

A Systematic Review and Meta-Analysis of Non-Invasive Nerve Stimulation Interventions on Dysphagia in Patients with Parkinson's Disease

Pengbo Wang¹, Hong Huo², Ying Zhang², Qianshi Zhang¹, Xinzhe Tan¹, Shiqiang Zhang³, Dongyan Wang^{1,2}

¹The Graduate School, Heilongjiang University of Chinese Medicine, Harbin, Heilongjiang Province, People's Republic of China; ²Department of Acupuncture, Heilongjiang University of Chinese Medicine Second Affiliated Hospital, Harbin, Heilongjiang Province, People's Republic of China; ³Hebei Province Key Laboratory of Integrated Traditional and Western Medicine in Neurological Rehabilitation, Hebei Province Cangzhou Hospital of Integrated Traditional Chinese and Western Medicine, Cangzhou, Hebei Province, People's Republic of China

Correspondence: Dongyan Wang, Heilongjiang University of Chinese Medicine, No. 24, Heping Road, Xiangfang District, Harbin, Heilongjiang, People's Republic of China, Email Doctor_WangDongyan@126.com

Background: Dysphagia is a non-motor symptom in patients with Parkinson's disease (PD). Non-invasive nerve stimulation therapy is used to treat dysphagia; it has the advantages of being non-invasive, painless, safe, and easily accepted by patients.

Design: Systematic review and meta-analysis.

Setting: Randomized controlled trials (RCTs) conducted on dysphagia treatment in patients with PD using non-invasive nerve stimulation as an adjuvant or standalone therapy were identified by searching PubMed, Web of Science, Embase, Cochrane Library, China National Knowledge Infrastructure, Wanfang Data, VIP database, and CBMdisc. Papers published between January 1, 2013, and July 31, 2023, were retrieved.

Participants: Patients with PD.

Interventions: Non-invasive nerve stimulation on dysphagia.

Primary and Secondary Outcome Indicators: The outcome indicators included Standardized Swallowing Assessment (SSA), Penetration-Aspiration Scale (PAS), Videofluoroscopic Swallowing Study (VFSS) scores, and clinical effectiveness rates. RevMan 5.4 software was used for the data consolidation analysis.

Results: This study included nine RCTs, with five and four interventions involving neuromuscular electrical stimulation (NMES) and repetitive transcranial magnetic stimulation (rTMS), respectively. In total, 613 participants were included in the study, 303 and 310 in the control and experimental groups, respectively. The meta-analysis showed heterogeneity in the combined effects of the SSA and PAS indicators. The subgroup analysis results showed that NMES and rTMS adjuvant therapies significantly reduced SSA scores. NMES as an adjuvant therapy significantly reduced PAS scores, but rTMS had no significant difference in improving PAS scores in the experimental group compared with the control group. Non-invasive nerve stimulation can significantly improve VFSS scores and clinical effectiveness rates.

Conclusion: NMES and rTMS can be an effective adjuvant therapy for treating dysphagia in patients with PD and improving their swallowing function. However, this conclusion is limited owing to the literature quality. Therefore, it should be verified using high-quality clinical RCTs.

Plain Language Summary:

- This study searched seven databases over the past decade for research on non-invasive neural stimulation therapy for swallowing disorders in patients with Parkinson's disease.
- This study summarized all non-invasive neural stimulation methods for treating swallowing disorders in patients with Parkinson's disease and conducted a subgroup analysis.
- This study summarized the stimulation parameters of non-invasive neural stimulation for the treatment of swallowing disorders in patients with Parkinson's disease.
- This study only searched databases in both Chinese and English, which may have led to a lack of research in other languages.



Keywords: non-invasive nerve stimulation, dysphagia, Parkinson's disease, meta-analysis, systematic review

Introduction

Parkinson's disease (PD) is a neurodegenerative disease that tends to occur in older adults.¹ Its incidence is increasing annually with the aging population.² PD generally involves motor symptoms as the core, but non-motor symptoms are essential in patients' daily lives, and dysphagia is a common PD complication.^{3,4} Dysphagia may involve one or more stages of swallowing and may occur at various stages of the disease.⁵ Presently, the mechanism of dysphagia in patients with PD is unclear; however, damage to the central nervous system that governs swallowing-related muscles, dopaminergic and non-dopaminergic mechanism disorders, muscle atrophy, bradykinesia, and muscle rigidity may be pathogenic factors.^{6,7} Dysphagia in patients with PD is characterized by structural and functional preservation but an abnormal swallowing mode, limiting the choice of food types and prolonging feeding time, resulting in malnutrition, electrolyte disorders, and other effects. Similarly, it complicates the intake of drugs, slowing patients' recovery and causing them a burden.^{8,9} Simultaneously, food accumulation in the mouth or throat can cause aspiration. The biggest risk is aspiration pneumonia, which is caused by aspiration, prolonging patients' hospitalization, increasing medical costs, and even endangering their lives. This is a crucial factor leading to poor prognosis in patients with PD.^{10,11} Therefore, improving the swallowing function in patients with PD is essential.

Presently, the clinical treatment of dysphagia in patients with PD mainly focuses on traditional swallowing, video-assisted swallowing, Lee Silverman speech and acupuncture therapies, expiratory muscle strength training, deep brain stimulation, repetitive transcranial magnetic stimulation (rTMS), surface electrical stimulation, botulinum toxin injection, dopaminergic drug therapy, nutrition management, and other methods.^{12–15} Conventional PD drugs positively affect motor symptoms, but improvements in swallowing function remain controversial.¹⁶ Botulinum toxin can be used to treat dysphagia due to spasms or a relaxation of the esophageal sphincter; however, it has a potential risk of respiratory and vocal disorders.¹⁷

Non-invasive nerve stimulation is a disease treatment method using physical factors such as electricity, magnetism, sound, light, and force acting on the human body surface as the main treatment method. It has the advantages of easy operation, safety, and easy acceptance by patients. rTMS, neuromuscular electrical stimulation (NMES), surface myoelectrical stimulation, transcranial direct current stimulation, biofeedback therapy, transcutaneous electrical stimulation, and other methods can improve the swallowing function,^{18,19} reducing the side effects of drug treatment.

There are many reports on the clinical research of non-invasive nerve stimulation in treating dysphagia in patients with PD; however, the efficacy evaluation indicators differ, as most research involved small sample trials, affecting the reliability of the results. Their effectiveness has not been fully confirmed, and no systematic evaluation exists. Therefore, we conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) on non-invasive nerve stimulation for treating dysphagia in patients with PD.

Methods

This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.²⁰ The study protocol was registered in PROSPERO (ID: CRD42023470003). URL: <https://www.crd.york.ac.uk/PROSPERO/recorddashboard>.

Data Sources and Search Strategy

The Chinese databases of the China National Knowledge Infrastructure, Wanfang Data, VIP database, and CBMdisc, and the English databases of PubMed, EMBASE, Cochrane Library, and Web of Science were searched using a computer. The keywords used were Parkinson's disease, dysphagia, deglutition disorder, swallowing disorder, rTMS, electrical stimulation, biofeedback therapy, NMES, and randomization. The retrieval time was between January 1, 2013, and July 31, 2023. According to the different databases, a comprehensive retrieval of subject and free words was performed to ensure the integrity of the retrieval.

Inclusion and Exclusion Criteria

The participants were patients diagnosed with PD complicated with dysphagia. No restrictions were considered on the basis of diagnostic criteria, age, sex, or race.

The intervention measures were non-invasive nerve stimulation as a separate or adjuvant treatment, including rTMS, NMES, surface muscle electrical stimulation, and biofeedback therapy. No restrictions were considered on the basis of the stimulation parameters, intervention time, or type of stimulation instrument used.

The control measures were sham stimulation, conventional PD treatment, other invasive stimulation therapy, swallowing rehabilitation therapy, and non-invasive nerve stimulation intervention.

The primary outcome indicator was Standardized Swallowing Assessment (SSA). The secondary outcomes indicators included Penetration-Aspiration Scale (PAS), Videofluoroscopic Swallowing Study (VFSS) scores, and clinical efficacy rates.

The SSA score was divided into clinical examination and observing the patient's swallowing condition using 5 and 60 mL of water. It included 18 items, with a total score of 18–46 points.

The mean PAS score was grade 8. The swallowing process recorded during the swallowing angiography was scored. Score 1 was no leakage or aspiration and food did not enter the airway. Scores 2–4 were classified as leakage of different degrees.

The VFSS score includes three parts: the oral phase, the pharyngeal phase, and the degree of swallowing error. The oral phase was scored 0–3 points, the pharyngeal phase was scored 0–3 points, the degree of swallowing error was scored 0–4 points, and the total score was 10 points. The swallowing process recorded during the swallowing angiography was scored.

The water swallow test (WST) graded, and its clinical efficacy was quantified. It was divided into four grades: cured: after treatment, the WST result was rated as grade I, without other symptoms; significant curative effect: the swallowing disorder of the patient was significantly reduced, and the WST evaluation results improved by two or more levels compared with those before the intervention; effective: after treatment, the WST evaluation result improved by one grade compared with that before the intervention; ineffective: WST assessment results did not change or decrease. The clinical effectiveness rate is the percentage of the total number of cured people, the number of people with significant curative effects, and the number of people for whom treatment was effective.

We only included RCTs of non-invasive nerve stimulation for treating dysphagia in patients with PD.

The exclusion criteria were re-published literature, literature without full-text extraction data, articles without baseline data, and articles with obvious errors in research design.

Data Screening and Extraction

Two researchers independently screened the retrieved literature and compared the screening results. If there were any differences, the research group discussed and decided whether to include them. Two researchers extracted information, including the first author's name, sample size, intervention measures, control measures, treatment course, outcome indicators, stimulation parameters, stimulation sites, and other information, from the included literature and cross-checked them.

Quality Assessment

On the basis of the bias risk assessment tool of the Cochrane Handbook, two researchers used the RevMan version 5.4 software to evaluate the quality of the included studies. If the evaluation results were inconsistent, the two researchers discussed and decided jointly and adopted them after consensus. If not, they decided after consulting a third researcher with a senior professional title.

Data Analysis

RevMan 5.4 software was used for data processing. The count data were expressed as relative risk (RR), and continuous variable data were expressed as the mean difference (MD); a 95% confidence interval (CI) was calculated for each effect. Heterogeneity among studies was tested using the I² value or P value. The test level was I² < 50% or P > 0.1 if the

heterogeneity was low, and the fixed effect model was used for analysis. However, if I^2 was $\geq 50\%$ or P was $\leq .1$, the heterogeneity was considered high; the source of heterogeneity was analyzed, and sensitivity or subgroup analysis was conducted if necessary. A random-effects model was selected for analysis if the heterogeneity remained large.

Patient and Public Involvement Statement

This study was a systematic review and did not involve patient or public participation.

Results

Literature Selection

In total, 847 papers were retrieved. After screening, nine studies were included. The literature screening process is illustrated in Figure 1.

Characteristics of the Included Literature

Of the nine included studies, NMES was used in five,^{21–25} and rTMS was used in four.^{26–29} Four studies^{23,25,28,29} compared true and false stimulations, and five^{21,22,24,26,27} compared non-invasive nerve stimulation combined with the control group treatment with only the control group treatment; all studies were single-center studies. The intervention

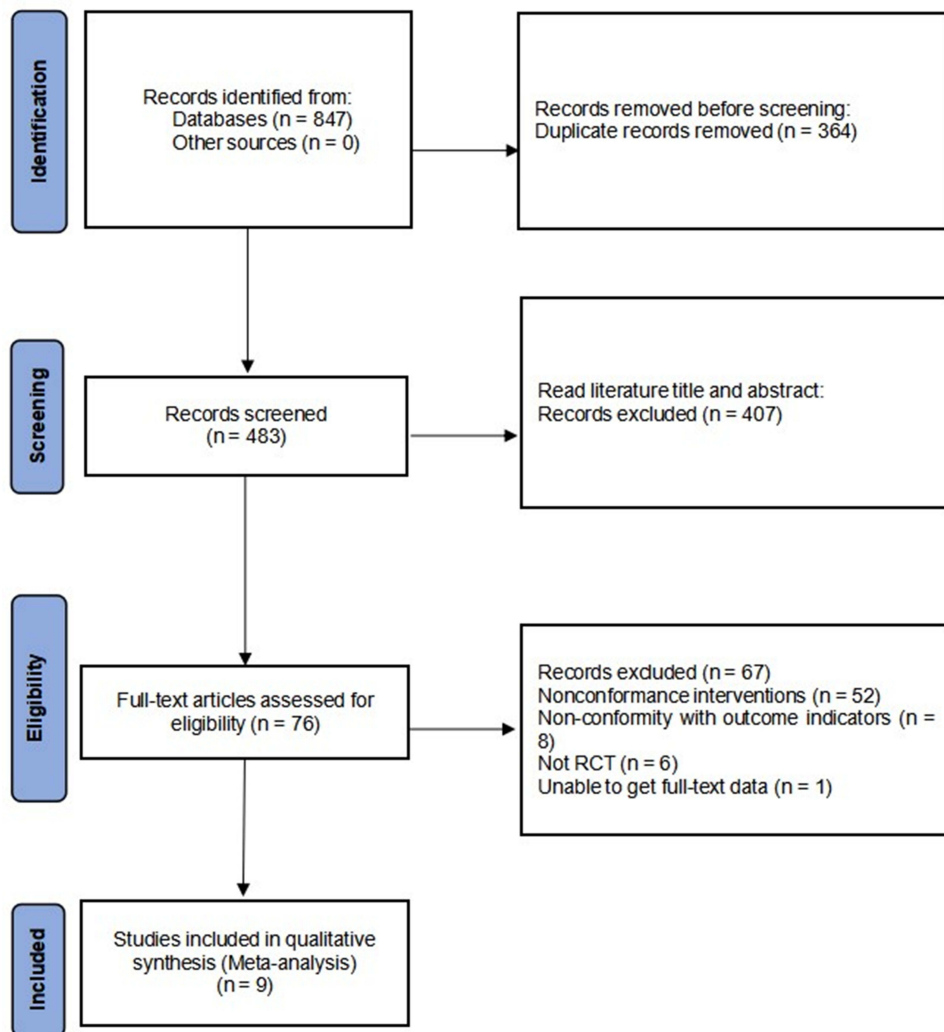


Figure 1 Flow diagram of article selection.

time was 14–30 days; the frequency range of NMES was 40–80 Hz, and 80 Hz was often used. The current parameter was 0–25 ma, which varied greatly in five studies;^{21–25} the wave width of three studies was 700 μ s,^{21,24,25} and two^{22,23} had undescribed wave widths. The stimulation site is usually located above or below the nape's hyoid bone, with a vertical arrangement and horizontal placement. The stimulation sites corresponded to the swallowing muscle groups, namely the suprahyoid and infrahyoid muscle groups. In the rTMS intervention, the stimulation frequency was 5 Hz, 10 Hz, and 20 Hz; two studies^{27,28} used a 5 Hz frequency. The stimulation intensity of three studies^{26–28} was set at 80% of the motion threshold, and one²⁹ was set at 90%. The three items^{27–29} described the stimulation sites, including the occipital and dorsolateral areas of the left prefrontal lobe, the anterolateral motor cortex of the head, the premotor area of the central anterior sulcus, and the brain's left and right hemispheres. The treatment frequency was once or twice daily, and the stimulation time was 20–45 min. The characteristics of the included studies are shown in [Table 1](#).

Risk of Bias in the Included Literature

A bias risk assessment was conducted for the nine included studies. Notably, all nine studies described randomized grouping, only three^{25,26,29} described allocation concealment, and the remaining six^{21–24,27,28} did not mention allocation concealment; therefore, they were identified as having ambiguous bias risk. Four studies^{23,25,28,29} used an anonymized study design for the participants, whereas the other five^{21,22,24,26,27} did not. One study²⁹ used an anonymized study design for the evaluator, and the other eight^{21–28} did not mention the anonymity; therefore, it was judged as an ambiguous bias risk. One study²⁹ had a small sample size, and the patient had a lot of shedding, so a high-risk bias was identified in terms of data integrity, and the other eight^{21–28} were judged as a low bias risk. The 9 studies included did not show any evidence of selective reporting or other sources of bias, so this review is judged as having a low bias risk. The risk of bias assessment is summarized in [Figures 2](#) and [3](#).

Results of the Meta-Analysis

SSA Score

Four studies reported the SSA scores, of which two were NMES and two were rTMS. The meta-analysis showed heterogeneity among the four studies ($P = 0.005$, $I^2 = 77\%$), and a subgroup analysis was conducted on the basis of the different intervention methods. The two RCTs in the NMES intervention group had no heterogeneity ($P = 0.28$, $I^2 = 16\%$) using a fixed effects model, and the results showed a significant difference in SSA scores between NMES combined with conventional treatment and conventional treatment alone (MD: -3.37 ; 95% CI: -4.07 , -2.66 ; $P < 0.0001$), with a more significant decrease in scores in the experimental group, indicating that NMES can improve swallowing function in patients with PD. Heterogeneity occurred between the two RCTs in the rTMS intervention group ($P = 0.001$, $I^2 = 90\%$); however, there were only two studies, and the cause of heterogeneity could not be determined. Therefore, a random-effects model was used, and the results showed a significant difference in SSA scores between the rTMS and control groups (MD: -3.96 ; 95% CI: -7.36 , -0.55 ; $P = 0.02$), with a more significant decrease in the experimental group's scores, indicating that rTMS can improve swallowing function in patients with PD ([Figures 4](#) and [5](#)).

PAS Score

Three studies reported the PAS scores, including two interventions with NMES and one with rTMS. The meta-analysis showed heterogeneity among the three studies ($P = 0.03$, $I^2 = 72\%$). Subgroup analysis based on different intervention methods showed no heterogeneity between the two RCTs in the NMES intervention group ($P = 0.26$, $I^2 = 22\%$). The fixed effects model showed a significant difference in the PAS score between NMES combined with conventional treatment and conventional treatment alone (MD: -0.84 ; 95% CI: -1.30 , -0.38 ; $P = 0.0003$). RCT results in the rTMS intervention group showed no significant difference between the two groups (MD: 0.10 ; 95% CI: -0.51 , 0.71 ; $P = 0.75$), possibly due to the small sample size and other factors ([Figure 6](#)).

VFSS Score

Two studies reported VFSS scores, one using NMES and the other using rTMS. Meta-analysis showed no heterogeneity between the two studies ($P = 0.42$, $I^2 = 0\%$). A significant difference was observed in the VFSS scores between the non-

Table I General overview of selected studies

Study	Sample Size (Male/Female)		Age (year) (mean ± SD)		Disease Duration (mean ± SD)		Intervention		Duration of Treatment	Outcomes	Stimulation Parameter	Stimulation region
	Experimental Group	Control Group	Experimental Group	Control Group	Experimental Group	Control Group	Experimental Group	Control Group				
Kang JL 2022 ²⁶	38 (22/17)	38 (22/16)	62.34 ± 5.07	61.77 ± 5.14	4.23 ± 0.47 y	4.57 ± 0.44 y	RT + warm acupuncture + rTMS	RT + warm acupuncture	4 w	WST	Stimulation frequency: 10 Hz, intensity: 80% MT, 20 min per session. Once a day	Undescribed stimulation site
Guo JY 2022 ²¹	33 (16/17)	32 (17/15)	65.42 ± 4.82	65.72 ± 4.79	4.00 ± 1.20 y	3.53 ± 1.34 y	RT+feeding training + NMES	RT + feeding training	20 d	WST and SSA score	Electric parameters: 0–25 mA, wave width approximately 700 µs; 45 min per session. Twice daily	Placed vertically and equidistantly above and below the hyoid bone in the midline of the neck
Tan JS 2019 ²²	17(9/8)	19 (12/7)	75.8 ± 8.4	73.9 ± 9.5	36.6 ± 7.6 w	39.1 ± 8.5 w	RT + NMES	RT	15 d	SSA score	Stimulation frequency: 80 Hz, Electric intensity 6.5–7.5 mA, 40 min per session. Once a day.	Both sides of the median line of the throat
Wang YF 2016 ²³	30 (19/11)	30 (16/14)	68.4 ± 6.1	67.2 ± 5.1	NA	NA	NMES	Sham NMES	14 d	PAS score	Electric intensity: 6–15 mA, 30 min per session. Twice daily	Undescribed stimulation site
Zhu YH 2021 ²⁷	40 (26/14)	40 (24/16)	62.7 ± 1.6	63.9 ± 1.7	8.9 ± 1.3 y	8.8 ± 1.2 y	RT + rTMS	RT	30 d	VFSS score SSA score	Stimulation frequency: 5 Hz, intensity: 80% MT, 20 min per session. Twice daily	Occipital region and left prefrontal dorsolateral region.
Zheng XQ 2018 ²⁸	45 (28/17)	45 (29/16)	64.5 ± 1.3	63.8 ± 1.5	5.3 ± 2.1 y	5.1 ± 1.9 y	rTMS	Sham rTMS	20 d	SSA score WST	Stimulation frequency: 5 Hz, intensity: 80% MT, 20 min per session. Once a day	Anterolateral motor cortex of the brain and precentral sulcus premotor area
Wang L 2020 ²⁴	79 (46/33)	79 (42/37)	65.13 ± 3.27	64.53 ± 3.06	5.6 ± 2.3 y	5.7 ± 2.0 y	RT + Mendelsohn therapy + NMES	RT + Mendelsohn therapy	4 w	VFSS score and WST	Stimulation frequency: 40–80 Hz, intensity: 7–10 mA, wave width: 700 µs, 20 min per session. Twice daily	Placed horizontally above the hyoid bone and The upper and lower parts of the thyroid cartilage
Park JS 2018 ²⁵	9 (5/4)	9 (3/6)	63.44 ± 13.55	54.67 ± 13.82	36.44 ± 7.5 w	36.11 ± 7.94 w	NMES	Sham NMES	4 w	PAS score	a fixed 80–Hz pulse rate and a fixed biphasic pulse duration of 700µs, 30 min per session, intensity of 1.0 mA	The electrodes were placed in the infrahyoid area, targeting the sternohyoid muscles
Khedr EM 2019 ²⁹	19(Data available for PAS: 9)	11(Data available for PAS: 6)	60.7 ± 8.8	57.4 ± 10.0	5.7 ± 3.9 y	6.5 ± 3.7 y	rTMS	Sham rTMS	2 w	PAS score	10 trains of 20–Hz stimulation. The stimulation intensity was set at 90% of the rMT for the first dorsal interosseous of the contralateral hand, with a total of 2000 pulses for each hemisphere.	Each hemisphere

Abbreviations: NMES, neuromuscular electrical stimulation; y, year; d, day; w, week; NA, not applicable; WST, water-swallow test; VFSS, Videofluoroscopic Swallowing Study; SSA, Standardized Swallowing Assessment; PAS, Penetration-Aspiration Scale; RT, regular treatment; MT, motion threshold; SD, standard deviation; rMT, resting motion threshold; rTMS, repetitive transcranial magnetic stimulation.

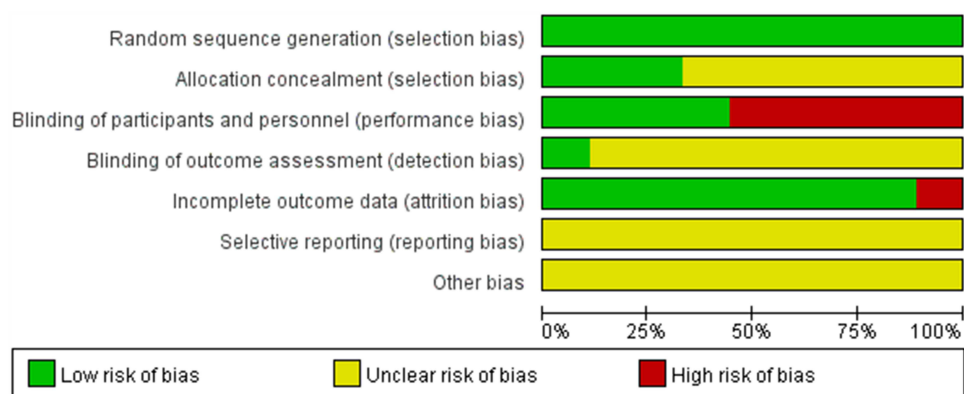


Figure 2 Risk of bias graph.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Guo JY 2022	+	?	-	?	+	?	?
Kang JL 2022	+	+	-	?	+	?	?
Khedr EM 2019	+	+	+	+	-	?	?
Park JS 2018	+	+	+	?	+	?	?
Tan JS 2019	+	?	-	?	+	?	?
Wang L 2020	+	?	-	?	+	?	?
Wang YF 2016	+	?	+	?	+	?	?
Zheng XQ 2018	+	?	+	?	+	?	?
Zhu YH 2021	+	?	-	?	+	?	?

Figure 3 Risk of bias summary.

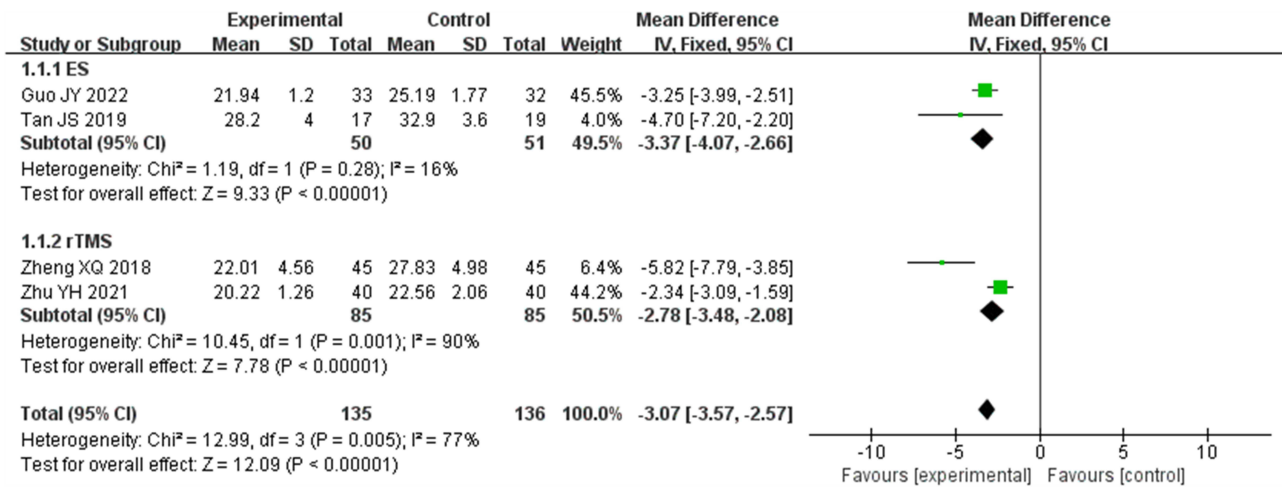


Figure 4 Forest plot of the Standardized Swallowing Assessment (SSA) scores comparison between the experimental and control groups, based on a subgroup analysis of different intervention measures.

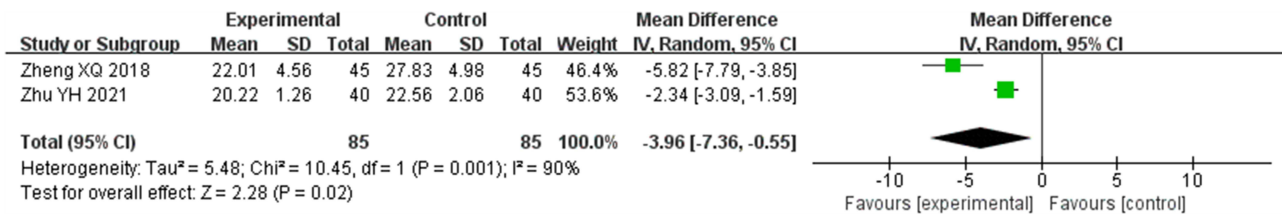


Figure 5 Forest plot of the Standardized Swallowing Assessment (SSA) scores comparison between the experimental and control groups.

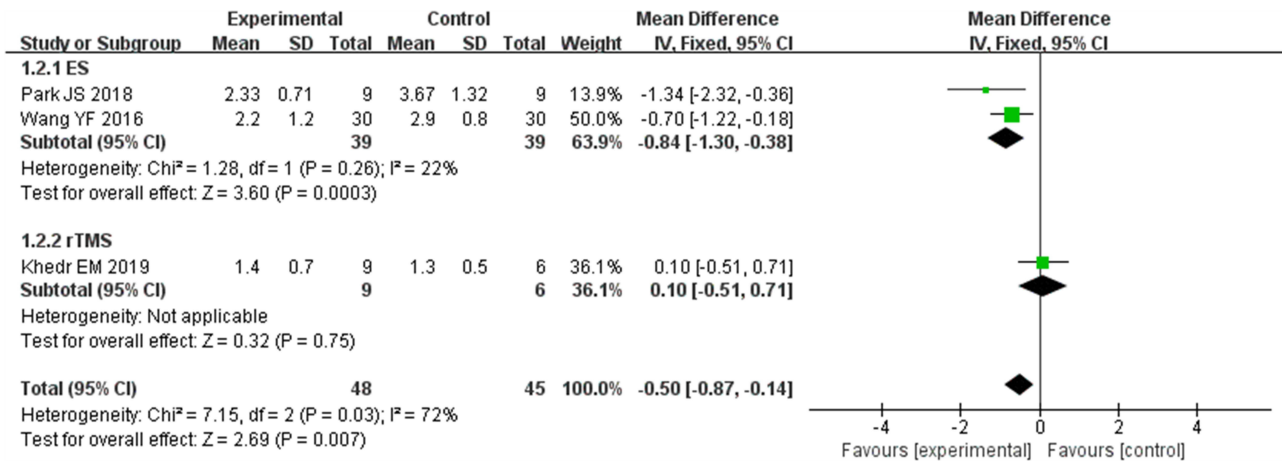


Figure 6 Forest plot of the Penetration-Aspiration Scale (PAS) scores comparison between the experimental and control groups, based on a subgroup analysis of different intervention measures.

invasive nerve stimulation and conventional treatment groups (MD: 1.35; 95% CI: 1.00, 1.70; P < 0.00001). However, a subgroup analysis was conducted, considering that the two items represent different intervention methods. The results showed a significant difference in the VFSS scores between the NMES combined with conventional treatment and conventional treatment alone (MD: -1.47; 95% CI: 1.02, 1.92; P < 0.00001), and there was a significant difference in the VFSS scores between the rTMS and control groups after treatment (MD: 1.18; 95% CI: 0.64, 1.72; P < 0.00001) (Figure 7).

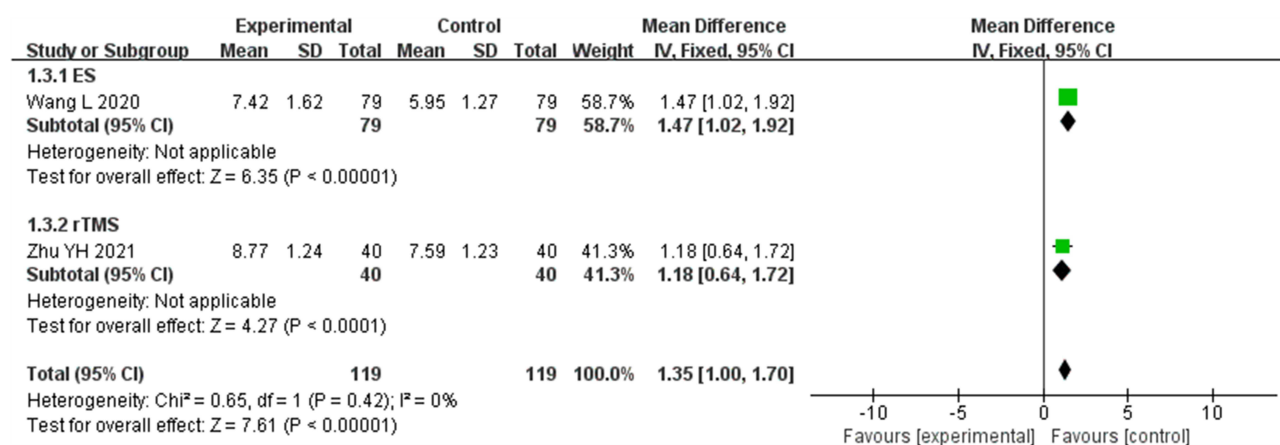


Figure 7 Forest plot of the Videofluoroscopic Swallowing Study (VFSS) scores comparison between the experimental and control groups, based on a subgroup analysis of different intervention measures.

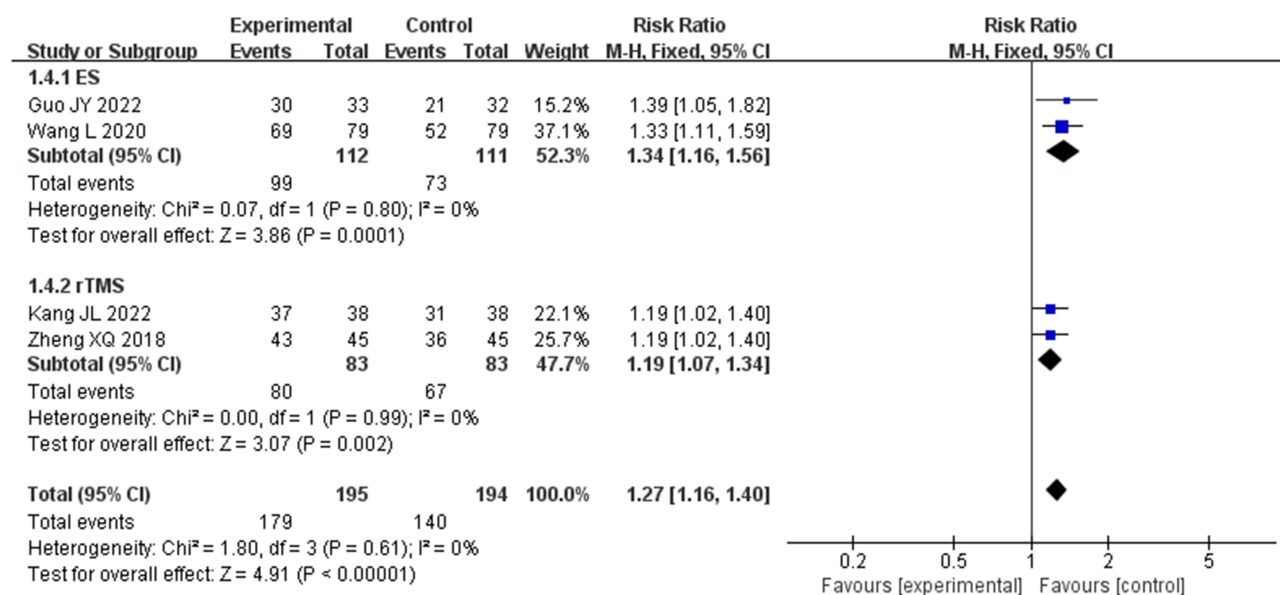


Figure 8 Forest plot of the clinical effectiveness rate comparison between the experimental and control groups, based on a subgroup analysis of different intervention measures.

Clinical Effectiveness Rate

Four studies reported the clinical effectiveness rate, including two NMES and two rTMS interventions. Meta-analysis showed no heterogeneity among the four studies ($P = 0.61$, $I^2 = 0\%$), and a significant difference was observed in the clinical efficiency between the non-invasive nerve stimulation and the conventional treatment groups (RR: 1.27; 95% CI: 1.16, 1.40; $P < 0.00001$). However, a subgroup analysis was conducted, considering that the two items represent different intervention methods. The results showed no heterogeneity between the two RCTs in the NMES intervention group ($P = 0.80$, $I^2 = 0\%$). The fixed effects model showed a significant difference in clinical efficacy between the NMES combined with conventional treatment and conventional treatment alone (RR: 1.34; 95% CI: 1.16, 1.56; $P = 0.0001$). The two RCTs in the rTMS intervention group showed no heterogeneity ($P = 0.80$, $I^2 = 0\%$). The results showed a significant difference in the clinical effectiveness rate between the two groups (RR: 1.19; 95% CI: 1.07, 1.34; $P = 0.002$), indicating that rTMS can improve the swallowing function of patients with PD (Figure 8).

Publication Bias

The number of studies included was <10; therefore, a funnel plot was not used for the publication bias studies.

Discussion

Main Results and Analysis

This study included nine RCTs and selected four indicators to evaluate patients' swallowing function. The SSA is a commonly used scale for assessing swallowing disorders that evaluates patients' swallowing status in multiple dimensions. The VFSS is an "ideal method" for checking swallowing function. It can comprehensively and dynamically observe the swallowing situation of patients, measure movement and time parameters during swallowing, check for residual leakage and risk of aspiration,^{30,31} and evaluate the swallowing function status of patients using the VFSS rating scale. The PAS scale is commonly used to assess a patient's swallowing leakage and aspiration. The WST is a widely used method to evaluate swallowing difficulties in clinical practice, and Chinese scholars often use it to quantify clinical efficacy. Therefore, we conducted a combined analysis of the effects of these four indicators to observe the improvements in swallowing in patients on the basis of multiple perspectives.

Our literature search found that the most commonly used non-invasive nerve stimulation methods in clinical practice currently include rTMS, NMES, surface electromyographic stimulation, transcranial direct current stimulation, biofeedback therapy, percutaneous electrical stimulation, etc. However, the nine studies that met the inclusion criteria only included two intervention methods: rTMS and NMES. No RCTs on transcranial direct current stimulation, surface electromyography stimulation, biofeedback therapy, or percutaneous electrical stimulation for the treatment of swallowing disorders in PD have been published in the past decade according to our literature search. Meta-analysis results show that non-invasive nerve stimulation may reduce the risk of inhalation and penetration and can improve swallowing function in patients with PD and dysphagia. However, heterogeneity among multiple studies may be associated with different intervention plans and the degeneration and complexity of PD. The subgroup analysis showed that NMES reduced the SSA and PAS scores and improved the VFSS score and clinical efficacy. rTMS can reduce the SSA score and improve the VFSS score and clinical efficacy. However, one study showed that rTMS did not significantly improve the PAS scores. Through a full-text reading, this result may be associated with factors such as a small sample size and short intervention time. However, we did not obtain sufficient evidence regarding the efficacy of non-invasive neural stimulation alone, which may be associated with the synergistic effect of non-invasive neural stimulation and other therapies. Notably, a limited number of studies are available to analyze the two intervention measures; therefore, it is essential to interpret this study's results cautiously. Therefore, our systematic evaluation and meta-analysis provide a reference and potential insight for future research on non-invasive neural stimulation for treating dysphagia in patients with PD.

Peripheral mechanisms are involved in PD swallowing disorders; swallowing-related muscle group movement and sensory disorders cause swallowing difficulties in patients with PD.⁹ As a peripheral stimulus, NMES stimulates the muscle around the face or neck through surface electrodes.³² It aims to strengthen the sensory input of the swallowing muscle group in these areas, activate sensory pathways, stimulate the nerves and nerve endplates in muscle fibers, promote the retraining of functional muscle contraction patterns, and improve swallowing muscle group function and hyoid motor ability, thus improving swallowing function.^{33–36}

Unlike invasive deep brain stimulation, rTMS regulates brain activity through electromagnetic induction and promotes changes in brain plasticity.^{33,37} On the basis of the principle of neural plasticity, research shows that rTMS can induce changes in neural plasticity in the swallowing motor cortex, increase the excitability of the swallowing cortex, and improve swallowing function.^{38–40} Khedr et al²⁹ found that rTMS can effectively improve pharyngeal transport time in patients with PD swallowing disorders, reduce the Arabic swallowing disorder index score, and improve swallowing function. However, a consensus on managing dysphagia in patients with PD, mainly published by Italian experts, suggests that using rTMS to treat swallowing disorders in patients with PD is currently not recommended in clinical practice because of the small sample size data obtained from a single study and a lack of standard treatment plans.⁴¹

Implications of This Research

PD is a neurodegenerative disorder. This study found that all included studies evaluated only short-term effects, with a maximum of 30 days. The short-term efficacy was good, but we could not determine whether non-invasive nerve stimulation could provide long-term efficacy. Although we found that non-invasive nerve stimulation has an adjuvant therapeutic effect, only two intervention methods, rTMS and NMES, were found to be effective. Further research is still required on other non-invasive nerve stimulation intervention methods, and the mechanism of action is not yet clear. In the future, new intervention measures for non-invasive nerve stimulation should be explored. This study found that non-invasive nerve stimulation has an adjuvant therapeutic effect; however, its mechanism of action is currently unclear, and large-scale clinical trials are lacking. Consequently, the nine included studies had different descriptions of stimulation sites and parameters. Future research should focus on stimulation sites and parameters to provide more objective references for clinical applications.

Standard treatment programs for non-invasive nerve stimulation remain unavailable. In the future, using consistent, comparable, and repeatable treatment methods for patients with PD to study the impact of non-invasive nerve stimulation on swallowing function is necessary. Therefore, a comprehensive description of testing methods and processes is required. In response to the different evaluation methods, future research is required to provide more details on instrument measurement methods for swallowing. Detailed information on the type and concentration ratio of barium used in the VFSS, equipment for data capture, and measurement methods is required. A quantitative evaluation of VFSS, such as the measurement of oral transport, soft palate lifting, hyoid bone displacement, and cricopharyngeal muscle opening times, is recommended.⁴² An anonymized setting for evaluators and researchers should also be ensured. In addition, current studies exist on staging treatments for swallowing disorders in patients with PD.⁴³ It is recommended to consider staging treatments on the basis of swallowing disorders in the future.

The manifestations and progression of dysphagia in patients with PD vary between individuals, and the potential mechanisms underlying the progression of dysphagia in patients with PD remain unclear. This poses a challenge in the management and treatment effectiveness of swallowing disorders.⁴⁴ A previous study reported changes in the neural networks of patients with PD with dysphagia. Patients with PD with swallowing difficulties have significantly increased functional connectivity in the cerebellum, left anterior motor cortex, auxiliary motor area, superior temporal gyrus, right temporal pole, inferior frontal gyrus, and insula than those without swallowing difficulties. The changes in the functional connectivity in the swallowing-related cortex may lead to swallowing difficulties in patients with PD.⁴⁵ Cortical swallowing activation was significantly reduced in all patients. In patients with PD, the brainstem, basal ganglia circuits, and the cortical regions regulate swallowing function in clinically relevant ways.⁴⁶ Therefore, future research on treating PD swallowing disorders should evaluate the impact on swallowing physiology and nerve control. It is necessary to further study the changes in the swallowing neural network after interventions to guide swallowing disorder treatment in patients with PD.

Limitations

This study followed the standards specified in PRISMA but has some limitations. The design of random trial methods in some of the included studies was not sufficiently standardized, and allocation concealment was not fully described, as the absence of anonymity for participants and outcome evaluators increases the risk of outcome bias. The evaluation criteria for the efficacy of the studies were different, and the main observation indicators of the studies were scales, lacking quantitative research on objective indicators. Notably, most studies focused on short-term clinical efficacy research and observation and lacked a long-term efficacy evaluation. Therefore, all these factors may cause bias in the system evaluation, have a specific impact on the reliability of the results, and even exaggerate the clinical efficacy.

Conclusion

NMES and rTMS are effective adjunctive therapies for treating dysphagia in patients with PD and improving the swallowing function in these patients. However, owing to the included literature's quality and quantity, the overall evidence for the efficacy of non-invasive nerve stimulation in treating swallowing disorders in patients with PD is still insufficient. Therefore, it is still necessary to further conduct high-quality clinical RCTs with multi-center, large samples, reasonable and standardized trial designs, and verify strict standard executions.

Data Sharing Statement

The dataset analyzed in this study can be obtained through the corresponding author.

Ethics Statement

Based on Article 32 of China's *Measures for Ethical Review of Life Sciences and Medical Research Involving Humans*, which outlines overarching principles for exemption from ethical review—specifically, that the research “does not cause harm to human subjects, involve sensitive personal information, or implicate commercial interests”—this study qualifies under its first and second clauses. The first clause permits the use of legally acquired public data, while the second allows research involving anonymized data, defined as information processed so that individuals cannot be identified, and the original identities cannot be restored.

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Disclosure

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