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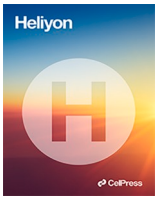

Research article

Pallidal versus subthalamic deep brain stimulation for Meige syndrome: A systematic review and meta-analysis

Xin Wu [a,1], Tao Xue [b,1], Shiqing Pan [c], Weikang Xing [a], Chuanjun Huang [a], Jianguo Zhang [b,**], Guozheng Zhao [a,*]

[a] Department of Neurosurgery, Suzhou Ninth People's Hospital, Suzhou, Jiangsu Province, China
[b] Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, Beijing, China
[c] A6 East in Department of Anesthesiology, The First Affiliated Hospital of Soochow University, Suzhou, Jiangsu Province, China

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ABSTRACT

Background: Globus pallidus internus (GPi) and subthalamic nucleus (STN) are two common deep brain stimulation (DBS) targets. This meta-analysis was to compared the efficacy and safety of these two DBS targets for the treatment of Meige syndrome (MS).

Methods: A systematic search was performed using EMBASE, MEDLINE, the Cochrane Library, and ClinicalTrials.gov to identify DBS trials for MS. Review Manager 5.3 was used to perform meta-analysis and the mean difference (MD) was analyzed and calculated with a random effect model. Pearson's correlation coefficients and meta-regression analyses were utilized to identify relevant predictive markers.

Results: Twenty trials involving 188 participants with GPi-DBS and 110 individuals with STN-DBS were eligible. Both groups showed improvement of the Burke-Fahn-Marsden Dystonia Rating Scale-Movement (BFMDRS-M) and Disability (BFMDRS-D) scores (BFMDRS-M: MD = 10.57 [7.74–13.41] for GPi-DBS, and MD = 8.59 [4.08–13.11] for STN-DBS; BFMDRS-D: MD = 5.96 [3.15–8.77] for GPi-DBS, and MD = 4.71 [1.38–8.04] for STN-DBS; all $P < 0.001$) from baseline to the final follow-up, while no notable disparity in improvement rates was observed between them. Stimulation-related complications occurrence was also similar between two groups (38.54 ± 24.07% vs. 43.17 ± 29.12%, P = 0.7594). Simultaneously, preoperative BFMDRS-M score and disease duration were positively connected with the relative changes in BFMDRS-M score at the final visit.

Conclusion: Both GPi-DBS and STN-DBS are effective MS therapies, with no differences in efficacy or the frequency of stimulation-related problems. Higher preoperative scores and longer disease duration probably predict greater improvement.

* Corresponding author. Department of Neurosurgery, Suzhou Ninth People's Hospital, No. 2666, Ludang Road, Wujiang District, Suzhou, Jiangsu Province, China

** Corresponding author. Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, No. 119 South 4th Ring West Road, Fengtai District, 100070, Beijing, China

E-mail addresses: zjguo73@126.com (J. Zhang), zgz1340788047@163.com (G. Zhao).

[1] Xin Wu and Tao Xue contribute equally to this work.

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1. Introduction

Meige syndrome (MS) is a segmental myodystonia characterized by blepharospasms, oromandibular myodystonia, and abnormal muscular activity in the neck [1]. The prevalence estimates of MS vary widely, which has been attributed to racial and ethnic differences. In the United States, the prevalence of MS ranged between 13 and 130 instances per million, whereas in Europe, the prevalence is 36 per million [2]. These symptoms are common in adulthood, with a greater frequency in females (male-to-female ratio 1:2) [3,4]. Age is an independent risk factor for MS, typically starting in the sixth decade of life [5]. The cause and underlying mechanisms of MS are still poorly understood, the most commonly recognized explanation for the pathophysiology of MS is dopaminergic and cholinergic disorders [2]. The lack of understanding of MS pathophysiology also poses challenges for its treatment. MS rarely remits autonomously [6]. Pharmacotherapy is the initial treatment option. However, most patients have adverse effects and some have perilous negative responses to medication [7,8]. Local application of botulinum toxin can alleviate MS symptoms, although, its effects persist for only 2–5 months, repeated treatments are necessary, and its effectiveness over time is potentially diminished [5, 9–11]. As a result, it is especially vital to create more effective treatment methods, including surgical procedures.

Research on the disease's pathology and physiology indicates a potential link to dysfunction in the circuitry of the basal ganglia, including the cortex-striatum-pallidum-thalamus [12–14]. According to this theory, deep brain stimulation (DBS) has the potential to block abnormal signals in MS that are transmitted through different pathways, including the direct (cortex-striatum-globus pallidus internus [GPi]/substantia nigra par reticulata [SNr]), hyper-direct (cortex-subthalamic nucleus [STN]-GPi/SNr), and indirect (cortex-striatum-GPi-STN-GPi/SNr) pathways [15]. The GPi is frequently targeted for MS treatment [16,17]. Hao and colleagues conducted a study involving 22 patients diagnosed with MS who underwent GPi-DBS for a maximum of 12 months. They found significant improvements in dystonia and quality of life and a decrease in depression among most patients [16]. Tian et al. reported similar outcomes [17–19]. The safety and effectiveness of STN have also been reported in other studies. Ouyang et al. showed the importance of focusing on the STN when treating MS. STN-DBS enhances patient motor symptoms and sleep conditions [20]. Therefore, we explored the use of DBS to treat MS because it has long been employed to treat primary myodystonia [21–23]. The efficacy of this method, both short- and long-term, is robust, making it a potentially reliable and efficient substitute for treating MS.

GPi and STN are the targets for DBS. Although the safety and efficacy of stimulating both targets have been demonstrated, there have been limited comparisons of the clinical outcomes. We conducted this systematic review and meta-analysis by gathering data from previously published trials to evaluate the effectiveness and safety of GPi- and STN-targeting DBS for managing MS.

2. Methods

2.1. Study protocol

A study protocol was written in the framework of the Cochrane Collaboration [24]. The systematic review process was registered retrospectively on INPLASY (INPLASY202360063) and can be accessed at https://inplasy.com (10.37766/inplasy2023.6.0063).

2.2. Criteria for inclusion and exclusion

The inclusion criteria were as follows: (1) language restriction: available in English; (2) participants: patients ≥18 years of age diagnosed with primary MS, based on the standard clinical diagnostic criteria; (3) intervention: GPi-DBS and STN-DBS; (4) outcomes: efficacy outcomes including objective scales Burke-Fahn-Marsden Dystonia Rating Scale-Movement (BFMDRS-M) and -Disability (BFMDRS-D), including total and sub-scores, and the absolute improvement rate of BFMDRS ((BFMDRSpre - BFMDRSpost)/BFMDRSpre * 100%); the safety outcomes was stimulation-related complications. Included studies were not required to include all the outcomes mentioned above but at least report BFMDRS score.

The exclusion criteria were as follows: (1) study type: conference articles, editorials, case reviews and reviews; (2) case report that included only one patient; (3) indications for surgery other than MS; (4) a stimulation target other than GPi or STN.

2.3. Search strategy

In the quest for papers related to MS, two autonomous researchers (XW and TX) thoroughly searched MEDLINE, EMBASE, the Cochrane Library, and ClinicalTrials.gov. The following search strategy was employed: ("globus pallidus interna" OR "subthalamic nucleus" OR "deep brain stimulation") AND "Meige Syndrome" in the title, abstract or keywords. The detailed search strategy can be found in the electronic supplementary material (Table S1). The search was limited to papers published before December 31, 2022. The reference lists of the included publications, pertinent systematic reviews, and meta-analyses were also independently and manually examined to ensure a complete investigation.

2.4. Study selection and data collection

According to the eligibility criteria listed above, two reviewers (XW and SQP) independently reviewed all titles, abstracts, and full-text articles found in the four databases, as well as the reference lists of the included studies and relevant systematic reviews or meta-analyses. If there were any disagreements between the two writers, they were resolved through discussion or, if necessary, by involving a third author (GZZ) who was not involved in data collection. Duplicate publications and research articles lacking entire texts were

eliminated.

After careful selection and review, data from the studies included were obtained, including the number of MS patients in each study, the patient's baseline characteristics (including sex, disease duration, age at surgery, and stimulation targets such as GPi or STN), as well as information regarding efficacy and safety outcomes (such as BFMDRS-M and BFMDRS-D scores at baseline and various follow-up times, follow-up duration, and any stimulation-related complications).

2.5. Quality of included studies

The quality of each study was assessed using the methodological index for nonrandomized studies (MINORS) [25]. The first subscale of the MINORS has eight items that address non-comparative research and the remaining 12 items address comparative studies. Together, these 12 items cover potential sources of bias. For the non-comparative and comparative investigations, the ideal global scores are 16 and 24, respectively, which are achieved by assigning a value of 0–2 to each component. The assessments were performed individually using WKX and CJH. Disagreements between the two researchers were resolved either by consensus or involvement of another independent investigator (XW).

2.6. Summary Measures and Synthesis of results

The direct evidence underwent a pairwise meta-analysis using Review Manager software (version 5.3). We used a random-effects model to calculate the mean difference (MD) for continuous outcomes and 95% confidence intervals (95% CIs). I^2 was then employed to calculate diversity in the following manner: $I^2 < 30\%$ indicated 'low diversity,' I^2 of 30%–50% suggested 'moderate diversity,' and $I^2 > 50\%$ denoted 'significant diversity.' This study aimed to evaluate whether there is a disparity in the outcomes of postoperative effectiveness between STN-DBS and GPi-DBS groups.

GraphPad Prism 8.0 software (GraphPad Software, San Diego, CA, USA) was utilized for all statistical computations. The average ±

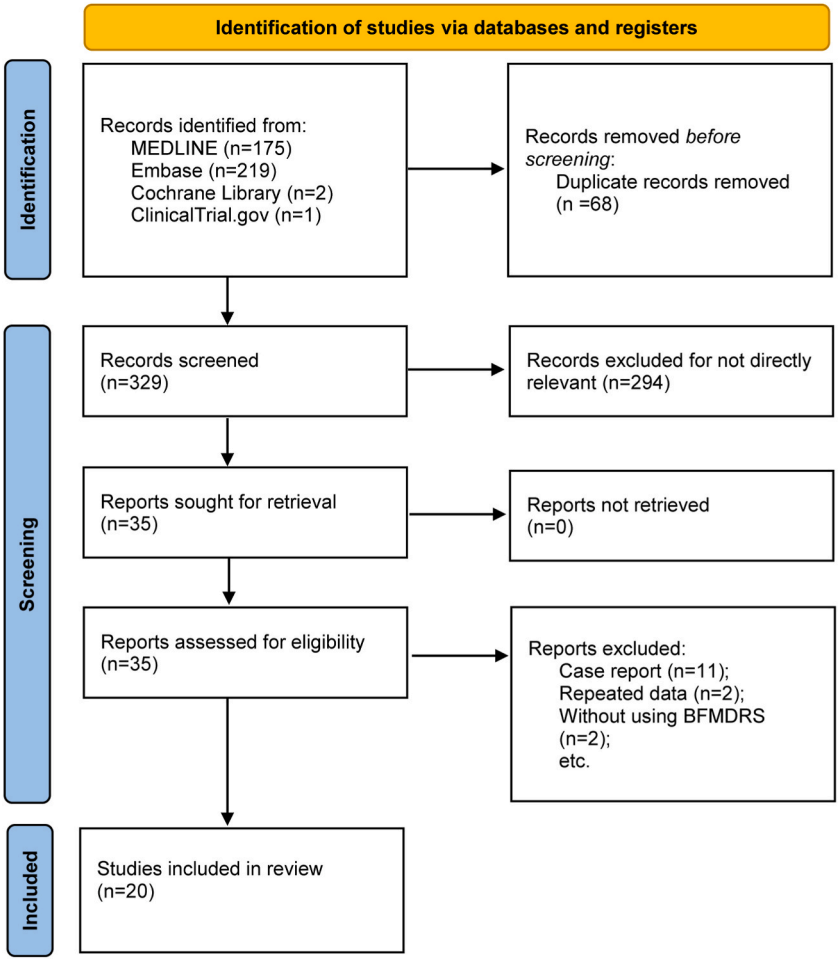


Fig. 1. The study search, selection, and inclusion process.

standard deviation of every data point is shown. The Kolmogorov-Smirnov test was used to determine if the datasets in each group followed a normal distribution. The variances across groups were compared using a two-tailed *t*-test for Student's t-distribution. To establish if there was a connection between the information obtained from both sets, we performed a Pearson's correlation analysis with a two-tailed approach. Meta-regression analyses were performed using a random-effects model to assess a linear association between the BFMDRS-M score and the outcome of interest. The regression line and its 95% prediction ranges were displayed if such an association exists. The threshold for statistical significance was $P < 0.05$.

3. Results

Overall, 397 titles and abstracts were found on Clinicaltrials.gov, EMBASE, MEDLINE, and the Cochrane Library, and 68 duplicate articles were excluded. Furthermore, 294 unrelated articles were eliminated following a brief evaluation, and an additional 35 articles were evaluated for suitability. Of these, 15 were excluded because of unsuitable publication types or participants; specifically, 11 were case reports, two articles presented duplicated data, and two trials did not meet our inclusion criteria as they failed to report the BFMDRS-M scores. The selection flowchart is shown in Fig. 1. The main features of the 20 studies are summarized in Table 1.

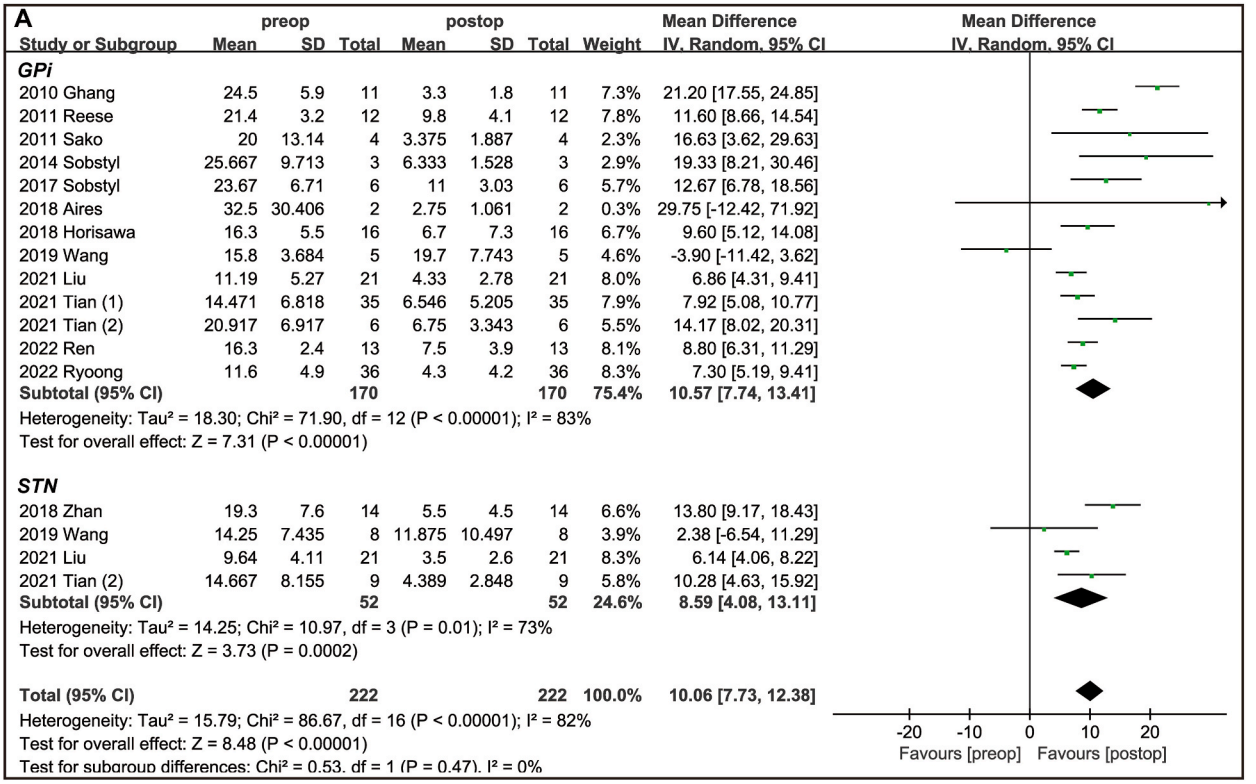
3.1. Effectiveness analysis of the Burke-Fahn-Marsden Dystonia Rating Scale-movement scores

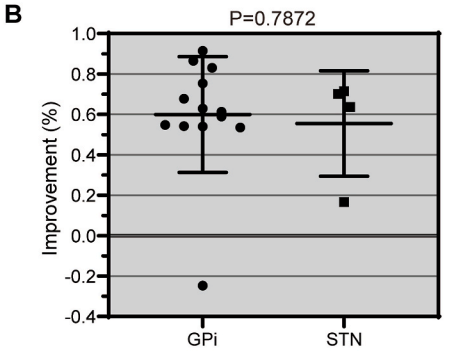
Patients who underwent GPi-DBS or STN-DBS had a notable reduction in their BFMDRS-M scores compared to their scores before surgery (GPi-DBS: MD = 10.57 [7.74–13.41], $P < 0.00001$, and $I^2 = 83\%$; STN-DBS: MD = 8.59 [4.08–13.11], $P = 0.0002$, and $I^2 =$

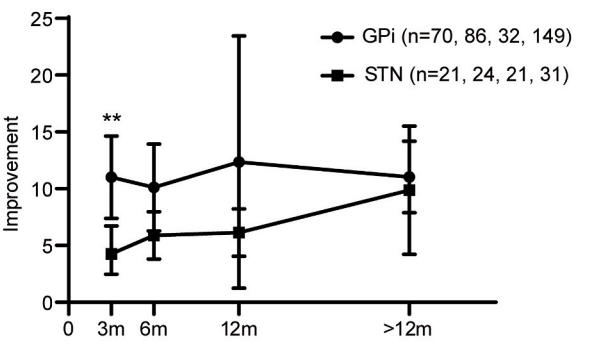
Table 1
Characteristics of the included studies.

Study	Number of patients	Male (%)	DU, ±SD(y)	AS, ±SD (y)	Stimulation target	BFMDRS-M score, ±SD		FU, ±SD (Ms)	Improvement(%) in BFMDRS-M score
						Pre-op	Post-op at the last FU		
Ryoong et al., 2022 [39]	36	25.0	5.6 ± 4.0	57.9 ± 11.5	GPi	11.6 ± 4.9	4.3 ± 4.2	24.6 ± 18.3	65
Ren et al., 2022 [40]	13	38.5	9.2 ± 2.1	46.9 ± 7.2	GPi	16.3 ± 2.4	7.5 ± 3.9	36.6 ± 11.0	54.6
Tian et al., 2021 (1) [41]	35	34.3	4.1 ± 1.8	56.9 ± 7.6	GPi	14.5 ± 6.8	6.5 ± 5.2	At least 2 years	54.8
Tian et al., 2021 (2) [42]	17	29.4	5.1 ± 3.2	56.0 ± 8.6	GPi:6, STN:11	16.7 ± 8.1	5.2 ± 3.1	30.1 ± 13.1	68.8
Liu et al., 2021 [43]	42	26.2	6.3 ± 6.0	59.1 ± 8.1	GPi:21, STN:21	10.4 ± 4.7	3.9 ± 2.7	12	62.4
Wang et al., 2020 [44]	32	46.9	6.0 ± 4.4	57.2 ± 9.4	STN:32	NR	NR	16.4 ± 7.2	NR
Wang et al., 2019 [32]	20	50.0	4.6 ± 4.4	60.1 ± 7.1	GPi:5, STN:15	13.7 ± 6.9	11.0 ± 9.8	18.2 ± 12.5	41.5
Zhan et al., 2018 [4]	14	NR	4.1 ± 2.7	53.0 ± 8.2	STN	19.3 ± 7.6	5.5 ± 4.5	28.5 ± 16.5	74
Yao et al., 2018 [33]	15	6.7	3.3 ± 2.0	56.4 ± 11.4	STN	NR	NR	14.8 ± 4.0	NR
Horisawa et al., 2018 [31]	16	56.3	5.9 ± 4.1	49.2 ± 13.9	GPi	16.3 ± 5.5	6.7 ± 7.3	66.6 ± 40.7	58.9
Aires et al., 2018 [45]	2	0.0	11.0 ± 8.5	70 0.0 ± 4.2	GPi	32.5 ± 30.4	2.8 ± 1.1	24	91.5
Sobstyl et al., 2017 [46]	6	33.3	12.5 ± 4.8	58.5 ± 8.6	GPi	23.7 ± 6.7	11.0 ± 3.0	31.0 ± 20.9	53.5
Wang et al., 2016 [37]	4	50.0	4.8 ± 3.3	53.5 ± 12.7	GPi:2, STN:2	16.9 ± 5.0	2.6 ± 2.1	At least 3 years	84.4
Sobstyl et al., 2014 [47]	3	33.3	14.7 ± 6.4	54.3 ± 10.2	GPi	25.7 ± 9.7	6.3 ± 1.5	22.7 ± 14.0	75.3
Sako et al., 2011 [30]	5	60.0	12.0 ± 4.6	65.0 ± 7.2	GPi	22.2 ± 12.4	3.1 ± 1.7	49.0 ± 43.7	86
Reese et al., 2011 [29]	12	50.0	8.3 ± 4.4	64.5 ± 4.4	GPi	21.4 ± 3.2	9.8 ± 4.1	38.8 ± 21.7	54.2
Limotai et al., 2011 [27]	6	66.7	11.3 ± 5.9	67.7 ± 14.6	GPi	NR	NR	36.8 ± 27.1	NR
Ghang et al., 2010 [26]	11	18.2	8.7 ± 7.5	58.2 ± 7.7	GPi	24.5 ± 5.9	3.3 ± 1.8	23.1 ± 6.4	86.5
Lyons et al., 2010 [28]	3	NR	NR	64.0 ± 8.5	GPi	NR	NR	48.0 ± 6.0	NR
Ostrem et al., 2007 [48]	6	100.0	8.2 ± 6.3	62.2 ± 6.7	GPi	22.0 ± 8.3	6.1 ± 4.2	6	72.3

DU: disease duration; AS: age at surgery; BFMDRS-M: Burke-Fahn-Marsden dystonia rating scale-motor score; Pre-op: pre-operation; Post-op: post-operation; FU: follow-up time; Ms: months; GPi: globus pallidus interna; STN: subthalamic nucleus; NR: not reported.







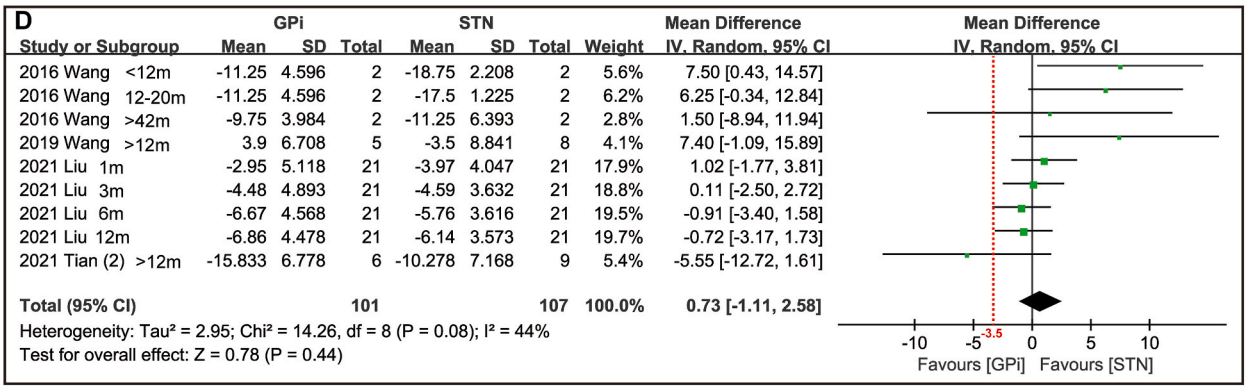


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Fig. 2. Efficacy outcome analysis of Burke-Fahn-Marsden Dystonia Rating Scale-movement score **A** Forest plot for Burke-Fahn-Marsden Dystonia Rating Scale-movement preoperative score and at the last postoperative follow-up **B** The comparison of the Burke-Fahn-Marsden Dystonia Rating Scale-movement score absolute improvement rates at the last postoperative follow-up in patients undergoing GPi-DBS and STN-DBS **C** The absolute value of postoperative Burke-Fahn-Marsden Dystonia Rating Scale-movement score improvement over time in patients undergoing GPi-DBS and STN-DBS. **D** Analysis of Burke-Fahn-Marsden Dystonia Rating Scale-movement score absolute improvement rates in patients undergoing GPi-DBS and STN-DBS in head-to-head studies. The red line represents the non-inferiority threshold, meaning crossing the line would demonstrate non-inferiority.
B and **C** present the data as mean ± SD.**P ≤ 0.01. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

73%) (Fig. 2A). Concurrently, when examining each subscale of the BFMDRS-M scores, both GPi-DBS and STN-DBS exhibited significant reductions in the scores of individuals with primary MS. Detailed effect sizes and P-values for the subscale analysis of the BFMDRS-M scores are summarized in Table 2. Fig. 2B shows no notable difference in the improvement rate between patients who underwent GPi-DBS and those who received STN-DBS (P = 0.7872). Additional subgroup analyses at various follow-up durations indicated that the overall enhancement in individuals receiving GPi-DBS was considerably higher than that in those who underwent STN-DBS within 3 months of surgery, and this disparity diminished as the follow-up period was extended (P = 0.003 at 3 months) (Fig. 2C). Moreover, an analysis combining multiple studies comparing GPi-DBS and STN-DBS demonstrated that STN-DBS exhibited greater efficacy than GPi-DBS in decreasing postoperative BFMDRS-M scores (Fig. 2D).

Two-tailed Pearson's correlation and meta-regression analyses were used to ascertain whether there was a linear association between absolute enhancements in the BFMDRS-M score and the desired outcome. The results showed an inverse correlation between improvements in BFMDRS-M scores and the number of patients (Pearson correlation analysis: r = −0.6933, P = 0.0029; meta-regression analysis: b = −0.19, 95% CI: −0.27–0.11). Additionally, there was a positive correlation between the improvements and the disease duration time (Pearson correlation analysis, r = 0.6024, P = 0.0135; meta-regression analysis, b = 0.93, 95% CI: 0.48–1.37), as well as the preoperative BFMDRS-M scores (Pearson correlation analysis: r = 0.9133, P < 0.0001; meta-regression analysis: b = 0.78, 95% CI: 0.56–0.99). Other factors are summarized in Table 3, which present the outcomes of the correlation and regression analyses regarding enhancements in the BFMDRS-M scores. Figs. S1–S18 present the detailed findings.

3.2. Effectiveness analysis of the Burke-Fahn-Marsden Dystonia Rating Scale-disability scores

Additionally, we conducted a meta-analysis of BDMDRS-D scores. After the operation, both operational teams showed a notable reduction in BFMDRS-D scores (GPi-DBS, MD = 5.96 [3.15–8.77], P < 0.0001, I^2 = 95%; STN-DBS, MD = 4.71 [1.38–8.04], P = 0.006, I^2 = 93%) (Fig. 3A). The method described in **Section 2.2** was used to calculate the absolute improvement values and rates of the BFMDRS-D scores. As shown in Fig. 3B, there was no notable disparity in the rate of improvement between patients who underwent GPi-DBS and those who underwent STN-DBS (P = 0.6073). Additionally, when conducting subgroup analyses at various follow-up periods, there was no notable disparity in absolute improvement between the two groups (Fig. 3C). However, upon conducting a comprehensive analysis of head-to-head research articles comparing the effects of GPi-DBS and STN-DBS, STN-DBS demonstrated superior efficacy in reducing postoperative BFMDRS-D scores (Fig. 3D).

3.3. Safety outcome analysis of stimulation-related complications

Safety assessments were focused on stimulation-related complications, which served as critical evaluation indicators. Table 4 shows the 80 complications related to stimulation in the 298 patients with MS who underwent GPi-DBS or STN-DBS. No significant difference was observed between the GPi-DBS and STN-DBS groups regarding stimulation-related complications (38.54 ± 24.07 vs. 43.17 ± 29.12%, P = 0.7594). Stimulation-induced complications were observed in the GPi-DBS and STN-DBS groups at rates ranging from

Table 2
Summary and detailed effects sizes for the subscale of BFMDRS-M; from all trials using random effects models.

Outcomes	No. of trials contributing to the meta-analysis	No. of participants contributing to the meta-analysis	MD (95% CI)	p value	I^2 (%)
Eye	**12**	**214**	**3.89 (3.46, 4.31)**	**<0.00001**	**37**
GPi	10	130	3.67 (3.26, 4.08)	<0.00001	0
STN	5	84	4.27 (3.55, 5.00)	<0.00001	54
Mouth	**12**	**214**	**3.03 (2.45, 3.61)**	**<0.00001**	**60**
GPi	10	130	3.10 (2.37, 3.83)	<0.00001	60
STN	5	84	2.85 (1.76, 3.94)	<0.00001	69
Speech and swallowing	**12**	**214**	**2.21 (1.41, 3.01)**	**<0.00001**	**74**
GPi	10	130	2.43 (1.32, 3.53)	<0.0001	72
STN	5	84	1.88 (0.48, 3.29)	0.009	81
Neck	**12**	**201**	**1.13 (0.60, 1.66)**	**<0.0001**	**60**
GPi	10	117	1.31 (0.57, 2.06)	0.0006	63
STN	5	84	0.88 (0.08, 1.69)	0.03	62

MD: mean difference; CI: confidence interval; GPi: globus pallidus interna; STN: subthalamic nucleus.

Table 3
Summary results of correlation and regression analysis of the improvements in Burke-Fahn-Marsden Dystonia Rating Scale-movement score with other factors.

Factors	Correlation		Regression
	r	*p*	b (95%CI)
Number of patients	−0.6933	**0.0029**	−0.19 (−0.27, −0.11)
Percentage of male	−0.2306	0.3903	1.16 (−5.82, 8.13)
Mean age at onset (years)	0.1159	0.6692	−0.07 (−0.23, 0.10)
Disease duration (years)	0.6024	**0.0135**	0.93 (0.48, 1.37)
Age at surgery (years)	0.4565	0.0755	0.09 (−0.09, 0.27)
Percentage of GPi	0.3309	0.2106	2.14 (−1.28, 5.57)
Pre-op BFMDRS-M scores	0.9133	**<0.0001**	0.78 (0.56, 0.99)
Follow-up time (months)	−0.0070	0.9792	0.04 (−0.04, 0.12)

CI: confidence interval; GPi: globus pallidus interna; pre-op: pre-operation; BFMDRS-M: Burke-Fahn-Marsden dystonia rating scale-motor score.

8.33% to 80.95% and from 20% to 85.71%, respectively. Furthermore, there was no notable disparity in the prevalence of dystonia among the two groups (24.77 ± 28.26% vs. 14.38 ± 14.66%, P = 0.5920).

3.4. Risk of bias in included studies

In the 20 studies that utilized the MINORS quality assessment, the risk of bias was minimal and no studies were excluded (Supplementary Table S2). Publication bias was assessed for the outcomes using a funnel plot, and the funnel plot was symmetrically distributed, indicating no publication bias in our study in Supplementary Figs. S19–20.

4. Discussion

The results of this study were based on 20 articles that included 298 patients with MS who were treated with GPi-DBS or STN-DBS. Our meta-analysis revealed that the GPi-DBS and STN-DBS groups experienced improvements in BFMDRS-M and BFMDRS-D scores at 3, 6, 9, and 12 months postoperatively. BFMDRS-M and BFMDRS-D scores did not increase with prolonged follow-up. The same results were observed for each sub-item of the BFMDRS-M. The GPi-DBS group had better BFMDRS-M scores than the STN-DBS group at 3 months postoperatively; although, both groups showed no significant difference in BFMDRS-M improvement thereafter. Similarly, no difference was observed in the improvement of BFMDRS-D scores between the GPI-DBS and STN-DBS groups.

Previous studies have revealed a preference for GPi-DBS as a stimulation target for MS. Many studies and case series have reported varying outcomes, including a 20%–86% improvement [26–30]. A recent study on GPi-DBS involving 16 patients with MS revealed a gain of 66% in BFMDRS-M scores after 3 months and 59% at the last follow-up [31]. Another study involving 40 patients who underwent GPi-DBS documented an overall 83% improvement at a mean follow-up of 15 months, with increases in 28 of the 40 patients within 1 week of stimulation [17]. However, recent large-scale studies have provided further evidence for MS treatment using STN-DBS [32,33]. A study involving 15 individuals who underwent STN-DBS demonstrated a 69% reduction in BFMDRS-M score [20]. Few studies have compared the efficacies of these two surgical methods. Our analyses revealed that during the most recent follow-up visit, patients in the GPi-DBS and STN-DBS groups exhibited significant enhancements in the BFMDRS-M and BFMDRS-D ratings, along with those in sub-categories related to vision, oral function, verbal communication, and ingestion.

Our research revealed no notable disparity in effectiveness between GPi-DBS and STN-DBS. Liu et al. conducted a comparative analysis of GPi-DBS and STN-DBS outcomes for MS treatment and obtained experimental results similar to ours. They observed that GPi-DBS and STN-DBS did not improve SF-36 or Pittsburgh Sleep Quality Index scores in patients with MS. Regarding the alleviation of depression and anxiety symptoms, the 17-item Hamilton Depression Rating Scale score indicated that STN-DBS is more effective than GPi-DBS [34]. Our analysis revealed that GPi-DBS outperformed STN-DBS indicated by BFMDRS-M scores within 3 months postoperatively.

To our knowledge, after our systematic and comprehensive literature search, we only found one meta-analysis published in 2019 on the application of these two DBS targets in MS [35]. They found that GPi-DBS and STN-DBS were both two effective therapies for even the refractory MS, while stimulation targets or other clinical factors did not constitute the outcome predictive factors. In comparison to their study, we have incorporated more recent studies since 2019, including trials comparing these two DBS targets head-to-head. On the other hand, further analysis of the BFMDRS-M scores demonstrated that the improvement rate of the BFMDRS-M scores was positively correlated with patient preoperative courses of the disease and their preoperative scores (reflecting disease severity at baseline). However, determining the duration of a preoperative disease course is inherently subjective. Patients may be more attentive to their symptoms at different stages; some patients may notice mild symptoms, whereas others may only report when they have multiple severe symptoms. A comprehensive study examined disease progression in 264 patients with ophthalmospasm symptoms and discovered that the mean time interval between the initial onset of the disease and the appearance of spasms was 7.9 ± 14.5 years [36]. This finding highlights the potential inaccuracy of the symptom timing. Previous studies have shown that preoperative disease severity is the sole MS predictor [32,35,37]. Neither the age at which dystonia first manifests, nor the disease duration predicts improvements in BFMDRS-M scores [37]. Horisawa et al. did not establish a clinically significant association, which is attributable to the study's relatively limited sample size [31]. Therefore, we contend that preoperative disease severity is the sole independent predictor of

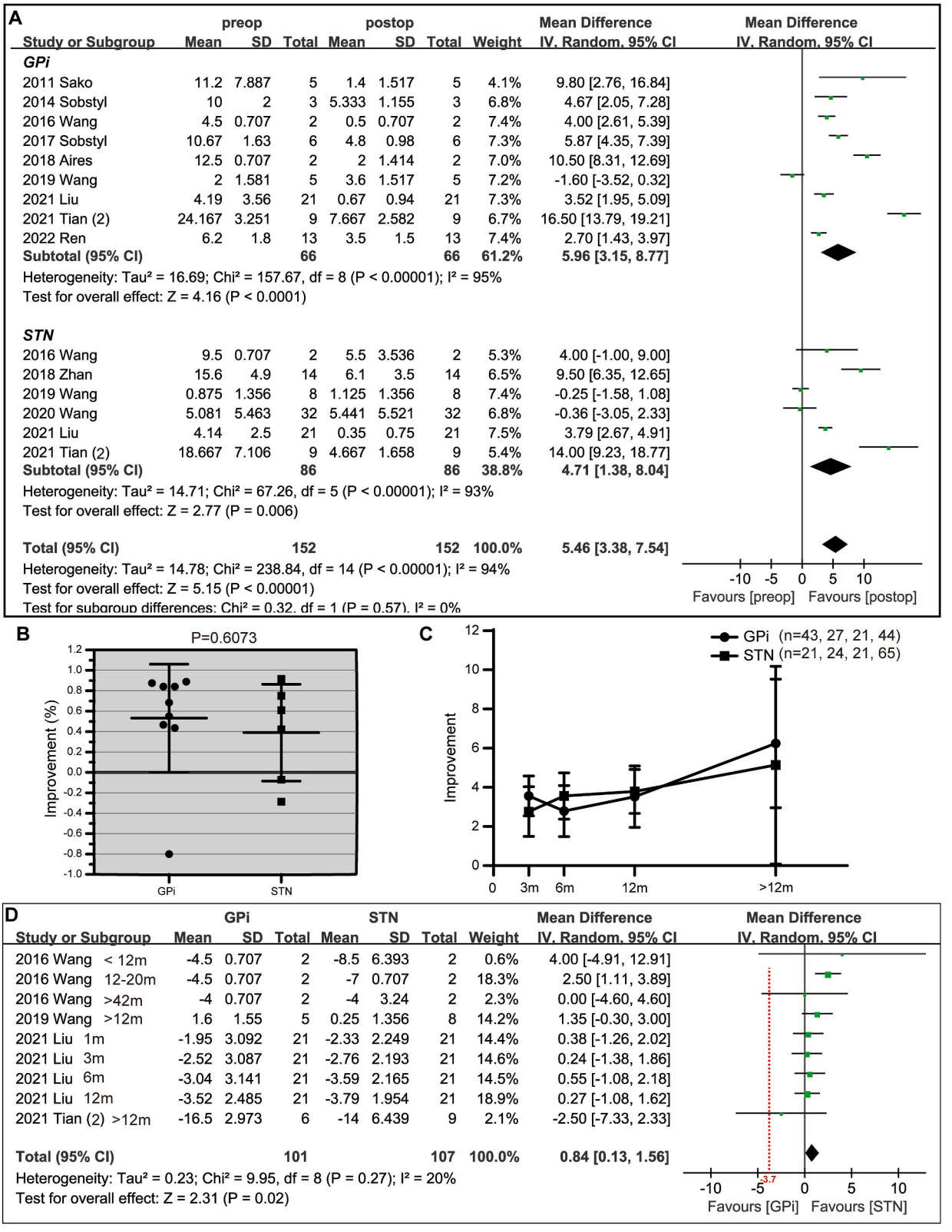

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Fig. 3. Efficacy outcome analysis of Burke-Fahn-Marsden Dystonia Rating Scale-disability score **A** Forest plot for Burke-Fahn-Marsden Dystonia Rating Scale-disability preoperative score and at the last postoperative follow-up **B** The comparison of the Burke-Fahn-Marsden Dystonia Rating Scale-disability score absolute improvement rates at the last postoperative follow-up in patients undergoing GPi-DBS and STN-DBS **C** The absolute value of postoperative Burke-Fahn-Marsden Dystonia Rating Scale-disability score improvement over time in patients undergoing GPi-DBS and STN-DBS **D** Analysis of Burke-Fahn-Marsden Dystonia Rating Scale-disability score absolute improvement rates in patients undergoing GPi-DBS and STN-DBS in head-to-head studies. The red line represents the non-inferiority threshold (crossing the line demonstrates non-inferiority). **B** and **C** present data as mean ± SD. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Table 4
Summary of stimulation-related complications.

Study name	*N*	Stimulation-related complications	Dysarthria	Dystonia	*n*
Studies including patients treated with STN-DBS					
Tian et al., 2021(2) [42]	11	0	0	0	0
Liu et al., 2021 [43]	21	Vertigo (1), dysarthria (4), paresthesia or numbness (12), stroke(1)	4	1	18
Wang et al., 2020 [44]	32	Dyskinesia (10)	0	10	10
Wang et al., 2019 [32]	15	Dystonia (3)	0	0	3
Zhan et al., 2018 [4]	14	Hemorrhage (3), infections (1), dystonia(1)	0	1	5
Yao et al., 2018 [33]	15	0	0	0	0
Wang et al., 2016 [37]	2	0	0	0	0
Studies including patients treated with GPi-DBS					
Ryoong et al., 2022 [39]	36	Seromatous fuid flling and leakage (1), paresthesia (1), cramps(1)	0	0	3
Ren et al., 2022 [40]	13	Dystonia (1), facial twitch (2), dysarthria (1), infections (1)	1	0	5
Tian et al., 2021(1) [41]	35	0	0	0	0
Tian et al., 2021(2) [42]	6	0	0	0	0
Liu et al., 2021 [43]	21	Vertigo (1), dysarthria (1), paresthesia or numbness (6), fall(1), disequilibrium sensation (1), dysphagia (2), fatigue (1), dysarthria (3), dyspnea (1)	1	2	17
Wang et al., 2019 [32]	5	Hematoma (1), cramps (1)	0	0	2
Horisawa et al., 2018 [31]	16	Dystonia (2), infection (1), lead breakage (1), DBS device erosion (1)	0	1	5
Aires et al., 2018 [45]	2	0	0	0	0
Sobstyl et al., 2017 [46]	6	Dislocation (1)	0	0	1
Wang et al., 2016 [37]	2	0	0	0	0
Sobstyl et al., 2014 [47]	3	Dislocation (1)	0	0	1
Sako et al., 2011 [30]	5	0	0	0	0
Reese et al., 2011 [29]	12	Infection (1)	0	0	1
Limotai et al., 2011 [27]	6	Dysarthria (1), dysphagia (1), fall (1), cognitive impairment (1)	1	1	4
Ghang et al., 2010 [26]	11	0	0	0	0
Lyons et al., 2010 [28]	3	Depression (1)	0	0	1
Ostrem et al., 2007 [48]	6	Ataxia (4)	0	4	4

GPi: globus pallidus interna; STN: subthalamic nucleus; DBS, deep brain stimulation; N, number of patients; n, number of stimulation-related complications.

clinical outcomes in patients with MS undergoing DBS.

The safety of different stimulation sites for treatment is crucial because DBS may directly or indirectly induce stimulation-related complications. The existing literature suggests that speech and movement disorders are caused by stimulation via the same cerebellothalamocortical fibers in DBS, including axons projecting into and out of the red nucleus and neighboring tracts [38]. Our analysis revealed no difference in stimulation-related complications incidence between the GPi-DBS and STN-DBS groups.

However, this meta-analysis has several limitations. Unlike other movement disorders such as Parkinson's disease, large randomized clinical trials on MS are unavailable. Therefore, our analysis was limited to non-randomized studies, including case reports

and series. Head-to-head experiments are more rigorous. Accordingly, we concluded that the therapeutic efficacy of STN-DBS surpassed that of GPi-DBS. However, the limited number of cases included in these experiments diminishes the overall reference value, which may affect the reliability of our conclusions. Further randomized controlled clinical trials are required to verify these findings. Additionally, in the meta-analysis comparing preoperative and postoperative outcomes, we discovered significant heterogeneity (all analyses had heterogeneity greater than 50%), which might be attributed to differences in case numbers, follow-up times, and so on. As a result, we did a thorough meta-regression analysis, examining each potential confounding factor for heterogeneity one by one. Finally, we discovered that the number of cases included, the length of the preoperative illness course, and the preoperative disease score all had an effect on postoperative scores, although the length of follow-up time had no meaningful correlation with outcomes.

Summarily, the results of our study showed that GPi-DBS and STN-DBS were both successful therapies for MS, with no notable disparity in their effectiveness. Moreover, the two groups had no significant difference in postoperative stimulation-related complications. Preoperative disease severity is a reliable prognostic factor for determining the outcome in patients with MS.

Contributions by the author

GZZ and JGZ was the principal investigator. The study was designed and the analysis plan was developed by XW and TX. XW and TX conducted data analysis and carried out a meta-analysis. Both XW and QSP were involved in the writing of the article. The manuscript was revised and the language was polished by WKX and CJH. The final submitted paper was read and approved by all authors.

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Data availability statement

All data generated or analyzed during this study are included in this published article and its supplementary information files.

CRediT authorship contribution statement

Xin Wu: Writing – original draft, Software, Methodology, Formal analysis. **Tao Xue:** Software, Methodology, Investigation, Formal analysis. **Shiqing Pan:** Writing – review & editing. **Weikang Xing:** Writing – review & editing. **Chuanjun Huang:** Writing – review & editing. **Jianguo Zhang:** Supervision, Project administration. **Guozheng Zhao:** Writing – review & editing, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Guozheng Zhao reports financial support was provided by Wujiang Science, Education, and Health Project. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e27945.

List of Abbreviations

Meige syndrome (MS)
deep brain stimulation (DBS)
globus pallidus internus (GPi)
subthalamic nucleus (STN)
Burke-Fahn-Marsden Dystonia Rating Scale-movement (BFMDRS-M)
Burke-Fahn-Marsden Dystonia Rating Scale -disability (BFMDRS-D)
globus pallidus internus deep brain stimulation (GPi-DBS)
subthalamic nucleus deep brain stimulation (STN-DBS)
substantia nigra par reticulata (SNr)

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