BMC Neurology

SYSTEMATIC REVIEW

Open Access

Therapeutic efficacy of repetitive transcranial magnetic stimulation on gait and limb balance function in patients with lower limb dysfunction post-cerebral infarction: a systematic review and meta-analysis

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Abstract

Background This investigation is designed to evaluate the effects of rTMS and its varying stimulation parameters and target sites on the therapeutic outcomes for post-stroke lower limb motor impairment and balance, with the objective of pinpointing stimulation locations and parameters that are both reasonable and applicable in clinical practice.

Materials and methods An exhaustive search was carried out across the PubMed, MEDLINE, Embase, CENTRAL, and Web of Science databases to identify RCTs that assessed the effectiveness of rTMS in the treatment of lower limb motor impairment following a stroke. Meta-analysis was performed usingR statistical environment (V.4.2.2, www.r-project.org). The review period encompassed the interval from the databases' origination through to February 18, 2024.

Results Research reveals that applying rTMS to the unaffected motor cortex markedly enhances gait speed in stroke patients,exhibiting a significant effect (SMD: 1.117, 95% CI:0.40, 1.82, $I^2 = 0.0\%$). rTMS sessions comprising 1000–1500 pulses (SMD: 0.92, 95% CrI:0.63, 1.21, $I^2 = 42\%$, six studies), with a total session count ≥ 10 (SMD: 0.85, 95% CrI:0.53, 1.18, I2 = 54.1%, six studies), and high-frequency rTMS (SMD: 0.83, 95% CrI:0.34, 1.09, $I^2 = 46.3\%$, three studies) exhibit significant efficacyin improving lower limb balance and gait post-stroke.

Conclusions The research indicates that rTMS has been instrumental in enhancing the post-stroke prognosis for gait and limb balance. Nevertheless, the therapeutic efficacy of rTMS is subject to the diversity in stimulation locations and parameter settings.

Keywords Stroke, Lower limb motor dysfunction, Repetitive transcranial magnetic stimulation, Meta-analysis

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Background

Stroke, a common neurological ailment, often leads to a decline in motor control, manifests as functional impairments including muscle atrophy, loss of balance, and challenges in ambulation [1]. Research highlights an escalating trend in stroke occurrences within China, especially amongst the elderly population. Over 60% of individuals who have suffered a stroke report experiencing different degrees of limb motor dysfunction [2], frequently resulting inlimitations indaily activities [2]. Furthermore, spasticity in the limbs, a condition frequently encountered by stroke survivors, not only hampers walking ability but also detracts from their overall well-being and diminishes the quality of life [3]. Meanwhile, An atypical walking pattern increases the likelihood of falls in post-stroke individuals [3]. Studies have demonstrated that post-stroke rehabilitation therapy is crucial in diminishing the incidence of disability in affected individuals [4]. Consequently, it is of utmost importance to discover a secure and efficient approach to rehabilitation.

Various therapeutic modalities, such as pharmacological intervention, physical rehabilitation, and occupational therapy, are employed to reclaim gait and balance capabilities in post-stroke patients. Nevertheless, the effectiveness of these treatments is often constrained [4]. rTMS entails the generation of electrical currents within the subjacent tissue by delivering a sequence of magnetic field pulses through an rTMS coil [5]. Frequencies ≤ 1 Hz are considered low frequency and can decrease neuronal excitability, while frequencies > 1 Hz, termed high frequency, can increase neuronal excitability [5]. rTMS adjusts synaptic plasticity by eliciting long-term potentiation or suppression [6], which in turn facilitates the reconfiguration of cortical function and the restructuring of the brain's network system through cortico-cortical connections [6]. The therapeutic mechanisms of rTMS encompass modifications in voltage-gated ion channels, adjustments in the flux rates of sodium and calcium ions, facilitation of neurotransmitter secretion, and stimulation of neurotrophic factor receptor activation [7, 8]. rTMS has demonstrated remarkable effectiveness in the treatment of a spectrum of conditions, including Parkinson's disease, stroke, depression, epilepsy, and sleep disturbances [6, 8, 9]. Scores of clinical investigations have elucidated substantial enhancements in various conditions including motor impairments, swallowing difficulties, aphasia, and chronic pain in stroke patients treated withrTMS, with a notable focus on the improvement of limb motor capabilities [10–12]. Nevertheless, certain research indicates that rTMS does not yield a substantial enhancement in gait improvement [13]. Moreover, substantial variations exist in patient demographics (age, disease duration, stroke site, severity), methodology (intervention frequency, assessment timing), rTMS parameters (stimulation protocol, target area), and outcome assessment [14–16].

Therefore, this research employed meta-analysis as a method to consolidate and scrutinize various treatment protocols, rTMS parameters, and stimulation locations aimed at enhancing limb motor function and addressing balance impairments following a stroke. The objective of this research is to assess the influence of rTMS along with varying stimulation parameters and target sites on the therapeutic outcomes for motor impairments in the lower limbs and balance issues following a stroke. The intent is to pinpoint stimulation locations and parameters that are both logical and applicable, thereby establishing a scientific foundation for the utilization of rTMS in improving walking ability and limb balance in post-stroke patients.

Methods

Protocol and registration

A systematic review and meta-analysis were administered the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [17]. The protocol number registered at https://inplasy.com/, registered under the identification number INPLASY202440112.

Study inclusion and exclusion criteria

Admission criteria, in adherence to the PICOS framework [18], were established as follows:(a) participants diagnosed with stroke;(b) intervention involving rTMS or its advanced variants; (c)comparison with a sham group; (d) outcomes comprising pre- and post-interventional assessments of gait velocity, balance or lower limb motor function or both; (e)study design including published randomized control trials (RCTs), whether individually designed, cluster designed, or the first phase of crossover trials. Exclusions were imposed on studies that investigated the immediate impacts of a solitary session on individuals post-stroke, as well as those that failed to delineate the precise stimulation site for rTMS, RMT, or the specific count of pulses administered per session. Unregulated single-arm studies, zoological investigations, individual case narratives, methodical assessments, scholarly examinations, seasoned expert insights, and symposium proceedings. Additionally, research lacking comprehensive documentation of averages and standard deviations in the outcomes, or where corresponding authors failed to furnish supplementary data upon request, were omitted from consideration.

Literature search and data extraction

A comprehensive search was performed across the PubMed, MEDLINE, Embase, CENTRAL, and Web of Science databases from their inception until February 18, 2024, with no language constraints. Specific search terms("rTMS" OR "iTBS") AND ('Stroke') AND ("balance" or "postural control" or "gait" or "walking" or "lower limbs") were utilized (online supplementary tables 1–5).The reference lists from the included studies and prior reviews were meticulously examined to identify any additional pertinent research. Ming-wei Liu performed the initial search and systematically eliminated duplicate entries. Subsequently, Qiu-juan Zhang and Bin-ran Zhang meticulously reviewed the titles and abstracts of distinct studies, adhering to a set of pre-established inclusion and exclusion criteria. Ming-wei Liu and Lin-ming Zhang conducted a thorough and independent assessment of the full texts that align with these criteria, with Ming-wei Liu addressing any inconsistencies that arose. Details of the search methodology are outlined in the Supporting File(see Search Strategy).

Study selection

The literature screening procedure was carried out by a quartet of independent reviewers, namely De-mei Jia, Xuan Li, Bin-cang Zhang, and Qiu-juan Zhang. They meticulously evaluated the titles, abstracts, and full texts to ascertain their conformity with the specified eligibility criteria. Titles, abstracts, and full-text screenings were done using Rayyan and Google spreadsheets, respectively [19, 20]. In instances where discrepancies emerged among the investigators, they adopted a consensus-driven method to arrive at decisions. Should further clarification be required, a fifth investigator, Ming-wei Liu, was brought in to aid in resolving any conflicts that occurred.

Data extraction

Following the preliminary examination of titles and abstracts, Qiu-juan Zhang and Ming-wei Liu meticulously evaluated the comprehensive content of all likely pertinent articles. During the thorough assessment, they extracted data regarding(1) participant characteristics, such as sample size, age, and gender; (2) intervention specifics, including the types of training and whether a professional physical therapist supervised it; (3) training-related variables; and (4) the main outcomes of this study (gait velocity, balance and lower limb motor function), and outcome measures were extracted. According to the office guidance of Cochrane Handbook for Systematic Reviews [21], the correlation coefficient (Corr) was set to 0.5 [22]. Additionally, the corresponding author of the manuscript was contacted in case of incomplete raw data. Studies were excluded where the authors could not be reached. All research evaluations were conducted separately by Qiu-juan Zhang and Bin-ran Zhang, utilizing the collated information as their basis. In the event of discrepancies concerning the inclusion of any study, Ming-wei Liu and Lin-ming Zhang were sought for their expert consultation. The collated data from the incorporated studies are presented in Table 1.

Assessment of risk of bias

The potential for bias within each individual study was meticulously evaluated by Lin-ming Zhang and Ming-wei Liu, utilizing the Cochrane Risk of Bias version 2 tool (RoB2) [23], including five domains. The evaluation criteria encompassed the generation of randomized sequences, potential biases arising from deviations from the planned intervention, the issue of incomplete data, inaccuracies in measurements, and partiality in the reporting of outcomes. Moreover, for cluster randomized controlled trials, the RoB2.0 instrument incorporates an extra category to gauge the risk of bias related to the timing of participant identification and enrollment, alongside the aforementioned five domains [24]. Each area was assessed as (1) high risk, (2) low risk and (3) some concern. For every investigation, should all evaluated domains present minimal risk, the cumulative risk of bias is deemed to be low; conversely, should any domain exhibit significant risk, or if several domains collectively elicit moderate concern, the aggregate risk of bias is rated as high. In all other instances, the overall risk of bias remains low. Any discrepancies among assessors were reconciled through mutual agreement or, when necessary, by consulting an additional reviewer.

Meta-analysis

We analyzed all the data based on the R statistical environment (V.4.2.2, www.r-project.org), and we used the "meta" package to merge the data results.To explore possible heterogeneity in our study, which aimed to examine the influence of rTMS-specific variables on our outcomes, the impact of various covariates, including rTMS types, dosage (pulses/session, total sessions, RMT (%)), and stimulation site, was analyzed using meta-regression and subgroup analysis by the "metareg" package.The Higgins score (I^2) test was utilized to explorethe diversity within clinical trial outcomes,a chi-square P value below 0.1 was deemed indicative of significant heterogeneity. $P > 0.1$ and $I^2 < 50\%$ implied a small heterogeneity among thesestudies, and thisfixed-effect model was implemented in such cases. $P \leq 0.1$ or $I^2 \geq 50\%$ indicated heterogeneity among the studies, and the random-effects model was utilized in these instances, followed by an analysis of heterogeneity

Table 1 Characteristics of the studies and subjects included in the review

Study	Mean age	Sample size (male/female)	Onset (months)	Side of lesion (left/right)	Intervention detail	Stimulation site	Outcomes
Chieffo et al. (2021)	60 ± 9	12 (6/6)	41.25 ± 24.12	5/7	rTMS: 20 Hz, 90% RMT, 1600 pulses/session, 3 weeks, 11 sessions	leg M1, unaffected	FMA-LE, 10 m WT
Choi et al. (2016)	rTMS: 67.1 ± 3.8 Sham: 68.7 ± 5.2	rTMS: 15(14/1) Sham: 15(13/2)	rTMS: 49.6 ± 28.3 Sham: 44 ± 29.9	rTMS: 8/7 Sham: 7/8	rTMS: 10 Hz, 90% RMT, 1000 pulses/session, 2 weeks, 10 sessions	trunk M1, bilateral	BBS
Forogh et al. (2017)	66 ± 6.5	26(16/10)	22 (84.6%) was more than 6 months	26(18/8)	rTMS: 1 Hz, 90% RMT, 1200 pulses/session, 1 weeks, 5 sessions	upper limb M1, unaffected	FMA-LE, BBS
Y.-N. Lin et al. (2015)	rTMS: 58.3 ± 10.8 Sham: 62.3 ± 11.7	rTMS: 16(10/6) Sham: 16(11/5)	rTMS: 1.35 ± 0.97 Sham: 1.11 ± 0.79	rTMS: 10/6 Sham: 7/9	rTMS: 1 Hz, 130% RMT, 900 pulses/session, 3 weeks, 15 sessions	leg M1, bilateral	FMA-LE
C. Wang et al. (2023)	H rTMS: 63.85 ± 9.54 L rTMS: 63.92 ± 10.28 Sham: 64.10 ± 9.96	H rTMS: 80(54/26) L rTMS: 80(51/29) Sham: 80(52/28)	H rTMS: 0.71 ± 0.09 L rTMS: 0.80 ± 0.11 Sham: 0.71 ± 0.1	H rTMS: 42/38 L rTMS: 39/41 Sham: 37/43	H rTMS: 10 Hz, 90% RMT, 1200 pulses/session, 3 weeks, 18 sessions L rTMS: 0.5 Hz,90% RMT, 1200 pulses/session, 3 weeks, 18 sessions	H rTMS: M1, affected L rTMS: M1, unaffected	FMA-LE, BBS
Yu et al. (2022)	rTMS: 54.6 ± 11.83 Sham: 57.37 ± 12.78	rTMS: 9(7/2) Sham: 9(8/1)	rTMS: 1.01 ± 0.32 Sham: 1.34 ± 0.27	rTMS: 4/5 Sham: 3/6	rTMS: 5 Hz, 80% RMT, 1200 pulses/session, 2 weeks, 10 sessions	left dorsolateral prefrontal cortex projection area	FMA-LE, BBS, 10 m WT
R.-Y. Wang et al. (2012)	rTMS: 64.90 ± 12.37 Sham: 62.98 ± 10.88	rTMS: 12(7/5) Sham: 12(8/4)	rTMS: 24 ± 29.52 Sham: 22.08 ± 13.92	rTMS: 6/6 Sham: 8/4	rTMS: 1 Hz, 90% RMT, 600 pulses/session, 1 week, 10 sessions	M1, unaffected	FMA-LE, MWT
Chieffo et al. (2014)	62.2 ± 6.25	10	21 ± 7.28	4/6	rTMS: 20 Hz, 90% RMT, 1500 pulses/session, 3 weeks, 11 sessions	hand or leg M1, bilateral	FMA-LE, 10 m WT
Huang et al. (2018)	rTMS: 62.2 ± 10.4 Sham: 61.2 ± 9.4	rTMS: 18(10/8) Sham: 20(13/7)	rTMS: 1.03 ± 0.85 Sham: 0.86 ± 0.6	rTMS: 11/7 Sham: 10/10	rTMS: 1 Hz, 120% RMT, 900 pulses/session, 2 weeks, 15 sessions	leg M1, bilateral	FMA-LE
Kim et al. (2014)	rTMS: 67.4 ± 7.8 Sham: 64.8 ± 11.7	rTMS: 22(11/11) Sham: 10(6/4)	rTMS: 0.54 ± 0.43 Sham: 0.50 ± 0.17	NA	rTMS: 1 Hz, 100% RMT, 900 pulses/session, 1 week, 5 sessions	M1, affected	10 m WT, BBS
Koch et al. (2019)	iTBS: 63 ± 11 Sham: 65 ± 12	iTBS:18(12/6) Sham:18(11/7)	iTBS: 14.52 ± 17.73 Sham: 11.87 ± 17.04	iTBS:6/12 Sham:8/11	iTBS: 90% RMT, 1200 pulses/session, 3 weeks, 21 sessions	leg M1, bilateral	FMA-LE, BBS
L.-F. Lin et al. (2019)	iTBS: 60.8 ± 8.1 Sham: 61.1 ± 9.7	iTBS: 10(9/1) Sham: 10(8/2)	iTBS: 11.96 ± 5.7 Sham: 12.8 ± 9	iTBS: 5/5 Sham: 6/4	iTBS: 100% RMT, 1200 pulses/session, 5 weeks, 10 sessions	leg M1, bilateral	FMA-LE, BBS, 10 m WT

Table 1 (continued)

Study	Mean age	Sample size (male/female)	Onset (months)	Side of lesion (left/right)	Intervention detail	Stimulation site	Outcomes
Rastgoo et al. (2016)	rTMS: 54.6 ± 11.78 Sham: 49.7 ± 11	rTMS: 10(8/2) Sham: 10(8/2)	rTMS: 30.2 ± 18.3 Sham: 27.4 ± 20.1	rTMS: 7/3 Sham: 6/4	rTMS: 1 Hz, 90% RMT, 1000 pulses/session, 1 week, 5 sessions	leg M1, unaffected	FMA-LE
Sasaki et al. (2017)	rTMS: 66.5 ± 16.6 Sham: 62.4 ± 10.3	rTMS: 11(8/3) Sham: 10(5/5)	rTMS: 0.37 ± 0.27 Sham: 0.35 ± 0.21	rTMS: 8/3 Sham: 4/6	rTMS: 10 Hz, 90% RMT, 1000 pulses/session, 1 week, 5 sessions	leg M1, unaffected	Brunnstrom Recovery Stages
R.-Y. Wang et al. (2019)	rTMS: 53.5 ± 13.7 Sham: 54.7 ± 12.2	rTMS: 8(7/1) Sham: 6(4/2)	rTMS: 31.8 ± 24.0 Sham: 25.3 ± 15.7	rTMS: 2/6 Sham: 4/2	rTMS: 5 Hz, 90% RMT, 900 pulses/session, 3 weeks, 9 sessions	leg M1, affected	FMA-LE, WT
Liao et al. (2021)	iTBS: 51.53 ± 9.22 Sham: 55.40 ± 8.10	iTBS: 15(12/3) Sham: 15(9/6)	iTBS: 2.35 ± 1.48 Sham: 2.88 ± 1.51	iTBS: 11/4 Sham: 9/6	iTBS: 80% RMT, 600 pulses/session, 2 weeks, 10 sessions	leg M1, unaffected	FMA-LE, BBS
Guan et al. (2017)	rTMS: 59.7 ± 6.8 Sham: 57.4 ± 14.0	rTMS: 21(16/5) Sham: 21(14/7)	rTMS: 0.13 ± 0.11 Sham: 0.16 ± 0.14	rTMS: 11/10 Sham: 12/9	rTMS: 5 Hz, 100% RMT, 1000 pulses/session, 1 week, 10 sessions	M1, unaffected	FMA-LE
Q. Wang et al. (2020)	H rTMS: 58.60 ± 10.58 L rTMS: 60.53 ± 14.11 Sham: 60.47 ± 12.08	H rTMS: 15(11/4) L rTMS: 15(10/5) Sham: 15(9/6)	H rTMS: 0.97 ± 0.57 L rTMS: 1.1 ± 0.66 Sham: 0.78 ± 0.33	H rTMS: 8/7 L rTMS: 7/8 Sham: 8/7	H rTMS: 10 Hz, 100% RMT, 1000 pulses/session, 2 weeks, 14 sessions L rTMS: 1 Hz, 100% RMT, 1000 pulses/session, 2 weeks, 14 sessions	M1, unaffected	FMA-LE

NA Non-available, *RMT* Resting motor threshold, *M1* Motor cortex, *rTMS* Repetitive transcranial magnetic stimulation, *iTBS* Intermittentθ-burststimulation, *FMA-LE* Fugl-Meyer assessmentlower extremity, *WT* Walking test

sources and a subgroup analysis of the factors that may contribute to heterogeneity. Due to the varied methodologies employed in assessing gait velocity, balance, and lower limb motor function, we adopted a random-effects model to ascertain the efficacy of rTMS across these diverse outcomes. Concurrently, our research amalgamates the effect sizes, which are articulated as the standard mean difference (SMD) along with 95% Confidence Interval (CI), with significant as $p < 0.05$, and the effect sizes of their findings were in alignment with the study conducted by Fisch et al.,which small effect size as SMD: < 0.5;moderate effect size as SMD0.5 to 0.8; and large effect size SMD > 0.8 [25].

Publication bias assessment

Furthermore, to ascertain the presence of publication bias, a funnel plot was employed. This allowed us to visually assess the risk of bias under particular conditions. Additionally, Egger's test, conducted using Stata software, indicated the likelihood of publication bias when the p-value was less than 0.05.

Results

Study selection

The preliminary literature search yielded a total of 1710 studies that appeared to be pertinent, as depicted in Fig. 1. Following the removal of 1265 duplicate entries and the exclusion of 186 studies after a meticulous review of their titles and abstracts, a selection of 201 full-text articles underwent thorough evaluation. Ming-wei Liu and Lin-ming Zhang meticulously examined these texts to ascertain the desired outcomes. In the end, the comprehensive systematic review and meta-analysis incorporated a total of 18 research studies [26–43], involving 690 participants. Sample sizes ranged from 6 to 80 individuals, with a mean age of 60.8 years (50–68.7 years).

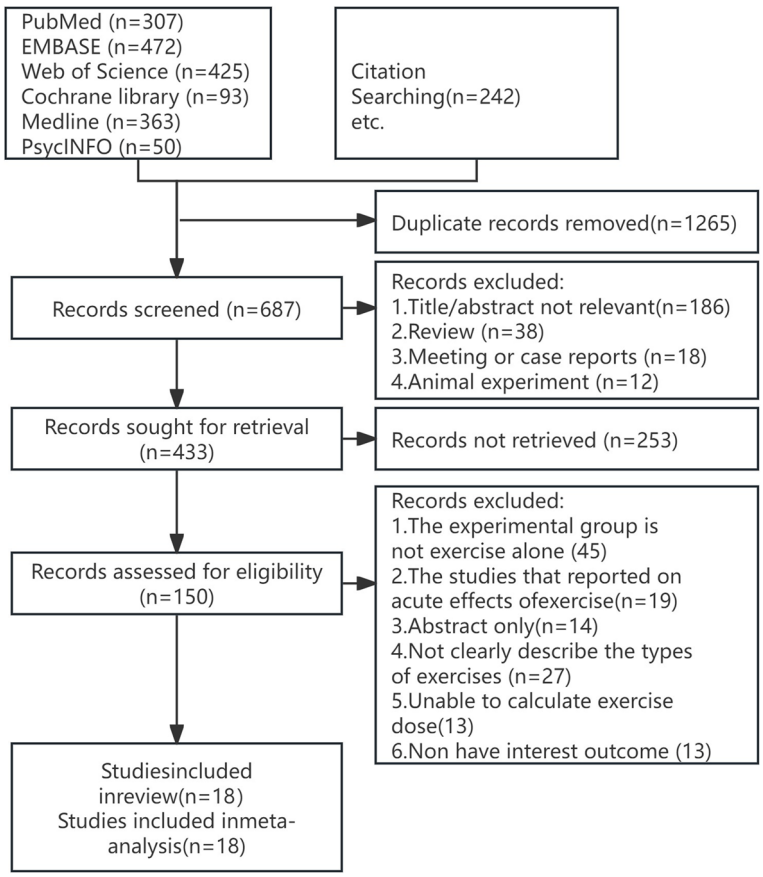

Figure1 Flow chart of literature screening

Study characteristics

The duration of rTMS treatment ranged from a span of 1 to 5 weeks, encompassing between 5 and 21 sessions, with each session delivering 600 to 1600 pulses, and an RMT intensity of 80–130%. Within the reviewed literature, six investigations were conducted to compare the effects of low-frequency rTMS with those of a control sham group [29, 31, 32, 36, 37, 41]. Seven studies directly compared high-frequency rTMS with sham groups (three studies with frequencies of 5 Hz [30, 42, 43], and two each with frequencies of 10 Hz [28, 38] and 20 Hz [26, 27]). Two studies involved direct comparisons of high-frequency and low-frequency rTMS [39, 40]. Moreover, three studies directly comparedintermittent Theta Burst Stimulation (iTBS)with sham groups [33–35] (Table 1).

Risk of bias

Of the 18 trials conducted, nine were identified as having an overall low risk of bias, eight triggered certain reservations, and one was classified as being at a high risk. Detailed assessments within specific domains indicated that, of the trials evaluated for their randomization process, 13 exhibited a low risk, whereas five prompted some concerns. In relation to deviations from the planned interventions, 17 trials posed a low risk, while two were marked by some degree of concern. With respect to the absent outcome data, fifteen studies were classified as having a low risk level; two studies prompted mild concerns, while one was identified as being at a high risk.All 18 trials exhibited a low risk in the assessment of outcome measurements, while in the reporting of selected results, 17 trials were deemed low risk, with only one trial prompting some reservations. The detailed results of the risk of bias analysis are presented in Fig. 2A-B.

Effect of rTMS on lower limb function in stroke patients

Sixteen investigations, encompassing 643 participants, were conducted to assess the functional capabilities of the lower limbs in stroke patients. The results indicated a marked improvement in lower limb function in these patients following rTMS treatment, when contrasted with a control group that received sham stimulation (SMD: 0.45, 95% CrI:0.25, 0.65, $I^2 = 35\%$, Fig. 3).

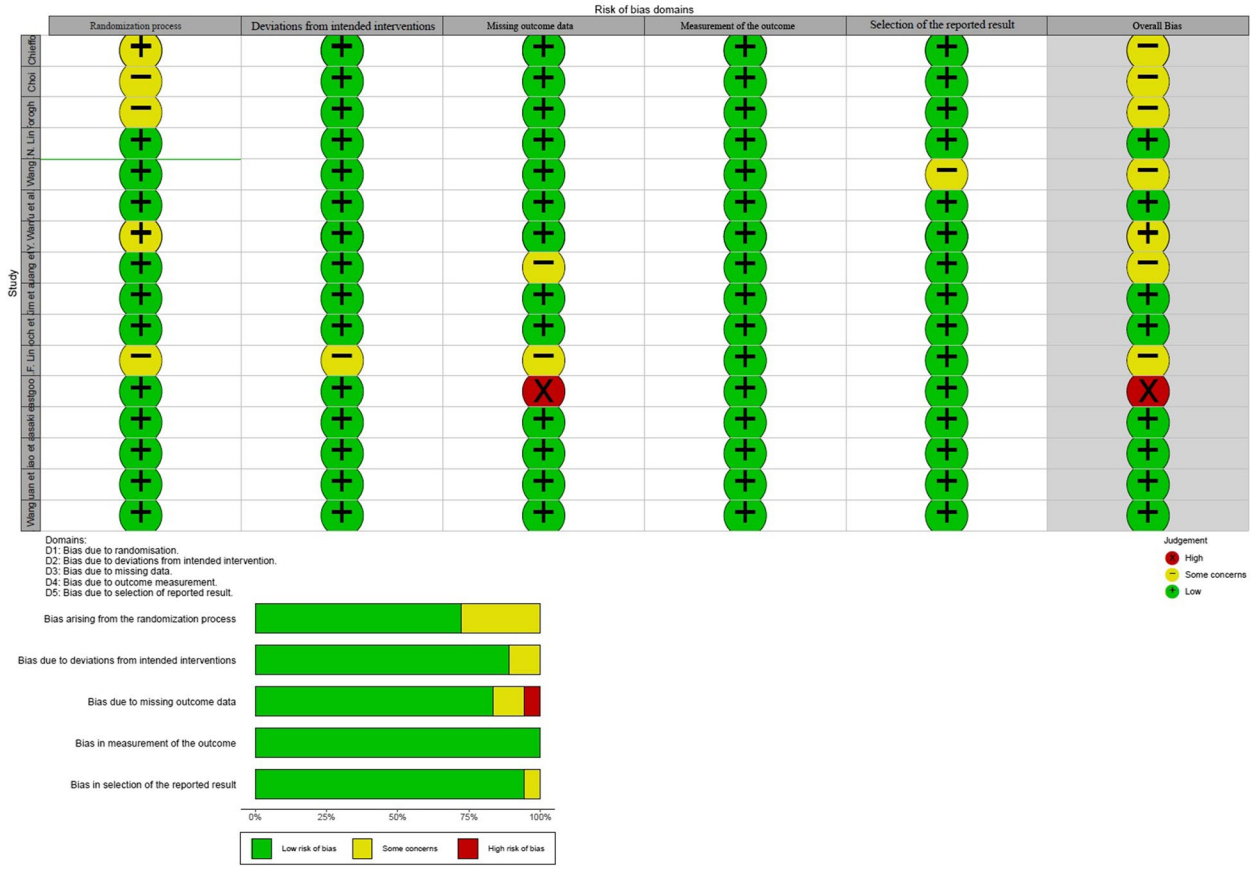

Figure2 Assessment of risk of bias. **A** Summary of risk bias assessment of the included studies. **B** Risk bias assessment of the included studies

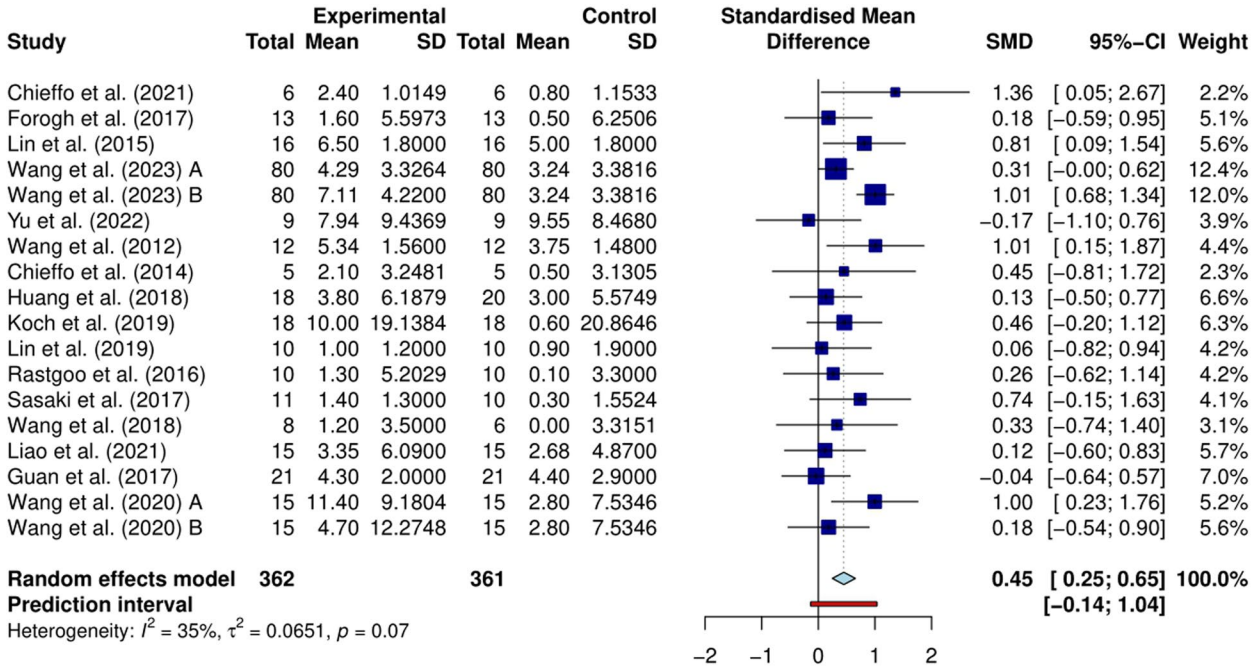

Figure3 Forest map of the effect of rTMS on lower limb function in stroke patients

Meta-regression findings suggest the absence of discernible risk factors impacting the results. Additionally, the subgroup analysis discloses that when targeting the non-motor cortical region, specifically the projection area of the left dorsolateral prefrontal cortex, rTMS failed to elicit a significant enhancement in lower limb functionality among stroke patients (SMD: −0.18, 95% CrI: −1.11, 0.75). Furthermore, it was observed that a recovery motor threshold exceeding 100% and a cumulative session count of less than 10 did not result in a significant improvement in lower limb functionality in stroke patients when contrasted with the control group receiving sham treatment. rTMS with ≥ 1500 pulses per session demonstrated a large effect size in improving lower limb functional ability in patients with stroke (SMD: 0.97, 95% CrI: 0.02, 1.93, $I^2 = 9.1\%$, from two studies) (Table 2).

Effect of rTMS on the gait velocity of stroke patients

Seven investigations encompassing 130 subjects were conducted to evaluate gait velocity in individuals post-stroke. Collectively, these studies revealed that rTMS failed to exhibit a significant enhancement in gait velocity when contrasted with the control group (SMD: 0.28, 95% CrI:−0.21, 0.78, $I^2 = 20\%$, Fig. 4). Meta-regression analysis has demonstrated that the location of stimulation plays a pivotal role in the outcomes ($p = 0.034$). It is imperative to underscore that notable enhancements in gait speed in stroke patients, as opposed to the control group, were exclusively evident when rTMS was administered to the motor cortex of the non-affected hemisphere.This intervention also demonstrated a large effect size(SMD: 1.117, 95% CrI:0.40, 1.82, $I^2 = 0.0\%$, from two studies) (Table 3).

Effect of rTMS on the balance ability of stroke patients

Eight investigations encompassing 512 subjects were conducted to evaluate the balance capabilities in individuals post-stroke. Collectively, these studies demonstrated that rTMS markedly enhanced the balance proficiency in stroke-affected patients, when contrasted with the control group receiving sham treatment (SMD: 0.72, 95% CrI:0.35, 0.1.09, $I^2 = 59\%$, Fig. 5). Meta-regression findings suggest that the number of pulses per session ($p = 0.044$) and the overall number of sessions ($p = 0.004$) were significant determinants of the observed outcomes. Furthermore, the subgroup analysis indicated that particularly when the stimulation was applied to regions outside the motor cortex, the effects were pronounced (left dorsolateral prefrontal cortex projection

Table 2 Summary of meta-regression and subgroup analysis results of rTMS on lower limb function in stroke patients

Covariate	Shared beta	Heterogeneity	Number of studies	SMD(95% CI)
	(mean and 95% CI), *P* value	(I^2)		
None	-	35.00%	16	0.45 (0.25, 0.90)[a]
Type	**−0.04 (−0.37, 0.28), 0.780**	**-**	**-**	**-**
High rTMS	-	27.40%	8	0.41 (0.10, 0.73)[a]
Low rMTS	-	49.00%	7	0.57 (0.22, 0.92)[a]
iTBS	-	38.10%	3	0.25 (−0.17, 0.68)[a]
Stimulation site	**−0.19 (−0.43; 0.07), 0.151**	**-**	**-**	**-**
M1, Affected	-	0.00%	2	0.32 (0.02, 0.62)[a]
M1, Unaffected	-	66.30%	10	0.57 (0.24, 0.90)[a]
M1, Bilateral	-	46.40%	15	0.40 (0.05, 0.74)[a]
LDPC	-	-	1	−0.18 (−1.11, 0.75)
Pulses/session	**0.08 (−0.37, 0.54), 0.702**	**-**	**-**	**-**
< 1000	-	14.90%	5	0.46 (0.09, 0.84)[a]
1000 to 1500	-	51.30%	9	0.42 (0.14, 0.69)[a]
≥ 1500	-	9.10%	2	0.97 (0.02, 1.93)[a]a
Total sessions	**0.18 (−0.13, 0.49), 0.234**	**-**	**-**	**-**
5	-	0.00%	3	0.39 (−0.10, 0.87)
6 to 10	-	3.70%	6	0.19 (−0.15, 0.52)
≥ 10	-	50.10%	7	0.61 (0.32, 0.90)[a]
Resting motor threshold (%)	**0.002 (−0.02, 0.02), 0.847**	**-**	**-**	**-**
80–100	-	40.90%	14	0.46 (0.23, 0.69)[a]
> 100	-	50.10%	2	0.46 (−0.22, 1.14)

M1 Motor cortex, *SMD* Standardized mean difference, *CI* Confidence interval, *LDPC* Left dorsolateral prefrontal cortex projection area, [a]significant therapeutic effect, a large effect size, b Potential factors significantly affect the results

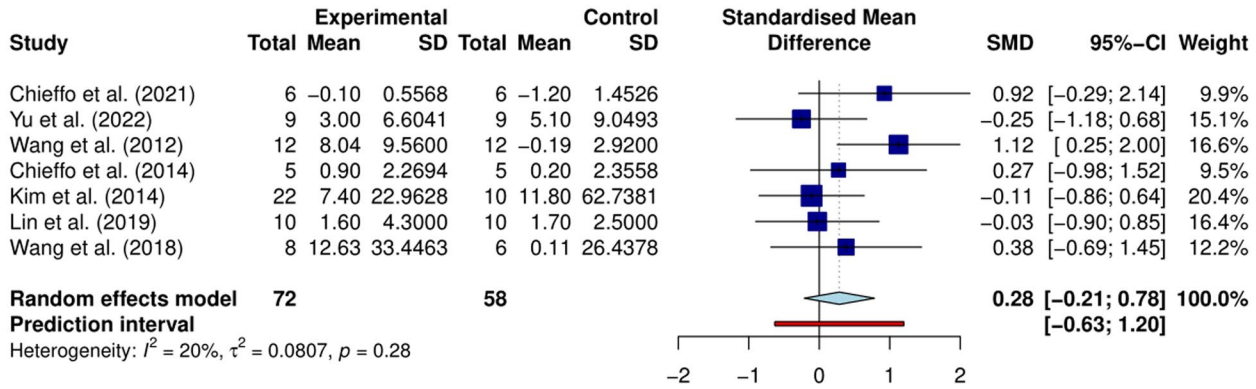

Figure4 Forest map of the effect of rTMS on the gait velocity of stroke patients

Table 3 Summary of meta-regression and subgroup analysis results of rTMS on gait velocity in stroke patients

Covariate	Shared beta	Heterogeneity	Number of studies	SMD
	(mean and 95% CI), *P* value	(I^2)		(95% CI)
None	-	20.00%	7	0.28 (−0.21, 0.78)
Type	**−0.10 (−0.94, 0.75), 0.781**	**-**	**-**	**-**
High rTMS	-	0.00%	4	0.27 (−0.27, 0.82)
Low rMTS	-	78.90%	2	0.51 (−0.74, 1.76)
iTBS	-	-	1	−0.03 (−0.91, 0.85)
Stimulation site	**−0.43 (−0.89, −0.02), 0.034b**	**-**	**-**	**-**
M1, Affected	-	0.00%	2	0.06 (−0.55, 0.67)
M1, Unaffected	-	0.00%	2	1.11 (0.40, 1.82)[a]a
M1, Bilateral	-	0.00%	2	0.08 (−0.64, 0.80)
LDPC	-	-	1	−0.27 (−1.19, 0.66)
Pulses/session	**0.00 (−0.78, 0.79), 0.989**	**-**	**-**	**-**
< 1000	-	57.90%	3	0.47 (−0.32, 1.26)
1000 to 1500	-	0.00%	2	−0.14 (−0.78, 0.50)
≥ 1500	-	0.00%	2	0.66 (−0.21, 1.53)
Total sessions	**0.11 (−0.17, 0.38), 0.365**	**-**	**-**	**-**
5	-	-	1	−0.11 (−0.86, 0.64)
6 to 10	-	-	1	0.41 (−0.66, 1.48)
≥ 10	-	41.30%	5	0.41 (−0.17, 1.00)
Resting motor threshold (%)	**−0.01 (−0.10, 0.08), 0.782**	**-**	**-**	**-**
80–100	-	20.00%	7	0.28 (−0.21, 0.78)
> 100	-	-	-	-

M1 Motor cortex, *SMD* Standardized mean difference, *CI* Confidence interval, *LDPC* Left dorsolateral prefrontal cortex projection area, [a]significant therapeutic effect, a large effect size, b Potential factors significantly affect the results

area)(SMD: 0.59, 95% CrI:−0.36, 1.53) and the affected motor cortex (SMD: 0.66, 95% CrI:−0.37, 1.70), rTMS did not significantly improve the balance ability of patients with stroke. Furthermore, low rTMS (SMD: 0.68, 95% CrI:−0.06, 1.42), iTBS (SMD: 0.63, 95% CrI:−0.10, 1.36), pulses/session < 1000 (SMD: 0.18, 95% CrI: −0.34, 0.70), and total sessions of five or fewer times (SMD: 0.31, 95% CrI:−0.24, 0.85) did not significantly enhance the balance ability forpatients with stroke compared to the sham group. rTMS with 1000–1500 pulses per session (SMD: 0.92, 95% CrI:0.63, 1.21, I^2 = 42%, from six studies), total session ≥ 10 times (SMD: 0.85, 95% CrI: 0.53, 1.18, I^2 = 54.1%, from six studies), and high rTMS (SMD: 0.83, 95% CrI: 0.34, 1.09, I^2 = 46.3%, from three studies) exemplified a large effect size in improving balance ability in stroke patients (Table 4).

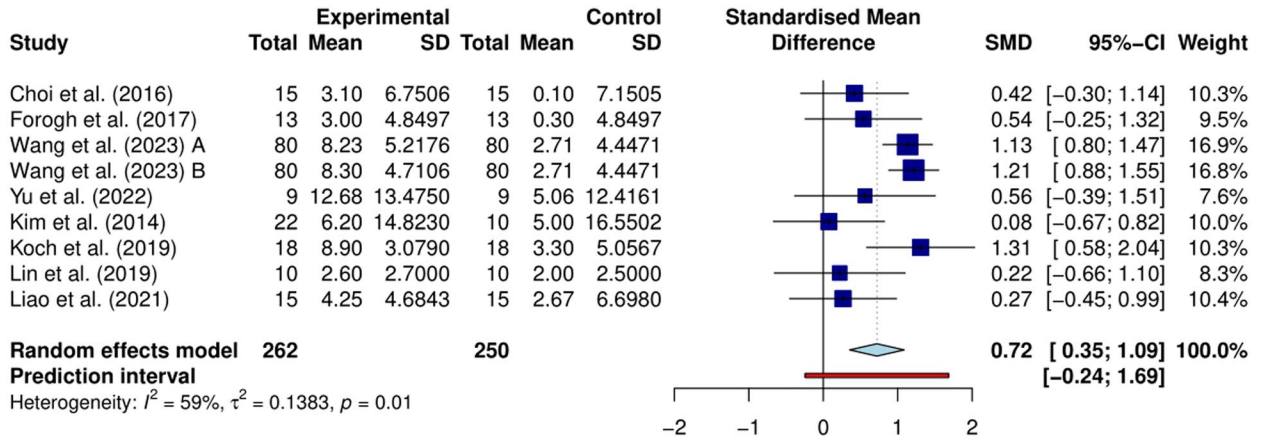

Figure5 Forest map of the effect of rTMS on the balance ability of stroke patients

Table 4 Summary of meta-regression and subgroup analysis results of rTMS on balance ability in stroke patients

Covariate	Shared beta	Heterogeneity	Number of studies	SMD
	(mean and 95% CI), *P* value	(I^2)		(95% CI)
None	-	69.00%	8	0.72 (0.35, 1.09)[a]
Type	**−0.08 (−0.60, 0.44), 0.721**	**-**	**-**	**-**
High rTMS	-	46.30%	3	0.83 (0.34, 1.33)[a]a
Low rMTS	-	76.80%	3	0.68 (−0.06, 1.42)
iTBS	-	62.70%	3	0.63 (−0.10, 1.36)
Stimulation site	**−0.04 (−0.50, 0.42), 0.849**	**-**	**-**	**-**
M1, Affected	-	84.50%	2	0.66 (−0.37, 1.70)
M1, Unaffected	-	70.50%	3	0.75 (0.11, 1.39)[a]
M1, Bilateral	-	56.30%	3	0.69 (0.02, 1.37)[a]
LDPC	-	-	1	0.59 (−0.36, 1.53)
Pulses/session	**0.75 (0.06, 1.56), 0.044b**	**-**	**-**	**-**
< 1000	-	0.00%	2	0.18 (−0.34, 0.70)
1000 to 1500	-	42.00%	6	0.92 (0.63, 1.21)[a]a
≥ 1500	-	-	-	-
Total sessions	**0.08 (0.03, 0.12), 0.004b**	**-**	**-**	**-**
5	-	0.00%	2	0.31 (−0.24, 0.85)
6 to 10	-	-	-	-
≥ 10	-	54.10%	6	0.85 (0.53, 1.18)[a]a
Resting motor threshold (%)	**−0.01 (−0.08, 0.05), 0.656**	**-**	**-**	**-**
80–100	-	69.00%	8	0.72 (0.35, 1.09)[a]
> 100	-	-	-	-

M1 Motor cortex, *SMD* Standardized mean difference, *CI* Confidence interval, *LDPC* Left dorsolateral prefrontal cortex projection area, [a]significant therapeutic effect, a large effect size, b Potential factors significantly affect the results

Publication bias assessment

A meticulous examination for publication bias was carried out across the 18 selected studies, with funnel plots meticulously constructed to illustrate the symmetrical distribution pertaining to lower limb function, high velocity, and balance capabilities in post-stroke patients, suggesting a minimal likelihood of publication bias (Fig. 6). Through Egger's test, it was found that the *p*-values were all greater than 0.05, indicating the absence of publication bias (Fig. 6).

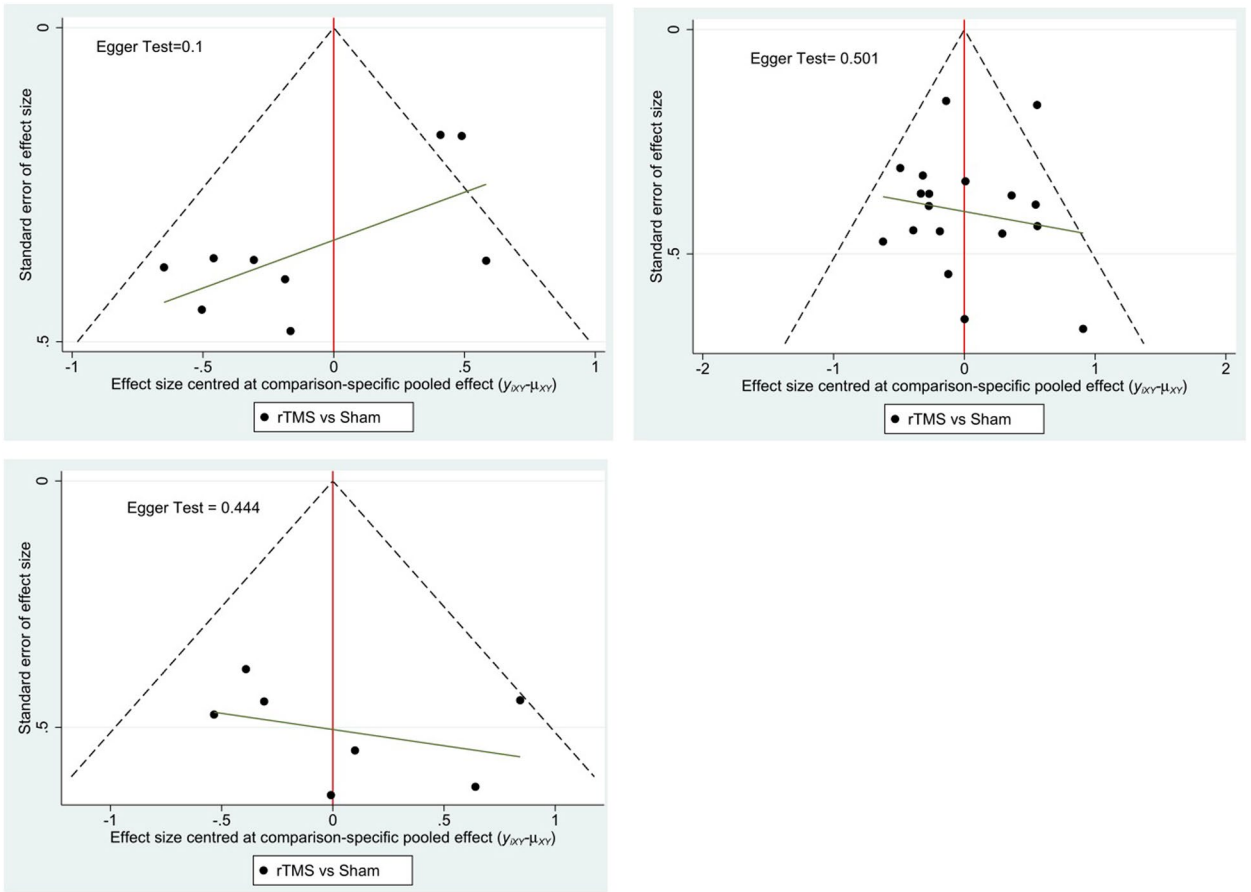

Figure6 The funnel plots of publication bias for lower limb function, high velocity, and balance ability in patients with stroke. A: balance ability; B: lower limb function; C: high velocity

Discussion

Ischemic stroke manifests abruptly, featuring clinical symptoms including aphasia, motor dysfunction of limbs, and dysarthria [44]. The majority ofpatients suffer from residual effects, encompassing impairments in speech, motor abilities, and swallowing. Among these, dysfunction of the lower limbs, a particularly prevalent sequela, is mainly manifested by diminished muscle strength, alterations in muscle tone, joint laxity, and a reduction in motor coordination [44]. Consequently, when the muscles of the lower limbs are affected by paralysis, they may encounter symptoms such as spasms, muscular weakness, limited joint mobility, reduced capacity for control, stiffness in limb movements, and an absence of distinct movement segmentation. This can lead to occurrences like contractures of the soft tissue, unsteady gait, and uneven walking patterns, which subsequently elevate the likelihood of falls in patients [45]. A survey revealed that the incidence of falls among patients with stroke aged ≥ 60 within a year was 28.9% [46]. The research team led by Wong [47] conducted a 6-month post-discharge follow-up with 46 hemiplegic patients, noting that those who had suffered falls demonstrated inferior motor abilities and a reduced level of limb coordination compared to their counterparts who had not fallen. This finding could be linked to diminished limb activity and a prolonged recuperation process following falls. Due to central nervous system impairment in stroke patients, an insufficiency in movement differentiation within the affected lower extremities leads to a narrowing of the range of motion in the affected knee, hip, and ankle joints, manifests as shortened stride length, diminished frequency and velocity of movement, and poses challenges in performing customary movements, ultimately resulting in atypical movement patterns and an abnormal gait. The robust limb primarily offsets this imbalance. While ambulating, the sturdy limb must commence the swing phase ahead of schedule to reposition the body's center of gravity, potentially resulting in wear and tear on the healthy joint and spinal curvature due to the sustained weight-bearing [3, 48]. Thus, the fundamental objective

and urgent demand of post-stroke rehabilitation is to facilitate the restoration of lower limb mobility, ambulatory function, and muscular strength in individuals with ischemic stroke, in order to mitigate the likelihood of falls and expedite their prompt reentry into the community.

Transcranial magnetic stimulation therapy is a non-invasive approach to brain stimulation. Throughout the course of treatment, the induced currents, produced by the pulsating magnetic field, directly influence the pertinent nerve function regions within the patient's cerebral cortex. This action is carried out through a consistent and repetitive pulsing mechanism, effectively modulating hemiplegia. This procedure is designed to rejuvenate the compromised condition of the patient's central nervous system, rectify the Atypical neuronal conduction, and reduce the dysregulation stemming from the irregular firing of central neurons. As a result, it facilitates the central nervous system's ability to stimulate motor nerves appropriately, thereby reinstating the normal motor abilities of the limbs and easing post-stroke lower limb spasticity [49–51]. Mei et al. [52] following rTMS intervention in cerebral ischemic rats, there was a significant increase inthe total length, density, number of dendritic branches, postsynaptic density, and synaptic curvature of the V-layer pyramidal cells in the undamaged motor cortex.The synaptic cleft width has notably diminished. Gao and colleagues [53] noted a marked elevation in the expression levels of postsynaptic density protein 95, glutamate receptor subunits 2 and 3, as well as synaptic protein-1 within the stimulated sensorimotor cortex of rats suffering from cerebral ischemia following rTMS therapy. This investigation further demonstrated that rTMS has the capacity to regulate intricate neuroimmune reactions, achieving this by lowering the levels of cytokines linked to the infiltration of peripheral immune cells. It also reduces the excessive expression of pro-inflammatory cytokines, minimizes the reactivity of microglia, and curbs the proliferation of astrocytes, consequently easing neuronal injury and mitigating oxidative stress [54–56]. Our examination integrated findings from 16 distinct investigations, encompassing a total of 723 participants, which were focused on evaluating the lower limb function in individuals post-stroke. The results indicated that rTMS notably improved the functional capabilities of the lower limbs in these patients when contrasted with the control group receiving sham treatment, showcasing a SMD of 0.45, with a 95% confidence interval ranging from 0.25 to 0.65.Considering the potential impact of various stimulation parameters and sites on lower limb function and balance in patients with stroke, further investigations were undertaken to explore these aspects.

The choice of stimulation site, or "hot spot," determines the local neurophysiological alterations and clinical efficacy [57], representing a pivotal factor in the rTMS stimulation protocol. The hemispheric rivalry model [58] provides a conceptual foundation for the application of rTMSin the rehabilitation of lower limb motor impairments post-stroke. Researchers have posited alternative theories, indicating that in cases of significant motor impairment, the activation of the unaffected hemisphere acts as a compensatory mechanism [54, 57]. The surrounding normal area adjacent to the lesion or the unaffected hemisphere may contribute to restoring lower limb function following a stroke [54]. Choi et al. [59] applied 10 Hz high-frequency rTMS to the cortical area of the affected trunk, resulting in improved lower limb movement and balance function in patients. Similarly, Goh et al. [60] administered a 5 Hz rTMS intervention targeting the left DLPFC in patients with left-sided stroke, leading to enhanced walking speed during regular and reverse walking tasks. The research team led by Kim [61] employed 1 Hz rTMS to bolster walking speed and equilibrium in the intact cerebellar regions of stroke patients. However, the investigation revealed that rTMSfailed to markedly augment the functional capabilities of the lower limbs in these patients when the stimulation was applied to areas of the non-motor cortex (projection area of the left dorsolateral prefrontal cortex) (SMD: −0.18, 95% CI:−1.11,0.75). Nevertheless, it was observed that when rTMS was applied to the intact motor cortex, it significantly improved gait velocity in post-stroke patients, showcasing a considerable effect size, with a SMD of 1.117 and a 95% Cl ranging from 0.40 to 1.82.These enhancements were especially pronounced in instances where the stimulation was targeted at regions beyond the motor cortex, particularly affecting the projection area of the left dorsolateral prefrontal cortex(SMD: 0.59, 95% CI: −0.36, 1.53) and the affected motor cortex area (SMD: 0.66, 95% CI: −0.37, 1.70), with no significant enhancement observed in the balance ability of patients with stroke. Thus, opting for a suitable stimulation location can significantly improve the lower limb motor function and equilibrium capabilities of these individuals.

Moreover, varying stimulation parameters profoundly influence the equilibrium and ambulatory velocity of the lower limbs in post-stroke patients undergoing rTMS therapy [62]. Typically, these parameters encompassed a total of 5 to 21 sessions, with each session delivering between 600 and 1600 pulses, and an intensity ranging from 80 to 130% of RMT. RMTs > 100% and total sessions < 10 did not significantly improve lower limb function in patients with stroke. rTMS with pulse/session ≥ 1500 significantly improves lower limb function in patients with stroke (SMD: 0.97, 95% CrI:0.02,

1.93, $I^2 = 9.1\%$). Conversely, low-frequency rTMS, with pulse/session < 1000 (SMD: 0.18,95% CrI:−0.34,0.70) and total session count of fiveor fewer (SMD: 0.31,95% CrI:−0.24,0.85), did not significantly improve the balance ability of patients with stroke. High-frequency rTMS, with 1000–1500 pulses/session (SMD: 0.92, 95% CrI:0.63,1.21, $I^2 = 42\%$) and total session count of ≥ 10(SMD: 0.85, 95% CrI:0.53,1.18, $I^2 = 54.1\%$), and high rTMS exhibited a significant effect on improving balance ability in patients with stroke. This research indicates that for individuals post-stroke undergoing rTMS therapy to enhance lower limb balance and gait velocity, the most favorable stimulation settings entail a dosage of 1000–1500 pulses per session, with a minimum of 10 sessions in total, and employing a high-intensity rTMS approach. Nevertheless, it has been demonstrated that rTMS, when administered with a pulse or session count of 1500 or more, significantly enhances lower limb functionality in post-stroke patients. Prospective patients should weigh the benefits against the potential drawbacks before opting to undergo this procedure.

Studies have shown that the magnetic and electrical impulses generated by low-frequency rTMSare capable of modulating the affected brain hemisphere in patients, thereby increasing its excitability and enhancing the motor cortex function from this angle. This occurrence has the potential to diminish the restrictive impact of stroke-related brain injury on the functionality of the brain hemispheres, thereby promoting the revival of the innate excitatory state in the innervation nerves of both cerebral hemispheres and enhancing the patient's limb coordination [63, 64]. After undergoing high-frequency rTMS specifically targeted at the primary motor area of the affected hemisphere, the subjects in the high-frequency rTMS group showcased a more pronounced motor recovery compared to those in the pseudo-stimulation control group. Moreover, this group experienced notable improvements in neurovascular remodeling, a significant upsurge in cortical excitability, activation in motor-evoked functional magnetic resonance imaging, and a targeted regulation of the neurovascular unit within the impaired brain motor region [65–67]. Further investigations revealed that, in contrast to the high-frequency rTMS group, the low-frequency rTMS group exhibited a significantly weaker effect on activating the M1 region in the ipsilateral limb related to motor functions [68]. Furthermore, it was observed that high-frequency rTMSproved to be more efficacious in enhancing the balance and gait velocity of the lower extremities in stroke patients, in contrast, low-frequency rTMS did not yield significant improvements in these aspects.

Previous research indicates that high-frequency rTMS may carry a risk of triggering epileptic seizures. Consequently, in therapeutic applications, low-frequency rTMS is more commonly utilized. Nevertheless, studies involving stroke patients have showcased their ability to withstand rTMS therapy, with no incidents of serious adverse effects reported [69–71]. For instance, Chieffo et al. [27] applied 20 Hz high-frequency rTMS to treat 12 patients with lower limb dysfunction after stroke. Three seasoned individuals experienced brief episodes of mild vertigo, while one reported a slight twitching in the shoulder muscles. Modulating the stimulation intensity down to 80% from the original 90% of the resting motor threshold (RMT) alleviated these symptoms, thus allowing all four participants to successfully undergo the entire treatment regimen. A meta-analysis [34] indicated that adverse events associated with high-frequency TMS are rare, with transient or mild headaches and local discomfort at the stimulation site being the most common. The study revealed that no instances of epilepsy or deterioration in NIHSS scores were observed following the initiation of rTMSin patients with acute intracerebral hemorrhage [72]. Moreover, active TMS was effectively endured by patients, exhibiting a minimal attrition rate due to adverse events (4.5%), which were predominantly mild and restricted to temporary scalp unease or soreness [73]. In the treatment of depression patients using theta burst and high-frequency rTMS, the most common treatment-related adverse event was headache in both groups (10 Hz rTMS: 131 [64%] of 204; iTBS: 136 [65%] of 208) [74]. Thus, it is widely regarded that high-frequency treatment is both secure and efficacious. Through meticulous patient selection, taking into account appropriate indications and contraindications, the likelihood of untoward events, including epilepsy, can be substantially reduced [75]. In our inclusion of 18 studies [26–43], there were no reports of rTMS causing epilepsy, however, some patients only have tolerable and mild headaches. Therefore, the use of high-frequency rTMS for treating patients with stroke with impaired balance and lower limb gait speed is considered both safe and effective.

There is a scarcity of studies investigating the concurrent application of low-frequency and high-frequency rTMS. Drawing on the principle of hemispheric mutual inhibition, it is observed that stimulation of the ipsilateral hemisphere at frequencies exceeding 1 Hz augments cortical excitability, whereas stimulation at frequencies of 1 Hz or below diminishes excitability in the unaffected hemisphere. Chinese scholars randomly divided 60 patients with acute cerebral infarction into high-frequency (10 Hz) and low-frequency rTMS groups. Following a fortnight of therapeutic intervention, the cohort subjected to concurrent low-frequency and high-frequency rTMS exhibited marked enhancements in both motor abilities and instrumental activities of daily living.

In terms of augmenting the excitability of the affected cortical regions, the synergistic application of both high-frequency and low-frequency rTMS proved superior to the isolated use of either frequency, yielding a notable increase in the excitability of the primary motor (M1) cortex in the affected hemisphere.In another study by Sasaki [76], patients were divided into two groups:one received high-frequency rTMS stimulation of the affected motor cortex combined with low-frequency rTMS stimulation of the contralateral motor cortex. Conversely, the remaining group underwent high-frequency rTMS exclusively on the impaired motor cortex. Following a 5-day course of consecutive therapy, individuals who received both high-frequency and low-frequency rTMS exhibited markedly superior motor function improvement compared to those who were administered high-frequency rTMS in isolation. Takeuchi [77] conducted a similar study where patients with stroke patients were randomly assigned to three groups. The initial cohort was administered low-frequency rTMS to the contralateral motor region, whereas the second cohort underwent high-frequency rTMS to the impaired motor area. The third cohort was treated with a concurrent regimen of low-frequency rTMS to the contralateral motor region and high-frequency rTMS to the affected motor region. Following the stimulation phase, a notable enhancement in motor function was observed among the patients, with the low-frequency rTMS and the group receiving combined stimulation demonstrating significant advancements relative to the initial baseline. In particular, the group that underwent combined rTMS stimulation achieved more exceptional results compared to both the high-frequency and low-frequency rTMS groups. Recent studies have found that high-frequency rTMS combined with sensory stimulationcan increase sensory and motor recovery, as well as functional independence, in participants with subacute stroke [78]. Nevertheless, the research highlighted that high-frequency rTMS is superior in improving balance and increasing gait velocity in the lower extremities of stroke survivors. Additional studies are required to ascertain if the amalgamation of low-frequency and high-frequency rTMS might produce more advantageous results than either frequency alone in the treatment of lower limb impairments following a cerebral infarction.

Limitation

The study demonstratethat the efficacy of rTMS is seemingly influenced by variations in stimulation sites and parameters; stimulation point M1 (Unaffected), HF rTMS, RMT 80–100, Total session count ≥ 10, Pulses/session 1500 are effective in treating patients with lower limb dysfunction in ischemic stroke. Nevertheless, this study has certain inherent limitations. Its literature search was confined to English and Chinese languages, which may have inadvertently excluded relevant works in other tongues. Moreover, given that this meta-analysis relies on previously published meta-analytic articles, it may have failed to incorporate initial studies that did not undergo meta-analytic treatment. This results show a high degree of statistical heterogeneity, and among the literature we included, one had a publication bias of "High" and eight had a publication bias of "Some concerns", both of which have a certain impact on the results. Therefore, in the future, larger, multicenter trials or systematic reviews with pre-specified protocols will be conducted to confirm these results.

In addition, various individual factors may influence the response to rTMS therapy. It is recognized that older participants exhibit reduced potential for plasticity changes induced by non-invasive neuromodulation [48]. Furthermore, the variable degrees of stroke severity and the differing locations of lesions among patients contribute significantly to the diversity in therapeutic outcomes. There are additional unconsidered factors that could also affect the final results. The age of the stroke patients included in the study ranges from 18 to 85 years, encompassing individuals with varying durations of stroke, which inherently introduces a certain degree of heterogeneity. Moreover, the research encompassed a diversity of rTMS parameters, such as frequency, intensity, treatment longevity, weekly session frequency, and the inclusion of various rehabilitation exercises within conventional physical therapy, which subsequently heightened the variability among studies.

Conclusion

The therapeutic impact of rTMSon enhancing balance and increasing walking velocity in post-stroke individuals with lower limb motor impairments is contingent upon the selection of diverse stimulation locales and parameters. Specifically, when the stimulation is directed at the unaffected motor cortex, rTMS markedly improves gait velocity in stroke survivors. Specifically, sessions with 1000–1500 pulses per session, totaling ≥ 10 sessions, and employing high-frequency rTMS exhibit more pronounced effects on lower limb gait and balance after stroke (Table 5). Conversely, low-frequency rTMS, sessions with < 1000 pulses, and a total session count offive or fewer times do not improve balance and gait among patients with lower limb dysfunction after stroke.These findings provide crucial insights for determining the optimal stimulation locations and parameters when administering rTMS therapy to individuals with gait and lower limb balance impairments post-cerebral infarction. Nevertheless,

Table 5 Optimal stimulation parameters and stimulation site

Items	Lower limb function	Gait velocity	Balance ability
Stimulated site	M1(Affected, Unaffected, Bilateral)	M1(Unaffected)	M1(Unaffected, Bilateral)
Stimulation method	rTMS	rTMS	rTMS
rTMS Frequency	HF or LF rTMS	HF or LF rTMS	HF rTMS
Resting motor threshold(%)	80–100	/	80–100
Total session count(times)	≥ 10	/	≥ 10
Pulses/session	≥ 1500	/	1000–1500

rTMS Repetitive Transcranial Magnetic Stimulation, *HF* High frequency

certain research indicates that high-frequency rTMS yields superior outcomes in enhancing walking pace compared to low-frequency rTMS, with peak effectiveness occurring at 20 treatment sessions. While for enhancing gait balance in stroke patients, LF-rTMS with the best therapeutic effect was observed at a frequency of 20–40 treatments [77]; Low-frequency rTMS is better than high-frequency rTMS stimulation in improving neurological function, motor function, and excitability of cortex in ischemic stroke. These studies are inconsistent with our research findings [78]. Consequently, it is crucial to delve deeper into the stimulation parameters and specific sites, customized for various stroke lesion locations and types of aphasia, through rigorous, high-caliber, randomized, and controlled clinical trials with ample sample sizes [79, 80]. These efforts are essential to enhance the quality of clinical research, yielding more dependable evidence regarding the effectiveness of rTMS in improving balance and gait in patients suffering from lower limb dysfunction following a stroke.

Abbreviations

RoB2	Risk of Bias version 2 tool
RCTs	Randomized control trials
rTMS	Repetitive Transcranial Magnetic Stimulation
CrI	credible interval
PRISMA-NMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Network Meta-Analyses
SMD	Standard mean differences

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12883-025-04112-9.

Supplementary Material 1

Authors' Contribution

D.M.J. J.T.Y. X.L. B.C.Z. L.M.Z. and M.W.L. had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. B.C.Z. B.R.Z. and Q.J.Z. contributed to the conceptualization, project administration, data curation, formal analysis and writing original draft. X.L. B.R.Z. Q.J.Z. and M.W.Z. contributed to the methodology and writing review and editing. D.M.J. L.M.Z. and B.C.Z. contributed to the validation. B.R.Z. Q.J.Z. and B.C.Z. contributed to the investigation (data collection). X.L. D.M.G. L.M.Z. and M.W.L. contributed to the supervision. All authors have read and agreed to the published version of the manuscript.

Funding

This study was supported by Nature Science Foundation of China under Grants [No. 81960350], Yunnan Applied Basic Research Project-Union Foundation of China under Grant [No.202201AY070001-091], and Key Science and Technology Special Plan of Dali Prefecture Science and Technology Bureau [No.2021NA07].

Data Availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Ethical approval was deemed not necessary for this study.

Consent for publication

De-mei Jia, Xuan Li, Bin-cang Zhang, and Ming-wei Liu had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Bin-cang Zhang, Bing-ran Zhang, and Qiu-juan Zhang contributed to the conceptualization, project administration, data curation, formal analysis and writing original draft. Xuan Li, Bing-ran Zhang, Qiu-juan Zhang, and Ming-wei Liu contributed to the methodology and writing review and editing. De-mei Jia, and Bin-cang Zhang contributed to the validation. Bing-ran Zhang, Qiu-juan Zhang, and Bin-cang Zhang contributed to the investigation (data collection). Xuan Li, De-mei Jia and Ming-wei Liu contributed to the supervision. All authors have read and agreed to the published version of the manuscript.

Competing interests

The authors declare no competing interests.

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Received: 30 October 2024 Accepted: 26 February 2025
Published online: 24 March 2025

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