Randomized controlled trial	USA		11	53.7 (41–66)	Parkinson's disease	STN-DBS	

(*Continued*)

Table 1

(Continued)

Study ID	Year of publication	Study design	Countries	Duration	Sample size	Age (y)	Type of movement disorders	Deep brain stimulation treatment	UPDRS III
Lizarraga *et al*	2016	Randomized controlled trial	USA	12 hours	22	65 (±9.6)	Parkinson's disease	STN-DBS	24.09 ± 2.76 48.68 ± 3.41
Agostino *et al*	2008	Randomized controlled trial	Italy	12 hours	14	62.4 ± 7	Parkinson's disease	Unilateral STN-DBS	19.7 ± 5.8 33.9 ± 9.32
Lubik *et al*	2006	Randomized controlled trial	Germany	22.5 months	12	62.25 (7.72)	Parkinson's disease	STN-DBS	32 ± 5 58 ± 12.5
Maciunas *et al*	2007	Randomized controlled trial	Ohio	3 months	5 5	28.2 (18–34) 27.4 (18–39)	Tourette syndrome	Bilateral implantation of DBS	
Marques *et al*	2013	Randomized controlled trial	USA		19	62.3 ± 5.7	Parkinson's disease	STN-DBS	14.6 ± 8.4 28.2 ± 11.0
McDonald *et al*	2012	Randomized controlled trial	UK		23 11	55.9 (6.3) 60.5 (6.1)	Parkinson's disease	STN-DBS	
Mercado *et al*	2006	Randomized controlled trial	Canada	12 hours	10	61 (42–78)	Parkinson's disease	STN-DBS	34.5 ± 13.2 47.6 ± 12.2
Michmizos *et al*	2015	Randomized controlled trial	Greece		20		Parkinson's disease	STN-DBS	25.6 ± 10.8 44.7 ± 15.1
Mikos *et al*	2009	Randomized controlled trial	USA	20 months	24 19	61.7 (4.9) 64.7 (6.6)	Parkinson's disease	STN or GPi DBS	22.1 (8.1) 42.8 (11.3) 31.2 (8.3)
Mondillon	2012	Randomized controlled trial	France		14	60.6 ± 1.6	Parkinson's disease	STN-DBS	14.75 ± 6.4 32.64 ± 11.8
Moreau *et al*	2010	Randomized controlled trial	France		11	69 median	Parkinson's disease	STN-DBS	28 ± 21.2 42.7 ± 15.3
Moro *et al*	2010	Randomized controlled trial	Canada	6 years	35 16	59.3 (1.6) 56.0 (2.1)	Parkinson's disease	STN-DBS GPi-DBS	30.1 (2.5) 52.7 (3.2) 32.6 (4.6) 43.9 (4.6)
Müller-Vahl *et al*	2021	Randomized controlled trial	Poland, Germany, USA	3 months	10	29.4 ± 10.2	Gilles de la Tourette syndrome (GTS)	pvi GPi stimulation pvi thalamic stimulation Sham stimulation	
Capecci *et al*	2005	Nonequivalent controlled study		24 months	13 PD	58.1 (6.8) years	Parkinson's disease	Chronic STN stimulation	(UPDRS at 24 months) 18.0 (4.7)
Cappon *et al*	2019	Double-blind, crossover, sham stimulation-controlled design	UK	3 months	11	Mean age = 34.3	Severe Tourette syndrome	Anteromedial GPi	
Castrioto *et al*	2011		USA		22	58 (8)	Parkinson's disease	Bilateral subthalamic nucleus (STN)	41.6 (13.9)
Nilsson	2005		Sweden	5 y	31	65 (50–77) (median and range)	Parkinson's disease	STN-DBS	(20.5 [17.4–35.1]) 12 months (median and first and third quartile)
Chang *et al*	2012	Controlled study	China	13 months postoperation	62	58.32 (4.18)	Parkinson's disease	STN-DBS	12.97 (4.79)

(*Continued*)

Table 1

(Continued)

Study ID	Year of publication	Study design	Countries	Duration	Sample size	Age (y)	Type of movement disorders	Deep brain stimulation treatment	UPDRS III
Charles *et al*	2014	Prospective, randomized, parallel-group, single-blind clinical trial		24 months	30	60 ± 6.8	Parkinson's disease	Bilateral STN-DBS	Mean difference 8.2 (2.5–13.9)
Okun	2012	Randomized controlled trial	USA	5y	101	60·6 (8·3)	Parkinson's disease	STN-DBS	MED-ON:15·1 (8·2)
Pedrosa	2014		Germany		14	62.29 (14.29)	Essential Tremor	Thalamic-DBS	
Visser	2008	Clinical trial	Netherlands	Not found	14 PD	50.28.3	Parkinson's disease	Bilateral STN stimulation	UPDRS: Motor score 51.4 ± 10.5////UPDRS: PIGDa 5.1±2.9
Dellapina *et al*	2012	Randomized, controlled, cross-over trial	France	6-month	16 patients (8 with pain and 8 without pain)	61.8 ± 7.6	Parkinson's disease	STN-DBS	13.1 ± 2.9
Deuschl *et al*	2006	Unblinded trial with a randomized-pairs design	Germany and Austria	6-month	156	60.5 ± 7.4	Parkinson's disease	Subthalamic nucleus	28.3 ± 14.7 at 6 month
Frank *et al*	2022		Germany			67 (60.8–71.2)	Parkinson's disease	STN-DBS	(On medication and on stimulation where applicable) 21 (15–31.5)
Gruber *et al*	2018	Prospective randomized double-blind, sham stimulation-controlled multicenter trial	Germany	3 months	25	62.0 ± 11.1	Dystonia	Pallidal neurostimulation	
Mügge *et al*	2023	Randomized controlled trial	Germany		23	57 (7.27)	Parkinson's disease	STN DBS	14.95 (9.55)
Welter *et al*	2017	Randomized, double-blind, controlled trial	France	3 month	16	12	Tourette's syndrome		
Volkmann *et al*	2014	Randomized controlled trial	Austria, Germany	3 months	32	57·1 (9·82)	Cervical dystonia	Pallidal neurostimulation	
Williams *et al*	2010	Randomized, open-label trial	UK	1 year	183 per group	59 (37–79)	Parkinson's disease	Subthalamic nucleus	UPDRS part III: motor (off medication) 47·6 (14·0)
Rocchi *et al*	2012	Randomized controlled trial	USA	6 months	15	61.4 ± 5.5	Parkinson disease	STN-DBS	51.1 ± 20.9
Vrancken *et al*	2005	Randomized controlled trial	Switzerland		14	50.3 ± 8.3	Parkinson's disease	STN-DBS	30.9 ± 8.1
Daniels *et al*	2011	Randomized controlled trial	Germany	6 months	61	59.7 (7.2)	Parkinson's disease	STN-DBS	18.8 (9.2)
Waldthaler *et al*	2023	Randomized controlled trial	Germany	3 months	19	57.0 (8.8)	Parkinson's disease	STN-DBS	38.9 (9.9)
Wojtecki *et al*	2011	A double blind, randomized	Germany		12	Mean age 64 years, SD 8	Parkinson's disease	STN-DBS	
Wang *et al*	2023	Randomized controlled trial	China	6 months	20	60 ± 9	Parkinson's disease	STN-DBS	28 ± 12 39 ± 16
Saatçi *et al*			Turkey	3 months	39	61.05 ± 9.9	Parkinson's disease	STN-DBS	11.1 ± 5.1
York *et al*	2008		USA	6 months	23	59.5 (11.8)			UPDRS total 49.5 (18.6)
Zangaglia *et al*	2009	Randomized controlled trial	Italy	3 months	32	58.84 6 7.70	Parkinson's disease	STN-DBS	29.3 (9.8)
Armen Sáez-Zea *et al*	2012	Non-randomized controlled study		6 months	9	54 (14)	Parkinson's disease	STN-DBS	43 (15)
Schüpbach *et al*	2007	A randomized, controlled trial	USA	18 months	10	48.4 ± 3.3	Parkinson's disease	STN-DBS	ON-MED:2.9 (3.0)/OFF-MED:32.7 (13.4)
Seger *et al*	2021	A randomized, controlled trial	Germany	1.5 year	20	63.1 ± 1.5	Parkinson's disease	STN-DBS	36.1 ± 4.6 (5–57)
St George *et al*	2014	A randomized, controlled trial	USA	6M	14	61.2 (69.3)	Parkinson's disease	GPI-DBS	
Tripoliti *et al*	2008	A randomized, controlled trial	UK		14	60 (6.5)	Parkinson's disease	STN-DBS	
Welter *et al*	2017	A randomized, controlled trial	France	5 years	7	30·8 (11·8)	Tourette's syndrome	GPI-DBS	
Williams *et al*	2010	A randomized, controlled trial	UK	6 years	183	59 (37–79)	Parkinson's disease	STN-DBS/GPI-DBS N:4	ON-MED: 16·0 (8·8)/OFF-MED:30·6 (15·2)

Statistical analysis

We conducted the analysis using RevMan 2.0 by analyzing the pooled mean difference between the STN DBS ON group and the STN DBS OFF group with a 95% confidence interval (CI). The results were considered to be statistically significant between the two groups if the Chi-square *P*-value was lower than 0.05[17].

The heterogeneity was assessed using chi-square and I-square. The heterogeneity was considered to be significant if the *P*-value was lower than 0.1 or the *I*2 more than 50%[17]. In addition, we used fixed-effect model in case of insignificant heterogeneity, otherwise, we used random-effect model.

The significant heterogeneity was handled by: (a) shifting to random-effect model[20]. (b) Conducting leave-one-out analysis[21], it works by leaving the study or studies that have caused this significant heterogeneity till the insignificant heterogeneity is achieved. (c) Doing publication bias if the number of studies was more than nine using funnel plot[22], so we could visually assess if there was a publication bias or not.

Results

UPDRS Part II:

The UPDRS Part III, evaluating motor symptoms in PD, showed significant improvement with an MD of −18.05 (95% CI [−20.17, −15.93]), $P < 0.00001$. This finding is based on data from 40 studies including 1200 participants, indicating that DBS substantially improves motor function. The heterogeneity was high ($I^2 = 88\%$), as illustrated in Fig. 2.

Hoehn and yahr stage:

Analysis of the Hoehn and Yahr Stage, which classifies the severity of PD, revealed a significant improvement with an MD

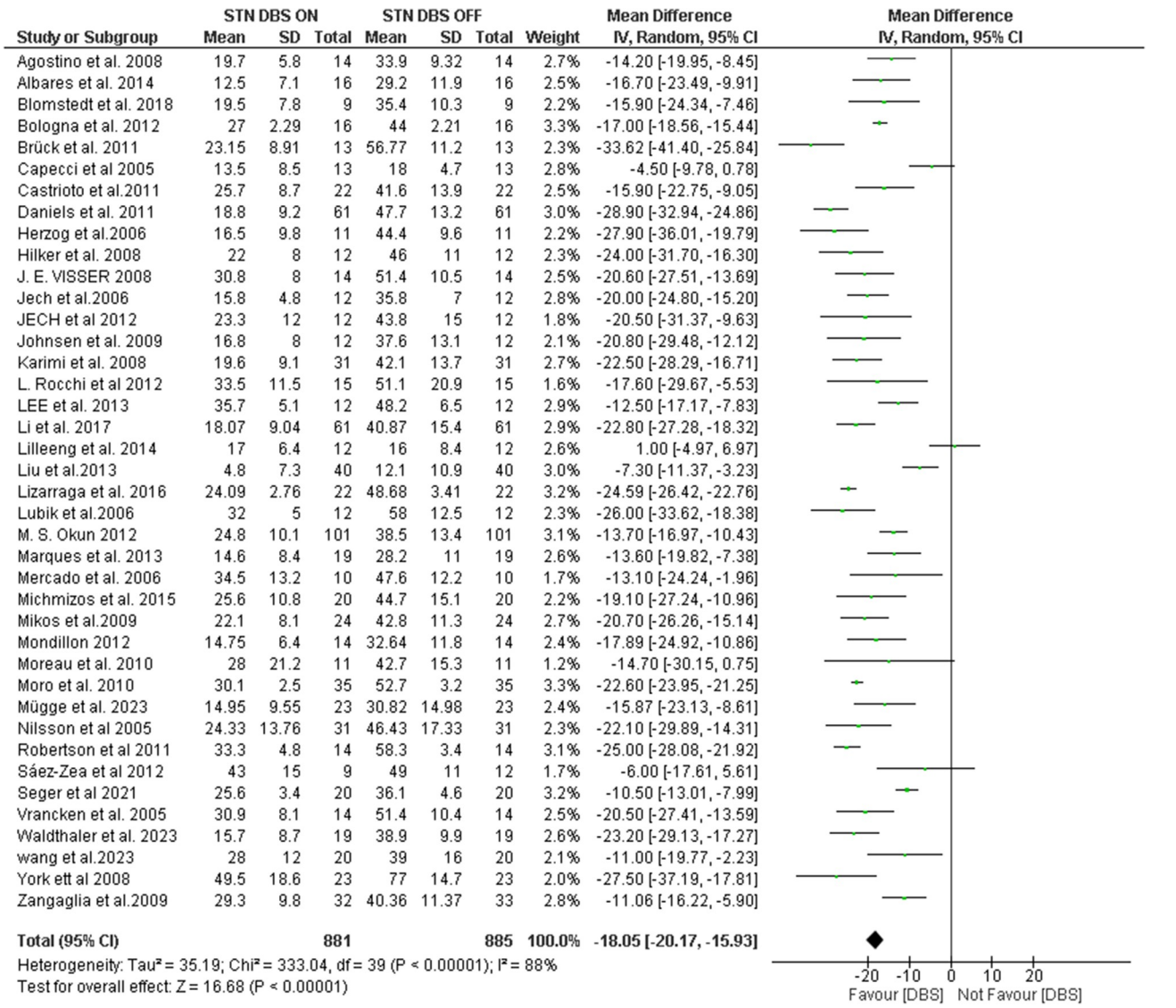

Figure 2. Analysis of mean difference of Unified Parkinson's Disease Rating Scale (UPDRS) Part III between DBS-ON and DBS-OFF.

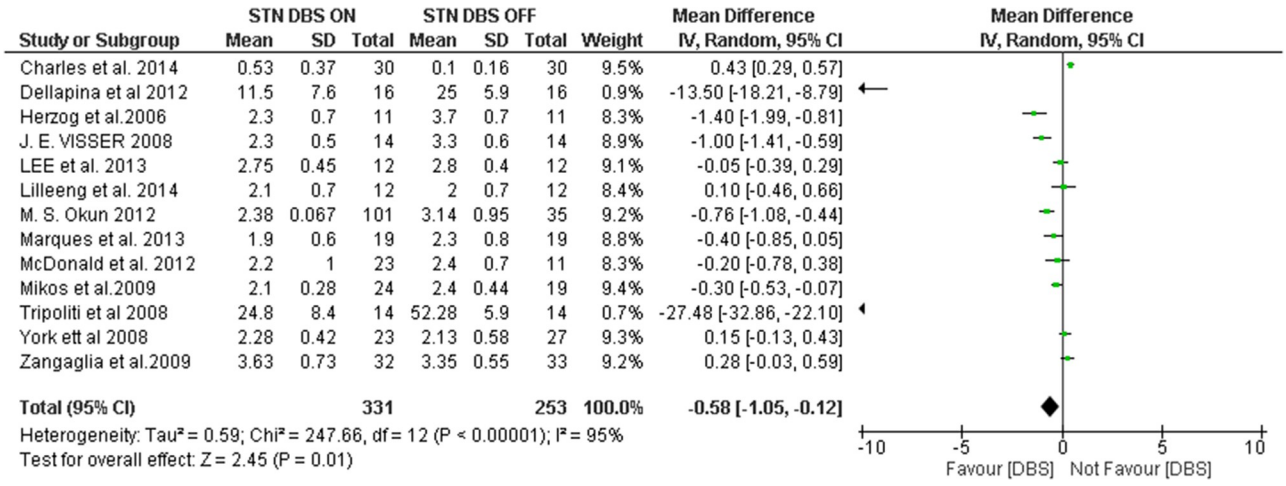

Figure 3. Analysis of mean difference of Hoehn and Yahr Stage between DBS-ON and DBS-OFF.

of –0.58 (95% CI [–1.05, –0.12]), P = 0.01. Derived from 13 studies, this result signifies that DBS is effective in reducing disease severity. Heterogeneity was high ($I2$ = 95%), indicating variability among study finding, as illustrated in Fig. 3.

Tremor severity

For tremor severity, assessing the intensity of tremor in patients, the meta-analysis found a significant reduction with an MD of –8.22 (95% CI [–12.30, –4.15]), P < 0.0001. This outcome, informed by four studies, highlights DBS's efficacy in alleviating tremor. There was high heterogeneity ($I2$ = 87%), as illustrated in Fig. 4.

Tremor

Analysis of overall Tremor, evaluating the presence and impact of tremor, showed a significant decrease with an MD of –2.68 (95% CI [–4.59, –0.77]), P = 0.006. This result, based on three studies, confirms the effectiveness of DBS in tremor management. The heterogeneity was low ($I2$ = 78%), indicating similar outcomes across different studies as illustrated in Fig. 5.

Gait velocity

The impact on gait velocity, a measure of mobility, demonstrated significant improvement with an MD of 0.13 (95% CI [0.08, 0.18]), P < 0.00001. Based on four studies, this outcome suggests that DBS enhances walking speed in individuals with movement disorders. Heterogeneity was insignificant ($I2$ = 10%), as illustrated in Fig. 6.

YGTSS Score

The analysis of YGTSS Score, indicating the severity of tics, revealed a significant reduction with an MD of –9.75 (95% CI [–14.55, –4.96]), P < 0.0001. This finding from four studies, shows that DBS is beneficial in reducing tic severity. The heterogeneity was moderate ($I2$ = 61%), suggesting variability that warrants further investigation, as illustrated in Fig. 7.

Publication bias

Visual inspection of funnel plots reveals a symmetry indicating potential publication bias, as illustrated in Figs. 8 and 9.

Discussion

DBS has emerged as a highly effective therapeutic option for patients with PD and other movement disorders, offering remarkable benefits across a spectrum of neurologic conditions[23]. PD, characterized by progressive neurodegeneration and a complex array of motor and nonmotor symptoms, presents significant challenges in management. Our meta-analysis, encompassing

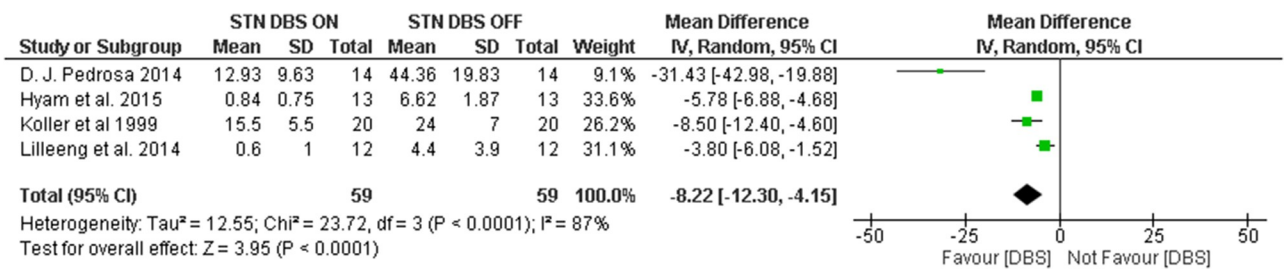

Figure 4. Analysis of mean difference of tremor severity between DBS-ON and DBS-OFF.

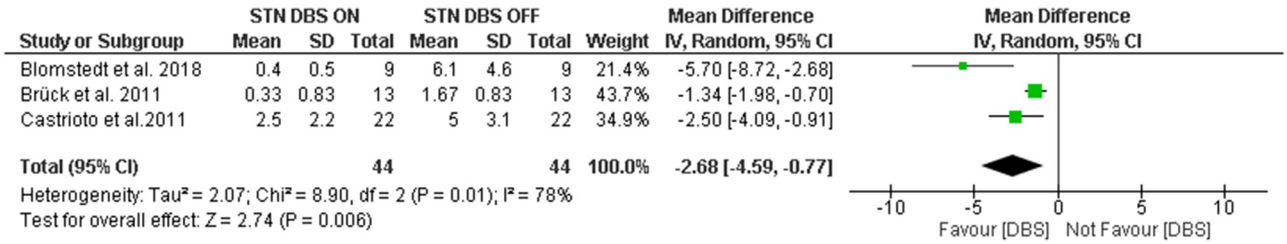

Figure 5. Analysis of mean difference of tremor between DBS-ON and DBS-OFF.

data from numerous studies, reaffirms the efficacy of DBS in improving motor function and disease severity in PD patients.

Over the past decade, DBS has transformed into a standard treatment modality for advanced PD, substantially enhancing motor function and overall quality of life for affected individuals.[24] By directly modulating pathological brain activity, DBS offers tailored and adjustable stimulation, effectively addressing symptoms in both neurological and psychiatric disorders linked to dysfunctional circuitry[25]. Notably, DBS targeting specific brain regions such as the ventral intermediate nucleus (VIM) of the thalamus, subthalamic nucleus (STN), or internal segment of the globus pallidus has demonstrated profound therapeutic effects, ranging from tremor relief to improvements in bradykinesia, rigidity, and gait disturbances[26]. The multifaceted mechanisms underlying DBS, including local and network-wide neuromodulatory effects, synaptic plasticity, and potential neuroprotective properties, underscore its versatility in addressing varied clinical presentations[27].

The observed improvements in motor symptoms, as indicated by reductions in UPDRS Part III scores, and disease severity, as reflected by changes in Hoehn and Yahr Stage ratings, highlight the therapeutic efficacy of DBS in ameliorating motor dysfunction and slowing disease progression in PD patients. Furthermore, our meta-analysis revealed a significant decrease in tremor severity and overall tremor presence following DBS treatment, underscoring its effectiveness in managing tremor symptoms, which often pose significant challenges for individuals with PD.

Despite the notable clinical success of DBS, the precise therapeutic mechanisms underlying its effects remain a subject of ongoing debate[28]. In light of this, patient safety remains paramount in neuromodulation interventions, with efforts focused on developing full-body MRI-safe systems to address concerns about potential heating of DBS systems during scans, ideally without the need for extension cables. Additionally, infection prevention strategies are crucial, given current infection rates ranging from 5% to 10%. Approaches such as utilizing antibacterial envelopes, proven effective in cardiac implantable devices, could be adapted for neurostimulation systems to mitigate infection risks. Moreover, vigilance regarding acute hardware failure is essential to prevent symptom rebound or severe events, such as neuroleptic-like malignant syndrome. Newer implantable pulse generators with improved battery capacity readouts offer potential for preemptive battery replacement, while future considerations may include implementing error-detecting servomechanisms[13]. Fig. 11 reflects the techincal surgical aspects that surgeons interest during DBS for movement disorders.

The improvement in gait velocity and reduction in tic severity further demonstrate the broad spectrum of benefits offered by DBS beyond motor symptoms, encompassing mobility enhancement and tic reduction in individuals with movement disorders.

DBS has shown promise in reducing tics associated with TS. Studies have explored different DBS targets, such as the thalamic centromedian parafascicular complex[29], STN[29], and anteromedial globus pallidus interna (amGPi)[30]. DBS has been found to modulate synaptic and tonic dopamine activity in the striatum, leading to a reduction in motor tic behavior[31]. Additionally, DBS treatment targeting the STN has shown significant improvements in tic severity and comorbid psychiatric symptoms in patients with TS[32]. Furthermore, amGPi-targeted DBS has demonstrated a decrease in tics, improvement in quality of life, and resolution of non-tic-related symptoms in refractory TS cases. These findings collectively support the efficacy of DBS in alleviating tics and associated symptoms in TS patients[33,34].

Accurately pinpointing the optimal stimulation location in the brain is crucial for enhancing the efficacy of DBS in PD. A recent study employed an individualized modeling technique, independent of standard brain atlases, to identify the most effective stimulation sites near the dorsomedial region of the STN. The

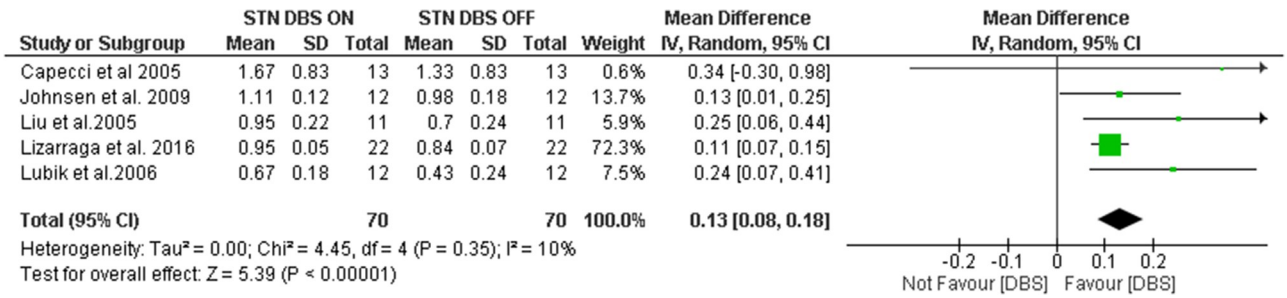

Figure 6. Analysis of mean difference of gait velocity between DBS-ON and DBS-OFF.

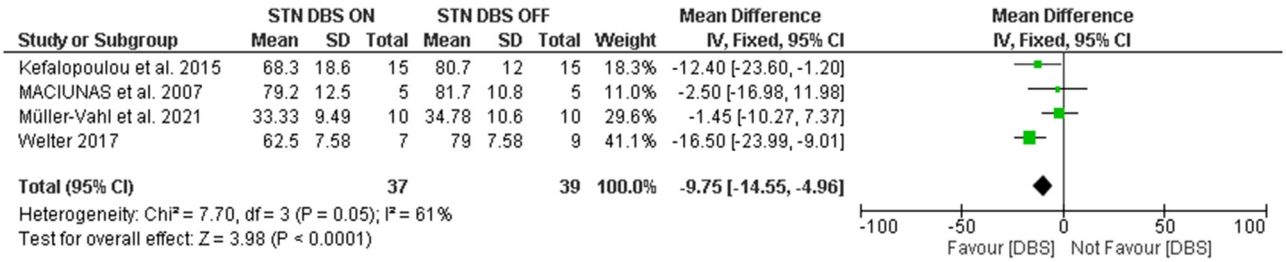

Figure 7. Analysis of mean difference of Yale Global Tic Severity Scale (YGTSS) Score between DBS-ON and DBS-OFF.

consistent improvement in motor symptoms across patients suggests the potential significance of targeting the caudal zona incerta in DBS therapy. This personalized modeling approach offers promise for tailoring DBS strategies to individual patients, not only in PD but also in other conditions like essential tremor and depression, facilitating improved clinical outcomes and minimizing side effects[35].

Furthermore, the observed improvement in plantar tactile cutaneous perception following STN-DBS highlights the potential of targeting sensory pathways alongside traditional motor-focused interventions. This suggests a promising avenue for developing novel therapy strategies aimed at enhancing sensory perception to augment motor performance and overall quality of life in PD patients[36].

While DBS effectively treats dopa-responsive motor symptoms and dyskinesia in the long term, it is important to acknowledge potential drawbacks. Some non-motor symptoms like pain may also improve with DBS, but it can lead to decreased verbal fluency, psychosocial issues, and may not alleviate postural instability, freezing of gait, or cognitive problems. In some cases, particularly among patients with preexisting intellectual impairment or over 70 years old, DBS may increase the risk of falls and impulsivity, with higher depression rates compared to other treatments. Therefore, thorough preoperative evaluation, including assessment of non-motor and psychiatric symptoms, is essential to optimize patient selection and minimize adverse effects. Additionally, in dystonia patients, pallidal stimulation can cause adverse effects such as bradykinesia and gait disturbance, while STN stimulation may induce dyskinesia without significant cognitive effects[37].

While DBS has expanded its scope to include other movement disorders like essential tremor and dystonia, PD remains its predominant indication. Despite potential risks, DBS stands as a valuable therapeutic avenue for patients grappling with PD, dystonia, and tremor, offering significant enhancements in motor function and quality of life. Nevertheless, ongoing research

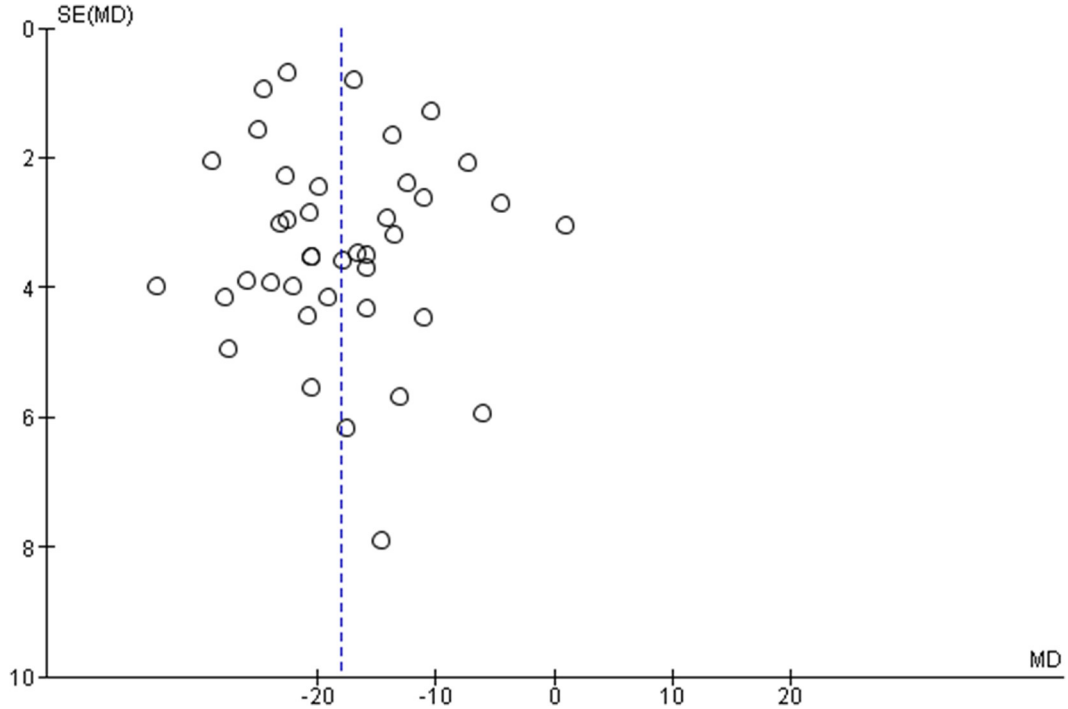

Figure 8. The publication bias for Unified Parkinson's Disease Rating Scale (UPDRS) Part III.

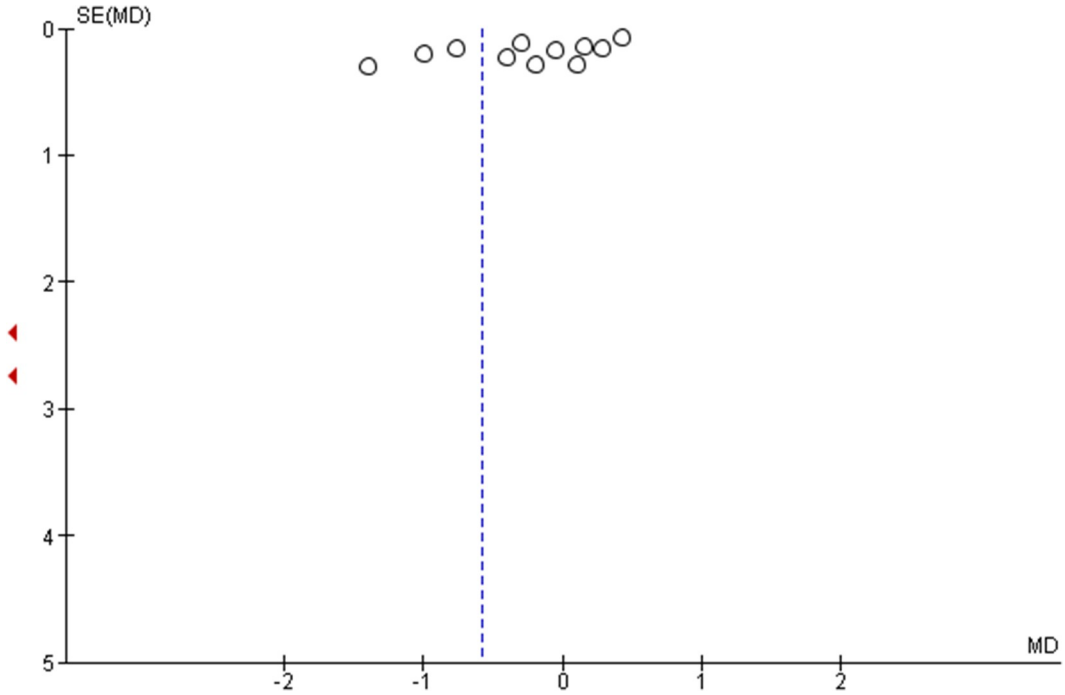

Figure 9. The publication bias for Hoehn and Yahr stage.

endeavors are imperative to unravel the precise mechanisms underlying DBS efficacy, refine patient selection criteria, and mitigate associated procedural complications.

DBS approaches and planes for movement disorders management

DBS has emerged as a promising treatment option for various neurological and neuropsychiatric disorders, including dystonia, PD, tremors, and Tourette's syndrome.

Parkinson's disease

DBS is an established treatment for PD, particularly for patients who have not responded well to medication or are experiencing disabling side effects[38]. The procedure typically targets the STN or the globus pallidus internus (GPi), two key regions involved in the motor symptoms of Parkinson's. DBS has been shown to significantly improve motor function, reduce tremor, and decrease the need for dopaminergic medications in Parkinson's patients. The long-term benefits of DBS for Parkinson's appear to be more durable compared to other movement disorders[37].

Essential tremor

DBS is also FDA approved for the treatment of essential tremor. The procedure involves implanting an electrode into the VIM of the thalamus. DBS can effectively reduce tremor severity and improve quality of life in patients with essential tremor[37].

Tourette's syndrome

DBS has also been explored as a treatment option for severe, treatment-refractory Tourette's syndrome. The targets for DBS in Tourette's have included the centromedian-parafascicular complex of the thalamus, the GPi, and the anterior limb of the internal capsule. While the results have been mixed, with an average response of around 40% improvement in tic severity, DBS has shown promise in reducing both motor and vocal tics in carefully selected patients with severe, disabling Tourette's symptoms that have not responded to other therapies.[38–40]

Dystonia

DBS has been approved for the treatment of dystonia, particularly primary or hereditary forms of the condition. The procedure involves implanting electrodes in the GPi, a specific region of the brain that is malfunctioning in dystonia patients[41]. The electrical stimulation from the implanted device helps to modulate the abnormal brain activity and reduce the severity of dystonic movements and postures. Studies have shown that patients with genetic dystonia can experience an 80%–99% improvement in their symptoms following DBS treatment. Patients with cervical dystonia (torticollis) often see a 40%–60% improvement in their neck movements and posture, though the response can vary. DBS has also been used to treat tardive dyskinesia, a movement disorder caused by certain medications, with up to 80% improvement in symptoms. However, the response to DBS in secondary dystonia associated with conditions like cerebral palsy is typically more limited, with only 0%–20% improvement[41].

It is important to note that the precise mechanisms by which DBS exerts its therapeutic effects in these different disorders are not yet fully understood. Ongoing research and larger, controlled studies are still needed to further elucidate the optimal targets and stimulation parameters for DBS in each condition, as well as to better define the patient selection criteria to ensure the best outcomes. In summary, DBS has demonstrated efficacy in

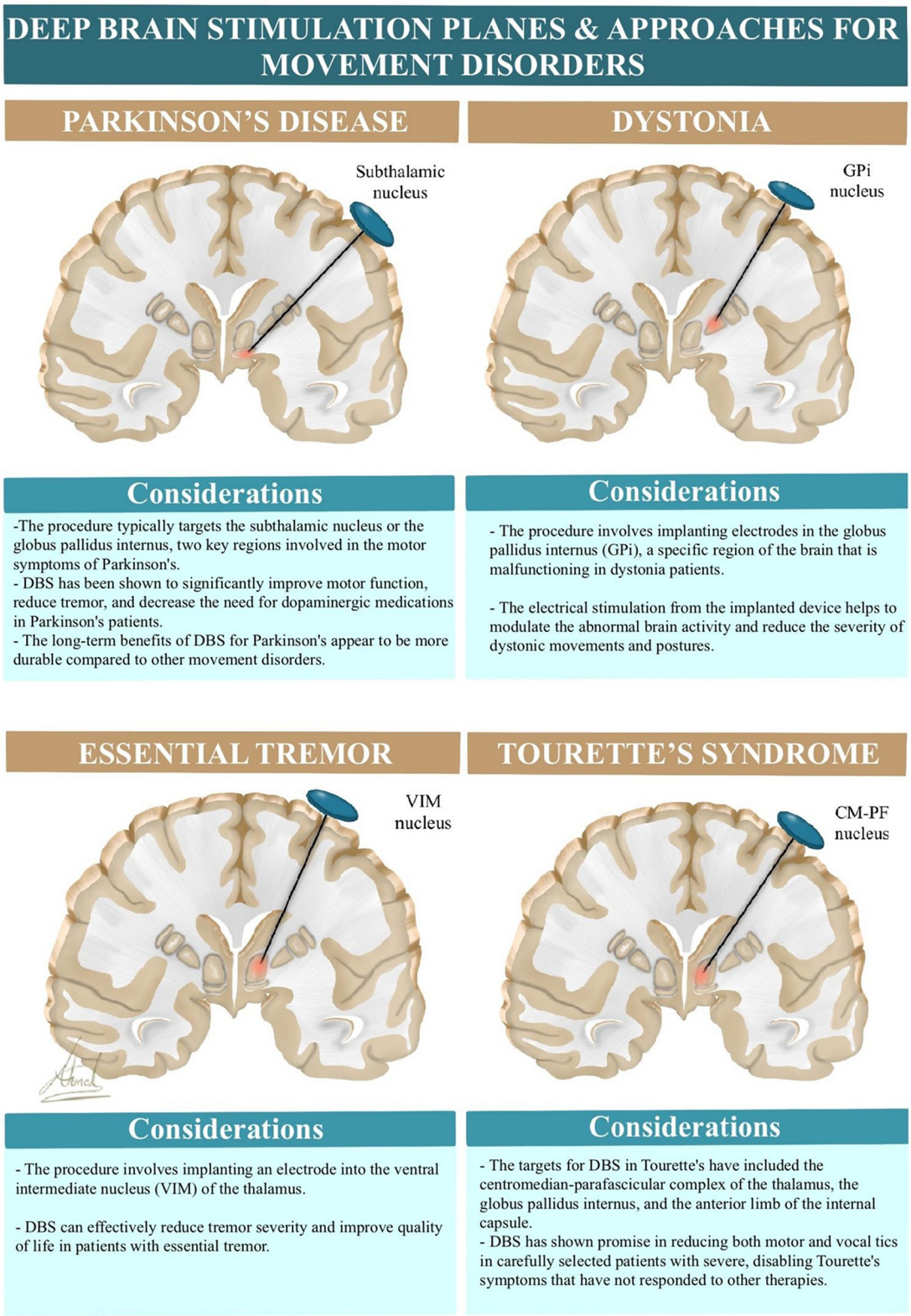

Figure 10. This figure reflects the approaches, planes, and considerations involved in deep brain stimulation (DBS) for movement disorders. The top-left section provides an anatomical illustration of target nucleus of parkinsons disease. The illustration shows the approaches and planes relative to the brain tissue, to illustrate the target nucleus . The top-right section provides an anatomical illustration of target nucleus of dystonia. The illustration shows the approaches and planes relative to the brain tissue, to illustrate the target nucleus . The bottom left section provides an anatomical illustration of target nucleus of essential tremor. The illustration shows the approaches and planes relative to the brain tissue, to illustrate the target nucleus. The bottom-right section provides an anatomical illustration of target nucleus of Tourette's syndrome. The illustration shows the approaches and planes relative to the brain tissue, to illustrate the target nucleus.

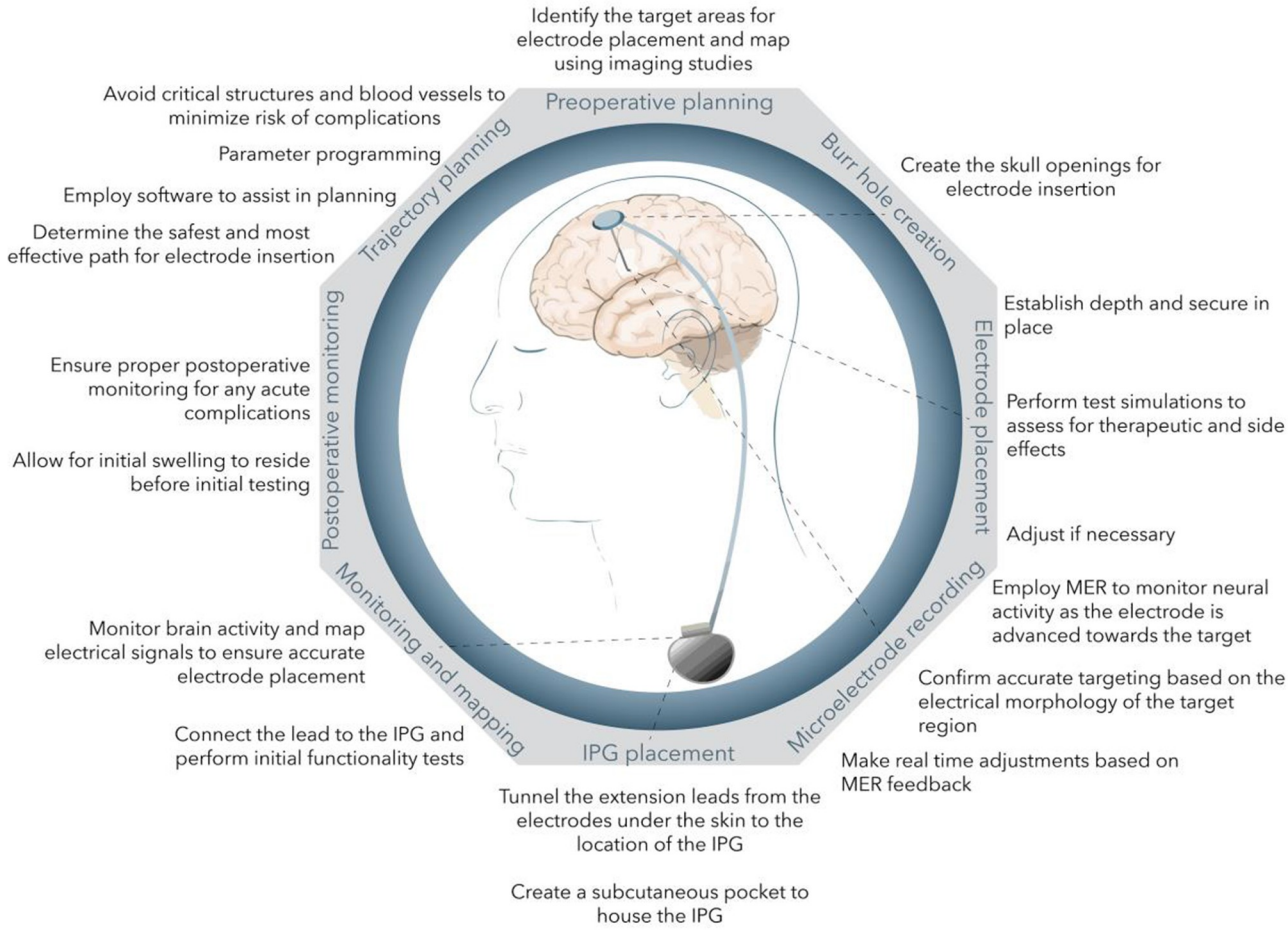

Figure 11. The techincal surgical aspects that surgeons interest during deep brain stimulation for movement disorders (Fig. 11). This figure illustrates the procedural steps involved in deep brain stimulation (DBS), from preoperative planning and trajectory optimization to electrode placement, intraoperative microelectrode recording (MER), and postoperative monitoring. It highlights key stages such as burr hole creation, mapping of neural activity, and placement of the implanted pulse generator (IPG), providing a general overview of the DBS surgical workflow. DBS, deep brain stimulation; MER, microelectrode recording; IPG, implanted pulse generator.

the treatment of dystonia, PD, and select cases of severe, treatment-refractory Tourette's syndrome. The specific brain targets and the degree of clinical improvement can vary across these different neurological and neuropsychiatric disorders, highlighting the need for a tailored, patient-specific approach to DBS therapy[42].

Comparison and efficacy

While DBS has been shown to be effective in all three conditions, the specific targets and approaches differ. In dystonia, DBS of the GPi is often used, whereas in PD, DBS of the STN is more common. In TS, DBS of the ventromedial thalamus and GPi have been used. The efficacy of DBS in these conditions is generally high, with significant improvements in motor function and symptom reduction reported in most studies. For example, in dystonia, DBS of the GPi has been shown to result in a 50% reduction in dystonic symptoms in 80% of patients. In PD, DBS of the STN has been shown to result in a significant improvement in motor function and a reduction in motor symptoms in patients, with a mean improvement of 60% in motor function. In TS, DBS of the ventromedial thalamus has been shown to result in a significant reduction in tic severity, with a mean improvement of 58% in tic severity. Overall, DBS has emerged as a promising treatment approach for these conditions, offering significant improvements in motor function and symptom reduction. Fig. 10 reflects the approaches, planes, and considerations involved in DBS for movement disorders.

In summary, DBS has demonstrated efficacy in the treatment of dystonia, PD, and select cases of severe, treatment-refractory Tourette's syndrome. The specific brain targets and the degree of clinical improvement can vary across these different neurological and neuropsychiatric disorders, highlighting the need for a tailored, patient-specific approach to DBS therapy. Implanted device helps to modulate the abnormal brain activity and reduce the severity of dystonic movements and postures. Studies have shown that patients with genetic dystonia can experience an 80%–99% improvement in their symptoms following DBS treatment. Patients with cervical dystonia (torticollis) often see a 40%–60% improvement in their neck movements and posture, though the response can vary. DBS has also been used to treat tardive dyskinesia, a movement disorder caused by

Table 2

Surgical intervention for movement disorders[44]

Technique	Features	Indications
Deep brain stimulation	Reversible procedure Modifiable effects Intracranial surgery Microelectrode recording Stimulation mapping Permanent implant Pacemaker-like generator Overnight stay in hospital	Essential tremor Parkinson disease Dystonia
Stereotactic radiosurgery	Irreversible lesioning Incisionless surgery No microelectrode recording No stimulation mapping Risk of radiation-induced neurotoxicity	Essential tremor Parkinson disease Dystonia
Focused ultrasound	Irreversible lesioning "Incisionless surgery Stimulation mapping Outpatient procedure	Essential tremor Motor symptoms of Parkinson disease Tremor-dominant Parkinson disease
Radiofrequency Ablation	Irreversible lesioning Intracranial surgery Microelectrode recording Stimulation mapping Older technology	Essential tremor Parkinson disease Dystonia

certain medications, with up to 80% improvement in symptoms. However, the response to DBS in secondary dystonia associated with conditions like cerebral palsy is typically more limited, with only 0%–20% improvement. Also, Table 2 shows comparison of DBS with newer interventions such as focused ultrasound

Applications of DBS

DBS is a sophisticated neurosurgical procedure that involves implanting electrodes into specific regions of the brain to modulate neural activity. Originally developed as a treatment for movement disorders, its applications have expanded significantly, making it a versatile tool in modern neuromodulation therapies. One of the most well-established uses of DBS is in the management of movement disorders. In PD, DBS targets the STN or the GPi, effectively alleviating symptoms such as tremors, rigidity, and motor fluctuations. It is also used to treat essential tremor by stimulating the VIM of the thalamus, providing substantial relief from tremors. For patients with dystonia, GPi stimulation has been shown to reduce involuntary muscle contractions and abnormal postures, enhancing their quality of life[41].

Beyond movement disorders, DBS has found significant application in neuropsychiatric conditions and epilepsy[43]. For obsessive-compulsive disorder, electrodes implanted in areas like the anterior limb of the internal capsule or the nucleus accumbens (NAc) have shown promising results, particularly in treatment-resistant cases. Similarly, DBS of the subgenual cingulate cortex (Brodmann Area 25) has been explored for patients with treatment-resistant depression, with ongoing research into its effectiveness and mechanisms. In TS, DBS targeting the centromedian thalamic nuclei or the globus pallidus has demonstrated potential in reducing the severity of tics, offering hope to patients with severe, refractory symptoms.

Chronic pain is another area where DBS has made an impact. For patients suffering from refractory pain conditions, such as neuropathic pain or cluster headaches, DBS of the periaqueductal gray or sensory thalamic nuclei has been utilized with considerable success. Additionally, the anterior nucleus of the thalamus has been targeted in patients with drug-resistant epilepsy, where DBS has been shown to reduce seizure frequency and severity[44].

Emerging evidence suggests that DBS may also play a role in managing cognitive disorders. In Alzheimer's disease, for example, DBS of the fornix and hypothalamus is being investigated to enhance memory and cognitive function. Similarly, for patients recovering from traumatic brain injury, DBS holds promise in modulating neural circuits involved in attention and arousal, potentially aiding in rehabilitation[45].

DBS is also being explored in addiction medicine. By targeting the NAs, researchers aim to modulate reward pathways, which could help treat substance use disorders such as alcohol, nicotine, and opioid addiction. Stroke rehabilitation is another area of interest, where DBS of regions like the cerebellum and primary motor cortex has shown potential in promoting motor recovery[40].

Additionally, DBS has shown promise in treating cluster headaches and migraines by targeting hypothalamic circuits, significantly reducing the frequency and severity of attacks in drug-resistant cases. Its role in sleep disorders is also under investigation, with preliminary studies exploring its effects on conditions such as sleep apnea and hypersomnia[41].

The development of closed-loop DBS systems is a major focus of research. These adaptive systems aim to provide real-time modulation based on patient-specific neural activity, potentially improving the precision and efficacy of DBS therapy. Furthermore, researchers are investigating the use of DBS in conditions such as bipolar disorder, schizophrenia, and neurodegenerative disorders like multiple system atrophy (MSA) and progressive supranuclear palsy (PSP). These advancements underscore the evolving nature of DBS and its potential to revolutionize the treatment landscape for a wide range of neurological and psychiatric conditions[42,43].

Case selection for DBS

DBS is primarily indicated for patients with movement disorders, such as PD, essential tremor (ET), and dystonia, who have not responded adequately to pharmacological treatments. For PD, suitable candidates typically present with motor fluctuations or dyskinesias that significantly impair daily activities and are refractory to medications. In ET, DBS is recommended for patients with severe tremor that significantly affects daily functioning and who have not benefitted from other treatments. Additionally, patients should exhibit stable disease progression and a clear benefit from symptom control, as DBS is most effective when symptoms are sufficiently severe but not so advanced that the procedure would not provide meaningful improvements. Candidates must also be cognitively and psychologically stable, with intact mental status, to ensure they can engage in rehabilitation and manage postoperative expectations[45].

Contraindications for DBS

Certain conditions are contraindications for DBS. Severe cognitive impairment, such as dementia or significant executive dysfunction, can limit the effectiveness of DBS and may worsen post-surgical outcomes. Active psychiatric conditions, including uncontrolled depression, psychosis, or mania, are also contraindications, as they can interfere with recovery and adjustment to the device. Medical comorbidities like uncontrolled cardiovascular disease, diabetes, or infections may increase surgical risk and are considered relative contraindications. Structural brain abnormalities, such as large tumors or extensive cortical atrophy, also present challenges for electrode placement and are therefore considered contraindications. It is essential to carefully evaluate these factors during pre-surgical screening to optimize patient selection and ensure safe and effective outcomes[25].

Advantages and disadvantages of DBS over magnetic resonance-guided focused ultrasound

DBS and magnetic resonance-guided focused ultrasound (MRgFUS) are two advanced therapeutic options for managing PD, each with distinct advantages and disadvantages. DBS has several advantages over magnetic resonance guided focused ultrasound, one of the significant benefits of DBS is its adjustability. Clinicians can fine-tune stimulation parameters to optimize therapeutic outcomes and minimize side effects. Additionally, DBS is reversible; if necessary, the system can be turned off or removed . DBS has a long-standing history of effectively managing motor symptoms in PD patients, particularly those with advanced disease stages. It is recognized as an evidence-based therapy for treating dopaminergic complications in PD. DBS targets, such as the STN and GPi, allow for comprehensive management of various motor symptoms, including tremor, rigidity, bradykinesia, and motor fluctuations. Conversely, MRgFUS is a non-invasive procedure that uses focused ultrasound waves to ablate targeted brain tissue without the need for incisions or implanted hardware, reducing the risk of infections and other surgical complications. Patients undergoing MRgFUS typically experience shorter recovery periods compared to those undergoing DBS, allowing for a quicker return to daily activities. Since MRgFUS does not involve implanted devices, the initial procedure may be less expensive, and there are no future costs related to hardware maintenance or replacements[43,44].

Regarding disadvantages of DBS compared to MRgFUS, DBS requires surgical implantation of electrodes and a pulse generator, making it an invasive procedure with associated surgical risks, such as infection, hemorrhage, and hardware complications. The procedure is costly, and patients may require regular follow-ups for device programming and battery replacements, adding to the long-term expense and maintenance burden. Not all patients are suitable candidates for DBS due to factors like age, comorbidities, or contraindications to surgery. Conversely, MRgFUS involves permanent ablation of brain tissue, making the effects irreversible. If complications or suboptimal outcomes occur, they cannot be undone. As a relatively newer treatment modality, MRgFUS lacks extensive long-term data on its efficacy and safety compared to DBS. Current applications of MRgFUS are primarily focused on tremor control. Its effectiveness in managing other PD symptoms, such as rigidity or bradykinesia, is less established[44,45].

Parkinsonism vs. parkinson's disease and indications for DBS in parkinsonism

PD is a neurodegenerative disorder primarily caused by the loss of dopamine-producing neurons in the substantia nigra and the most common form of parkinsonism, but other types include MSA, PSP, corticobasal degeneration (CBD), and drug-induced parkinsonism. PD patients typically present with a combination of rest tremor, rigidity, bradykinesia, and postural instability. PD patients often respond well to dopaminergic therapies, such as levodopa, especially in the early stages[40].

Conversely, parkinsonism is an umbrella term that encompasses a group of neurological disorders characterized by motor symptoms such as tremor, rigidity, bradykinesia, and postural instability, includes disorders like MSA, PSP, and CBD, each with distinct pathophysiological mechanisms. Parkinsonism conditions may present with additional symptoms not typical of PD, such as autonomic dysfunction in MSA, vertical gaze palsy in PSP, or asymmetric cortical deficits in CBD. Atypical parkinsonian disorders generally have a poor or transient response to dopaminergic therapies. The role of DBS in atypical parkinsonian disorders is less well-defined. While DBS is an established treatment for managing motor complications in PD, its application in other forms of parkinsonism remains limited due to the limited response to dopaminergic medications and the distinct pathophysiology of these disorders, DBS outcomes have been less favorable compared to those in PD. Consequently, DBS is not routinely recommended for atypical parkinsonism and is generally considered on a case-by-case basis, often within clinical trial settings or specialized centers[41].

Take-home message

DBS has revolutionized the management of movement disorders such as PD, dystonia, and essential tremor. It provides significant motor improvement, reduces medication requirements, and enhances the overall quality of life for patients with refractory symptoms.

Therapeutic efficacy

DBS effectively modulates dysfunctional neural circuits, offering sustained symptom relief and addressing both motor and non-motor aspects of movement disorders. Recent insights into the neural pathways influenced by DBS has expanded its applications and improved understanding of its effects on cognition, mood, and behavior. Innovations like adaptive (closed-loop) DBS and improved electrode designs are paving the way for personalized and more precise therapies. While DBS shows immense potential, challenges such as patient selection, programming optimization, and accessibility remain. Future research should focus on addressing these barriers, exploring new targets, and integrating DBS with complementary therapies.

DBS stands as a cornerstone in movement disorder management, combining clinical efficacy with promising research avenues to improve patient outcomes further.

Overview of weaknesses

This review was limited by the small number of studies, the nonuniform reporting of outcomes and our various methodological assumptions. In addition, not all subgroups were based on a priori hypotheses, and arbitrary thresholds were used for

comparisons. Nonetheless, this is the first review to report pooled estimate demonstrating improved motor scores after DBS for PD. It may lack long-term follow-up data on DBS efficacy, which is crucial for assessing sustained benefits and risks. The review could benefit from a deeper exploration of the limitations in patient selection and the impact of comorbidities on outcomes. Additionally, the neurobiological mechanisms discussed might be oversimplified, requiring more nuanced discussion. The review also underemphasizes the role of advancements in DBS technologies, such as closed-loop systems. Lastly, the discussion on adverse effects and complications could be more thorough. There is also limited consideration of the cost-effectiveness and accessibility of DBS across different healthcare systems.

Conclusion

Our meta-analysis affirms the substantial therapeutic efficacy of DBS in the treatment of PD and related movement disorders. DBS has been shown to result in significant improvements in motor function, disease severity, tremor reduction, gait velocity, and tic management. While there are some concerns regarding potential publication bias, the overall findings solidify DBS as a highly effective and versatile treatment option that enhances patient outcomes in movement disorders.

While the benefits of DBS are well-established, there remains a critical question about whether it should be considered earlier in the disease course than current guidelines suggest. Although subgroup analysis yielded promising results, the limitations of the data prevent definitive conclusions about the ideal timing for DBS. Additional well-conducted RCTs are necessary to determine the optimal treatment window for DBS to maximize its efficacy. Moreover, a standardized approach to assess the severity and causes of serious adverse events is essential for future studies to minimize bias and improve the reliability of meta-analytic results. Most importantly, a deeper understanding of DBS's mechanisms in relation to the pathophysiology of the basal ganglia is crucial for explaining the therapeutic benefits observed in PD patients and for identifying predictive factors that may help select candidates who are most likely to benefit from DBS.

Ethical approval

Ethics approval was not required for this review.

Consent

Informed consent was not required for this review article.

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All authors have contributed equally in formation of all forms of manuscript.

Conflicts of interest

Not applicable.

Research registration unique identifying number (UIN)

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Bipin Chaurasia.

Provenance and peer review

Ok.

Data availability statement

Not applicable.

References

1. Singer HS, Mink JW, Gilbert DL, *et al*. Movement disorders in childhood. Academic press; 2015.
2. Klein C. Movement disorders: classifications. J Inherit Metab Dis 2005;28:425–39.
3. Pandey S. Classification of movement disorders: the problem of terminology. Neurol India 2018;66:S12–S14.
4. Stoessl AJ, Mckeown MJ. Movement disorders. Handb Clin Neurol 2016 ;136:957–69.
5. Picillo M, Munhoz RP. Medical management of movement disorders. Prog Neurol Surg 2018;33:41–49.
6. Ferreira JJ, Rodrigues FB, Duarte GS, *et al*. An MDS evidence-based review on treatments for Huntington's disease. Mov Disord 2022;37:25–35.
7. Jankovic J. Treatment of hyperkinetic movement disorders. Lancet Neurol 2009;8:844–56.
8. Damato V, Balint B, Kienzler AK, *et al*. The clinical features, underlying immunology, and treatment of autoantibody-mediated movement disorders. Mov Disord 2018;33:1376–89.
9. Ferreira JJ, Mestre TA, Lyons KE, *et al*. MDS task force on tremor and the MDS evidence based medicine committee. MDS evidence-based review of treatments for essential tremor. Mov Disord 2019;34:950–58.
10. Fox SH, Katzenschlager R, Lim SY, *et al*. Movement Disorder Society Evidence-Based Medicine Committee. International Parkinson and movement disorder society evidence-based medicine review: Update on treatments for the motor symptoms of Parkinson's disease. Mov Disord 2018;33:1248–66. Erratum in: Mov Disord. 2018 Dec;33(12):1992. PMID: 29570866.
11. Nielsen G, Stone J, Matthews A, *et al*. Physiotherapy for functional motor disorders: a consensus recommendation. J Neurol Neurosurg Psychiatry 2015;86:1113–19.
12. Delorme C, Giron C, Bendetowicz D, *et al*. Current challenges in the pathophysiology, diagnosis, and treatment of paroxysmal movement disorders. Expert Rev Neurother 2021;21:81–97.
13. Krauss JK, Lipsman N, Aziz T, *et al*. Technology of deep brain stimulation: current status and future directions. Nat Rev Neurol 2021;17:75–87.
14. Pycroft L, Stein J, Aziz T. Deep brain stimulation: an overview of history, methods, and future developments. Brain Neurosci Adv 2018;2:2398212818816017.
15. Larson PS. Deep brain stimulation for movement disorders. Neurotherapeutics 2014;11:465–74.
16. Page MJ, McKenzie JE, Bossuyt PM, *et al*. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Syst Rev 2021;10:89.
17. Cochrane Handbook for Systematic Reviews of Interventions [Internet]. [cited 2023 Aug 21]. https://training.cochrane.org/handbook.

18. Sterne JA, Hernán MA, Reeves BC, *et al*. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ 2016;355:i4919.
19. RoB 2: A revised Cochrane risk-of-bias tool for randomized trials| Cochrane Bias [Internet]. [cited 2023 Sep 27]. https://methods.cochrane.org/bias/resources/rob-2-revised-cochrane-risk-bias-tool-randomized-trials. [Accessed 18 October 2011].
20. Dettori JR, Norvell DC, Chapman JR. Fixed-effect vs random-effects models for meta-analysis: 3 points to consider. Global Spine J 2022;12:1624–26.
21. Willis BH, Riley RD. Measuring the statistical validity of summary meta-analysis and meta-regression results for use in clinical practice. Stat Med 2017;36:3283–301.
22. Cochrane Collaboration. 10.4. 3.1 Recommendations on testing for funnel plot asymmetry. Cochrane Handbook for Systematic reviews of interventions version. 2011;5(0).
23. Perlmutter JS, Mink JW. Deep brain stimulation. Annu Rev Neurosci 2006;29:229–57.
24. Breit S, Schulz JB, Benabid A-L. Deep brain stimulation. Cell Tissue Res 2004;318:275–88.
25. Lozano AM, Lipsman N, Bergman H, *et al*. Deep brain stimulation: current challenges and future directions. Nat Rev Neurol 2019;15:148–60.
26. Hariz M, Blomstedt P. Deep brain stimulation for Parkinson's disease. J Intern Med 2022;292:764–78.
27. Herrington TM, Cheng JJ, Eskandar EN. Mechanisms of deep brain stimulation. J Neurophysiol 2016;115:19–38.
28. Miocinovic S, Somayajula S, Chitnis S, *et al*. History, applications, and mechanisms of deep brain stimulation. JAMA Neurol 2013;70:163–71.
29. Rusheen AE, Rojas-Cabrera J, Goyal A, *et al*. Deep brain stimulation alleviates tics in Tourette syndrome via striatal dopamine transmission. Brain 2023;146:4174–90.
30. Dai L, Xu W, Song Y, *et al*. Subthalamic deep brain stimulation for refractory Gilles de la Tourette's syndrome: clinical outcome and functional connectivity. J Neurol 2022;269:6116–26.
31. Cagle JN, Okun MS, Cernera S, *et al*. Embedded human closed-loop deep brain stimulation for Tourette syndrome: a nonrandomized controlled trial. JAMA Neurol 2022;79:1064–68.
32. Kisten R, Van Coller R, Cassimjee N, *et al*. Efficacy of deep brain stimulation of the anterior-medial globus pallidus internus in tic and non-tic related symptomatology in refractory Tourette syndrome. Clinical Parkinsonism Relat Disord 2022;7:100159.
33. Mukhammedaminov B, Kajita Y. O036/# 970 thalamic deep brain stimulation for the disabling tics in Tourette's syndrome: track 2: deep brain stimulation for movement disORDERS. Neuromodulation 2022;25:S65.
34. Malaga KA, Costello JT, Chou KL, *et al*. Atlas-independent, N-of-1 tissue activation modeling to map optimal regions of subthalamic deep brain stimulation for Parkinson disease. Neuroimage Clin 2021;29:102518.
35. Heß T, Themann P, Oehlwein C, *et al*. Does impaired plantar cutaneous vibration perception contribute to axial motor symptoms in parkinson's disease? Effects of medication and subthalamic nucleus deep brain stimulation. Brain Sci 2023;13:1681.
36. Toda H, Saiki H, Nishida N, *et al*. Update on deep brain stimulation for dyskinesia and dystonia: a literature review. Neurol Med Chir (Tokyo) 2016;56:236–48.
37. Casagrande SC, Martino D. Deep brain stimulation in Tourette's syndrome: evidence to date. Neuropsychiatr Dis Treat 2019;15:761–75.
38. Neuroscience, a new map of brain connections to aid treatment of diseases such as Parkinson's disease, Tourette's syndrome and dystonia. https://www.santannapisa.it/en/news/neuroscience-new-map-brain-connections-aid-treatment-diseases-such-parkinsons-disease. [Accessed 23 February 2024].
39. Deep Brain Stimulation – Tourette Association of America. (n.d.). https://tourette.org/research-medical/deep-brain-stimulation/. [Accessed December 2021].
40. Deep Brain Stimulation for Dystonia – VCU Health. (n.d.). https://www.vcuhealth.org/services/parkinsons-and-movement-disorders-center/our-services/deep-brain-stimulation-dbs/dbs-for-dystonia. [Accessed 4 October 2024].
41. Tian X, Hu R, He P, *et al*. Efficacy and safety of magnetic resonance-guided focused ultrasound for Parkinson's disease: a systematic review and meta-analysis. Front Neurol 2023;14:1301240.
42. Ko TH, Lee YH, Chan L, *et al*. Magnetic resonance-guided focused ultrasound surgery for parkinson's disease: a mini-review and comparison between deep brain stimulation. Parkinsonism Relat Disord 2023;111:105431.
43. Lee KS, Clennell B, Steward TGJ, *et al*. Focused ultrasound stimulation as a neuromodulatory tool for parkinson's disease: a scoping review. Brain Sci 2022;12:289.
44. França C, Carra RB, Diniz JM, *et al*. Deep brain stimulation in Parkinson's disease: state of the art and future perspectives. Arq Neuropsiquiatr 2022;80:105–15.
45. Artusi CA, Rinaldi D, Balestrino R, *et al*. Deep brain stimulation for atypical parkinsonism: a systematic review on efficacy and safety. Parkinsonism Relat Disord 2022;96:109–18.