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REVIEW

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Safety and effectiveness of non-invasive brain stimulation on mobility and balance function in children with cerebral palsy: a systematic review and meta-analysis

Mengru Zhong[1†], Yage Zhang[1†], Jie Luo[1], Tingting Chen[1], Jingbo Zhang[1], Tingting Peng Sr.[1], Mingshan Han[1], Wen Le[1,2], Tingting Peng Jr.[1] and Kaishou Xu[1*]

Abstract

Background Children with cerebral palsy (CP) experience significant mobility and balance impairments. Non-invasive brain stimulation (NIBS), including transcranial direct current stimulation (tDCS) and repetitive transcranial magnetic stimulation (rTMS), has emerged as a potential therapeutic intervention. Nevertheless, the safety and effectiveness of NIBS in children with CP remain uncertain and require further investigation. This study aimed to evaluate the safety and effectiveness of NIBS in improving mobility and balance function in children with CP.

Methods Randomized controlled trials written in English were searched in five databases (PubMed, Embase, Scopus, Web of Science, and ProQuest), from the first available records in each database to April 2024. Statistical analysis focused on outcomes related to mobility and balance function immediately following intervention and one-month follow-up.

Results A total of 16 studies encompassing 346 children with CP, aged 3–14 years, were included. The meta-analysis indicated that NIBS is safe and well-tolerated [Risk Difference = 0.16, 95% CI − 0.01–0.33], with a low incidence of adverse events. Significant improvements were observed in mobility post-intervention and at one-month follow-up, particularly in Gross Motor Function Measure scores [standard mean difference (SMD) = 0.47 to 0.63, $P < 0.05$]. Gait parameters, including gait velocity (SMD = 1.28, $P < 0.01$) and stride length (SMD = 0.70, $P = 0.01$) showed immediate improvements. However, no significant improvements were found in balance post-tDCS or at follow-up.

Conclusions Our findings support the use of NIBS as a safe and feasible tool for enhancing mobility in children with CP, demonstrating both immediate and sustained improvements in gait parameters such as velocity and stride length. However, the impact on balance remains inconclusive. Future research should focus on extending follow-up periods, increasing sample sizes, and exploring tailored stimulation protocols to better understand the long-term efficacy and optimal application of NIBS in pediatric populations.

Keywords Cerebral palsy, Transcranial direct current stimulation, Transcranial magnetic stimulation, Safety, Mobility, Balance

†Mengru Zhong and Yage Zhang are Co-first authors.

*Correspondence:
Kaishou Xu
xksyi@126.com
Full list of author information is available at the end of the article

Introduction

Cerebral palsy (CP) is a neurological disorder caused by brain damage that occurs during fetal development, infancy, or early childhood. This damage can result in permanent issues with movement and posture, significantly impacting a child's ability to move and maintain balance [1]. The underlying pathophysiology of CP is often associated with structural abnormalities in critical areas of the brain involved in motor function, most notably the primary motor cortex (M1) and the corticospinal tracts [2, 3]. These brain regions are crucial for motor control and coordination, and their damage results in the characteristic motor deficits seen in children with CP.

Recent global estimates suggest a prevalence rate for CP ranging from 1.6 to 3.4 per 1000 live births, underscoring its importance as a public health issue [4]. The etiology of CP is multifactorial, including genetic predisposition, perinatal complications, and brain infections. Recent neuroimaging techniques, including Magnetic Resonance Imaging with Cortical Spinal Tractography (MRICS), have revealed structural abnormalities in the brains of children with CP, which are closely associated with the altered cortical excitability and impaired activation of the corticospinal and somatosensory pathways [5]. Such structural and functional abnormalities contribute to the motor deficits seen in children with CP, affecting their ability to perform tasks requiring motor coordination and balance.

Given the profound impact of CP on motor and balance functions, there has been growing interest in exploring non-invasive brain stimulation (NIBS) as a potential therapeutic intervention [6–8]. The two most common forms of NIBS include transcranial direct current stimulation (tDCS) and repetitive transcranial magnetic stimulation (rTMS). These techniques modulate cortical excitability through electrical currents or magnetic fields without the need for invasive procedures. tDCS applies low-intensity (1–2 mA) direct electrical current through surface electrodes, with anodal stimulation facilitating neuronal depolarization and cathodal stimulation promotes neuronal inhibition through hyperpolarization [9]. In contrast, rTMS uses time-varying magnetic fields induce currents in specific brain regions [10, 11]. High frequency rTMS (above 1 Hz) increases cortical excitability, whereas low frequency rTMS (at or below 1 Hz) has the opposite effect [11, 12]. Both modalities target the motor cortex, enhancing cortical excitability and synaptic efficacy via the corticospinal tracts, potentially leading to improvements in motor function [13, 14].

Both techniques have been demonstrated to enhance motor functions in patients with stroke [15, 16], Parkinson's disease [17], multiple sclerosis, and neurodegenerative conditions like Alzheimer's disease [18]. It also enhances athletic performance and cognitive functions in healthy people [19] and aids in pain management for chronic pain sufferers [20]. However, the effects of NIBS in children with CP have been less consistently reported. While some studies [21, 22] have evaluated the impact of NIBS on motor function in children with CP, the findings have been mixed, particularly with respect to balance function. While some studies have assessed the impact of NIBS on upper limb function in CP, its effects on mobility and balance remain less explored [23]. A previous systematic review [21] in 2017 summarized the impact of NIBS on pediatric patients following brain injury. Since then, seven randomized controlled trials (RCTs) [24–30] have expanded the evidence base, necessitating a comprehensive review of the effects of NIBS on mobility and balance in children with CP. This review aims to systematically evaluate the safety and effectiveness of NIBS in improving mobility and balance in children with CP.

Method

This study was conducted according to the guidelines of the Cochrane Handbook for Systematic Reviews of Interventions and the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) [31] and was registered in the PROSPERO database with the registration number CRD42023412290.

Search strategy

Our literature search was designed to identify relevant papers from five electronic databases: PubMed, EMBASE, Web of Science, ProQuest and Scopus. The search encompassed articles published until March 2024. The details of our search strategy are outlined in Table 6 of the appendix.

Inclusion and exclusion criteria

Adhering to the PICOS framework [32], our study selection focused on RCTs involving children and adolescents under the age of 18 with CP, who received NIBS interventions, specifically tDCS or rTMS, alongside control groups. Outcomes were evaluated using mobility-related measures (e.g., gait analysis, the 6-min Walk Test [6MWT], the 10 m Walk Test [10MWT], Timed Up and Go Test [TUGT], Gross Motor Function Measure [GMFM], and Pediatric Evaluation of Disability Inventory [PEDI]) and balance-related measures (e.g. center of pressure [COP], and the Pediatric Balance Scale [PBS]). Exclusions were based on non-CP neurological conditions, non-empirical articles, and articles not published in English or without full-text availability. The details of the eligibility criteria are outlined in Appendix Table 7.

The GMFM is a standardized tool assessing gross motor function in children with CP, divided into five

domains: (A) lying and rolling, (B) sitting, (C) crawling and kneeling, (D) standing, and (E) walking, running, and jumping. Specifically, we focused on standing performance (GMFM-D) and walking ability (GMFM-E) [33]. The COP evaluates postural control and balance, measuring anteroposterior (AP) and mediolateral (ML) stability with eyes open (EO) and closed (EC) [34]. These parameters provide insights into visual and sensory integration effects on balance.

Study selection and data extraction

Two reviewers (MRZ and YGZ) independently selected studies and extracted data, with disagreements resolved by a third (KSX). After de-duplication with Endnote 20, we screened titles and abstracts, followed by full-text review against our inclusion criteria. Detailed data from the articles were extracted using a standardized form designed for this study. In cases where data were presented graphically, WebPlotDigitize version 4.6 was used for manual data extraction [35]. Missing data were sought from the authors of article.

Quality assessment

The methodological quality of the intervention studies was appraised using the Physiotherapy Evidence Database (PEDro) scale [36], which grades studies on 11 criteria, excluding the first for external validity. For each aspect, a score of 1 point was given if the criteria were met ("yes") and 0 points if they were not met ("no"). Studies were categorized as follows: excellent (9 or 10), good (6 to 8), fair (4 to 5), and poor (less than 4) [37, 38]. The Revised Cochrane Risk of Bias Tool for Randomized Trials (RoB 2) [39] was used to assess the quality of the included studies, with independent reviews by two evaluators, resolved by discussion and a third party when needed (KSX).

Statistical analysis

To assess the safety of NIBS, we quantified dropout rates and documented adverse effects. The effectiveness of NIBS was examined by comparing motor outcomes post-intervention and at one-month follow-up. Meta-analysis was conducted at these two time points (each supported by at least two studies): immediately post-intervention and at one-month follow-up. Data from other time points were described narratively. Outcome measures were categorized into two domains: mobility and balance. Mobility was assessed through gait analysis, 6MWT, 10MWT, TUGT, GMFM-D, GMFM-E, and the Mobility and Self-care domains of the PEDI. Balance was evaluated using the COP and PBS. We used the Review Manager software for statistical analysis [40], comparing outcomes with standardized mean difference (SMD), 95% confidence interval (CI), and risk difference (RD). Statistical significance was set at $P < 0.05$, with effect sizes categorized as small (0.20), medium (0.50), and large (0.80) [41]. Heterogeneity was assessed using chi-square test and I^2 index, with high heterogeneity indicated by $P > 0.1$ and $I^2 > 50\%$ [42, 43]. The random-effects model was used when high heterogeneity; otherwise, the fixed-effects model was applied. Sensitivity or subgroup analyses were conducted to investigate sources of heterogeneity. Funnel plots were generated to assess publication bias in analyses that included more than ten studies [44]. For outcomes that were not part of the meta-analysis, a descriptive summary was provided instead of statistical analysis.

Result

Description of studies and participant characteristics

The study selection process is shown in Fig. 1. A total of 487 studies were initially retrieved from databases. After removing 142 duplicates, the remaining 345 studies were further screened. Among them, 293 records were excluded after reviewing the title and abstract since they were not related to the topic of this research article; 36 records were excluded after reviewing the full text of 52 articles; 16 studies were ultimately included in this review. Of these 16 studies, 11 studies [24–26, 45–52] employed tDCS, while the remaining five [27, 28, 53–55] utilized rTMS. A meta-analysis was conducted on 16 studies [24–28, 45–55] to evaluate the acceptability and tolerability of NIBS. Additionally, a meta-analysis was conducted on 14 studies [24–27, 45–53, 55] to assess the effectiveness of NIBS in improving mobility and balance function in children with CP.

Table 1 summarizes the characteristics of the included articles. This review encompassed a total of 346 children with CP, aged between 3 and 14 years. The active NIBS group consisted of 171 children (51.5%), and the sham group included 161 children (48.5%). Among the 16 included studies, nine articles reported the gender distribution of participants in detail [24, 25, 27, 45, 48, 49, 51, 53, 55]. In these reports, a total of 117 males (55.2%) and 95 females (44.8%) were included. Specifically, in tDCS studies, the ratio of males to females was 1.1:1, while in rTMS studies, it was 1.2:1. Overall, the gender distribution was well-balanced. Eleven articles provided detailed information on the Gross Motor Function Classification System (GMFCS) levels of the study participants, with severity ranging from level I–IV. Specifically, 69 participants (28.4%) were classified as GMFCS level I, 109 (44.9%) as level II, 63 (25.9%) as level III, and 7 (3%) as level IV. This distribution highlights a predominance of participants with GMFCS levels I–III, which indicates that the studies focused on participants with mild to moderate motor impairments.

Eleven RCTs [24–26, 45–52] utilized tDCS and included 260 participants with CP, which is 75.1% of the total sample size. Among them, 164 participants (63.1%) had diplegia, 34 (13.1%) had hemiplegia, six (2.3%) had ataxia, 24 (9%) had unspecified types of spastic CP, and 32 (12.3%) had unknown CP subtypes.

Five studies [27, 28, 53–55] used rTMS and involved 86 participants with CP. The majority, 69 participants (80.3%) had hemiplegia, while 17 participants had quadriplegia (19.7%). Together, these participants represented 24.9% of the total sample.

NIBS protocols summary

The intervention parameters, including dose, site, duration, and intensity, varied across different studies, as presented in Table 2.

tDCS

In the tDCS studies [24–26, 45–52], the intensity was set at 1 mA, with the number of sessions varying from a single session to up to 15 sessions. Fajardo et al. [25] conducted a 15-day tDCS intervention, while Grecco et al. [50] and Lazzari et al. [52] assessed the effect of a single tDCS session. Eight studies [24, 26, 45–49, 51] implemented a treatment protocol consisting of 10 sessions, each lasting 20 min. The stimulation site were as follows: M1 of the dominant hemisphere in 44 participants [48, 50]; Non-dominant hemisphere in 24 participants [47]; Contralateral to the most affected motor cortex in 74 participants [25, 45]; Unspecified side in 133 participants [24, 26, 51, 52]; Over the cerebellum in 6 participants with ataxic CP [49]. Regarding cathode placement, it was positioned over the inion in two studies [24, 26], and over the supra-orbital region on the contralateral side in others [25, 45, 47–52].

rTMS

Our review compiled information from five RCTs [27, 28, 53–55] that investigated the use of rTMS for treating spastic CP. These studies applied rTMS at frequencies of 1 Hz, 5 Hz, or 10 Hz, and one study by Valle et al. [55] explored the effects of rTMS at both 5 Hz and 1 Hz rTMS on spastic CP. The details are provided in Table 2. Resting motor threshold was reported at 90% or 100% of the intensity in five studies [27, 28, 53–55]. Additionally, one study [27] utilized a two-channel Neuro-EMG–MS digital system to determine the motor threshold and measure the resting motor threshold. The duration of the intervention varied between 1 and 6 weeks across the studies, with sessions ranging from 5 to 24 min. The majority administered either 15^{-28} or 20-minute [28, 53, 54] sessions, while Valle et al. [55] defined session length in terms of 1500 pulses.

The timing of the evaluation

Outcome measures were assessed at two key times: immediately after intervention in ten studies [24, 26, 28, 45, 50–55], and one month later in seven studies [25, 45–49, 51]. Specific time points for assessment included 20 minutes [55], one week [47–49], two weeks [26], ten weeks [24], 12 weeks [26], and three months post intervention [27, 49]. In the meta-analysis, two key assessment time intervals were specified: immediately after the intervention and one-month post-intervention. These time points were selected as they provided sufficient replications for each outcome measure (i.e., more than two studies) and are consistent with the current clinical context.

Associated treatment

Participants in the intervention group received NIBS stimulation complemented by physical therapy that encompassed virtual reality, treadmill training, gait training [26], mobility training [52] or neurodevelopmental treatment [25], as well as lower limb occupational therapy [54]. In contrast, the control group received either placebo NIBS, exercises, or a combination of both treatments [28, 50, 55].

Assessment of quality

Table 3 presents the scores from the PEDro scale for the included studies. Two articles [45, 46] were of excellent quality, while six studies [24–26, 28, 49, 52] were rated as fair quality, and the remaining studies [27, 47, 48, 50, 51, 53–55] were deemed to be good quality.

Risk of bias assessment

The results of risk of bias assessment are shown in Fig. 2. Over half of the studies had low risk or only some concerns regarding bias. Among the 16 articles, 15 [24–27, 45–55] provided detailed accounts of the randomization process. Participants in all trials received the allocated interventions, and complete outcome data was available. Three studies [45, 48, 53] used an intention-to-treat approach when conducting data analysis. Furthermore, 13 articles [27, 28, 45–55] reported the blinding of participants or personnel during the studies. With the exception of three studies [24, 26, 52], all RCT described the implementation of blinding for outcome assessment. One study [26] exhibited signs of selective reporting, whereas the remaining studies provided full results.

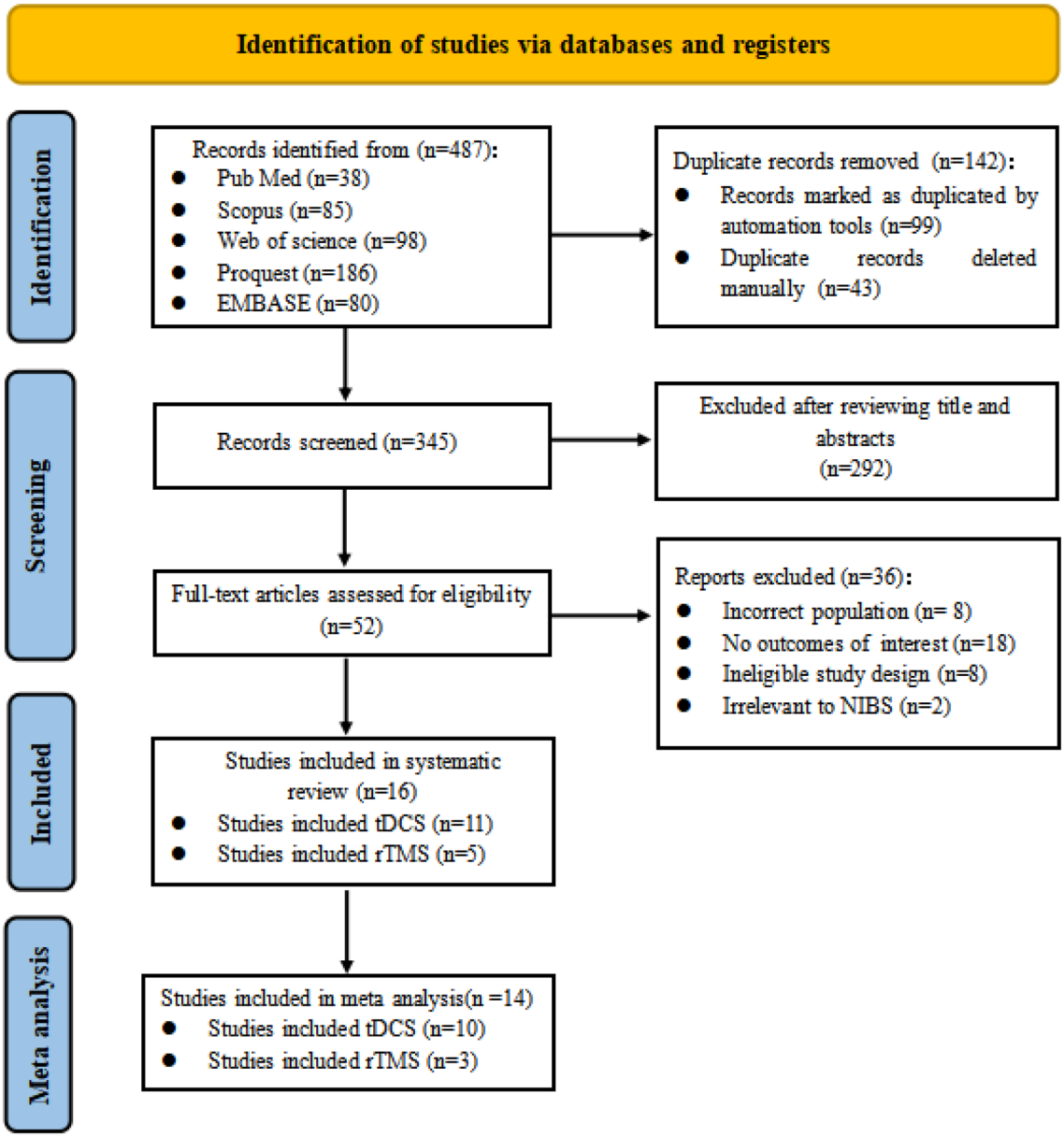

Fig. 1 PRISMA flow chart for study selection

Outcomes

Tolerability and safety

A meta-analysis encompassing the 16 included studies [24–28, 45–55] revealed no significant difference in dropout rates between the active group (1 of 142) and the control group (5 of 136) (RD = − 0.03, 95% CI − 0.08–0.03, I^2 = 0%), as depicted in Fig. 3A. In total, six participants withdrew from the studies: one from the active group due to the unavailability of static balance assessment, and five from the control group, with four leaving for personal reasons and one due to the unavailability of assessment.

Six trials [24, 45, 46, 49, 50, 53] provided precise figures for participants experiencing adverse events in the active group (29 out of 73 participants) and the control group (16 out of 74 participants), as illustrated in Fig. 3B. The pooled estimate showed no significant difference between the two groups (RD = 0.16, 95% CI − 0.01–0.33, I^2 = 63%). The adverse events experienced by participants were mostly mild to moderate in severity. The most frequently reported events were headaches (3%), redness

Table 1 Characteristics of included randomized controlled trials

Intervention type	Study name	Sample size (M/F)	Age (Mean SD) (years)	Diagnosis (GMFCS levels)	Types of CP
tDCS	Grecco et al.,2015	20(11/9)	8.5 ± 1.37	II(n = 7); III(n = 13)	Diplegic:20
	Fajardo et al.,2022	24(12/12)	5.25 ± 2.08	II(n = 4); III(n = 14) IV(n = 6)	Hemiplegic:9 Diplegic:15
	Grecco et al.,2014a	24(7/17)	7.9 ± 2.57	II(n = 16); III(n = 8)	Spastic:24
	Elsadany et al.,2019	40 (-/-)	7.73 ± 1.08	I /II (-/-)	Diplegic:40
	Radwan et al.,2023	40(23/17)	8.53 ± 1.53	I(n = 26); II(n = 4)	Diplegic:40
	Grecco et al.,2017	6(3/3)	7.17 ± 2.14	I(n = 2); II(n = 4)	Ataxic:6
	Duarte et al.,2014	24(-/-)	7.95 ± 1.74	I(n = 5); II(n = 13); III(n = 6)	Hemiplegic:5 Diplegic:19
	Lazzari et al.,2017	20(14/6)	7.45 ± 2.05	I(n = 10); II(n = 5); III(n = 5)	NI
	Grecco et al.,2014b	20(-/-)	7.50 ± 1.64	I(n = 6); II(n = 8); III(n = 6)	Hemiplegic:7 Diplegic:13
	Lazzari et al.,2015	12(-/-)	4–12	I/II/III (-/-/-)	NI
	Grecco et al.,2023	30(-/-)	9.9 ± 1.74	I(n = 9); II(n = 14); III(n = 7)	Hemiplegic:13 Diplegic:17
rTMS	Valle et al.,2007	17(8/9)	9.08 ± 3.17	NI	Quadraplegic:17
	Dadashi et al.,2019	4(-/-)	4–14	II(n = 3); IV(n = 1)	Hemiplegic:4
	Marzbani et al.,2018	4(-/-)	9 ± 3	NI	Hemiplegic:4
	Mahgoub et al.,2021	30(16/14)	10.55 ± 3.39	NI	Hemiplegic:30
	He et al.,2024	31(23/8)	6.94 ± 2.69	I(n = 11); II(n = 16); III(n = 4)	Hemiplegic:31

tDCS Transcranial direct current stimulation; *rTMS* Repetitive transcranial magnetic stimulation; *M* Male; *F* Female; *GMFCS* Gross Motor Function Classification System; *NI* No information; *SD* Standard deviation; *CP* Cerebral palsy

(14%), and mild tingling (30%). A detailed summary of these adverse effects is presented in Table 4. No serious adverse reactions such as epilepsy or sleep disorders were documented. In summary, dropout rates were not correlated with the occurrence of adverse effects.

Effectiveness of NIBS on mobility capacity

A meta-analysis of 12 studies [24–26, 45–51, 53, 55] assessed the effectiveness of NIBS on children with CP, focusing on mobility outcomes like the 6MWT, 10MWT, TUGT, gait analysis, GMFM, PEDI scores post-intervention and one month after the active intervention (Figs. 4, 5, 6).

Overall effect on walking ability Walking capacity was assessed through the 6MWT, 10MWT, TUGT, and gait analysis post-intervention and one month later. The results are summarized below.

The 6MWT showed significant improvements following NIBS intervention (SMD = 1.37, 95% CI 0.58–2.16, $P < 0.05$, $I^2 = 62\%$). Sensitivity analysis excluding studies utilizing rTMS [53] resolved the heterogeneity ($I^2 = 0\%$), as depicted in Table 5. Follow-up at one month of the 6MWT continued to show significant benefits (SMD = 0.96, 95% CI 0.55–1.42, $P < 0.05$, $I^2 = 0\%$), as showed in Fig. 7A. [46, 50]

Studies by Marzbani et al. [27] and He et al. [53] demonstrated that NIBS, particularly rTMS, significantly enhanced performance on 10MWT. However, due to limited data from rTMS studies, only tDCS studies were included in the meta-analysis for this measure. The TUGT, however, did not show significant improvements following tDCS interventions. The meta-analysis indicated no change in performance immediately post-intervention (SMD = − 0.38, 95% CI − 0.94–0.18) or at one-month follow-up (SMD = − 0.19, 95% CI − 0.74–0.37) (Fig. 7B). Studies specifically focusing on tDCS interventions also failed to demonstrate significant improvements in TUGT outcomes, suggesting that this measure may not be as responsive to NIBS as the 6MWT or 10MWT.

Significant improvements in gait parameters were noted, particularly in gait velocity and stride length. Post-intervention gait analysis across five trials [24, 26, 45, 48, 50] revealed significant post-intervention improvements in velocity (SMD = 1.28, 95% CI 0.67–1.88, $P < 0.05$, $I^2 = 61\%$) and stride length (SMD = 0.70, 95% CI

Table 2 NIBS parameters in the reviewed studies

Intervention type	Study name	Group condition	Stimulation parameters			Measurement time	Outcome measures
			Stimulation site	Stimulation intensity 、duration and frequency	Sessions		
tDCS	Grecco et al.,2015	IG:n = 10 active tDCS + VR CG:n = 10 sham tDCS + VR	Anode: the primary motor cortex of the contralateral hemisphere to lower limb with greater motor impairment Cathode: over the supraorbital region on the contralateral side	1 mA 20 min 5 times per week for 2 weeks	10	1: immediately following intervention 2: post-intervention 3:one mouth follow-up	Gait parameters GMFM PEDI
	Fajardo et al.,2022	IG:n = 14 active tDCS + NDT CG:n = 10 only NDT	Anodal: over the leg area of the primary motor cortex which was opposite to the lower limb with greater motor impairment Cathode: over the supra-orbital region on the opposite side	1 mA 20 min 3 times per week for 5 weeks	15	1: immediately following intervention 2: post-intervention 3:one mouth follow-up	GMFM MAS
	Grecco et al.,2014a	IG:n = 12 active tDCS + treadmill training CG:n = 12 sham tDCS + treadmill training	Anodal: over the primary motor cortex of the dominant hemisphere Cathode:over the supra-orbital region on the contralateral side	1 mA 20 min 5 times per week for 2 weeks	10	1:one week before the intervention 2:one week after the intervention 3:one mouth follow-up	6MWT GMFM Gait parameters
	Elsadany et al.,2019	IG:n = 20 activetDCS + PT + gait training CG:n = 20 sham tDCS + PT + gait training	Anodal: targeting right and left lower limb motor cortices (Cz) Cathode: positioned over the inion	1 mA 20 min 5 times per week for 2 weeks	10	1: before intervention 2: two weeks after intervention 3:12 weeks follow-up	Gait parameters
	Radwan et al.,2023	IG:n = 20 active tDCS + PT CG:n = 20 VR + PT	Anodal: corresponds to the motor of lower limb motor cortices (Cz) Cathode: positioned over the inion	1 mA 20 min 5 times per week for 2 weeks	10	1: before the intervention 2: post-intervention 3: ten weeks after intervention	Spatiotemporal parameters Kinetic parameters
	Grecco et al.,2017	IG:n = 3 active tDCS + treadmill training CG:n = 3 sham tDCS + treadmill training	Anodal: the cerebellar region Cathode: over the central supraorbital region	1 mA 20 min 5 times per week for 2 weeks	10	1:one week before intervention 2:one week after intervention 3:one month follow-up 4: three months follow-up	COP PBS PEDI

Table 2 (continued)

Intervention type	Study name	Group condition	Stimulation parameters			Measurement time	Outcome measures
			Stimulation site	Stimulation intensity 、duration and frequency	Sessions		
	Duarte et al.,2014	IG:n = 12 active tDCS + treadmill training CG:n = 12 treadmill training + sham tDCS	Anodal: over the primary motor cortex of the non-dominant hemisphere Cathode: over the supra-orbital region on the contralateral side	1 mA 20 min 5 times per week for 2 weeks	10	1:one week before intervention 2:one week after intervention 3:one mouth follow-up	COP PBS PEDI
	Lazzari et al.,2017	IG:n = 10 active tDCS + VR CG:n = 10 sham tDCS + VR	Anodal: over the primary motor cortex Cathode: over the supra-orbital region on the contralateral side	1 mA 20 min 5 times per week for 2 weeks	10	1: before the intervention 2: immediately following intervention 3:one mouth follow-up	COP PEDI TUG
	Grecco et al.,2014b	IG:n = 10 active tDCS CG:n = 10 sham tDCS	Anodal: over the primary motor cortex of the dominant hemisphere Cathode: over the supra-orbital region on the contralateral side	1 mA 20-min	1	1: before the intervention 2: immediately following intervention	COP Gait parameters
	Lazzari et al.,2015	IG:n = 6 active tDCS + mobility training + VR CG:n = 6 sham tDCS + mobility training + VR	Anode: over the primary motor cortex Cathode: over the supra-orbital region on the contralateral side	1 mA 20 min	1	1: before intervention 2:immediately following intervention	COP
	Grecco et al.,2023	IG:n = 15 active tDCS + dual task(treadmill gait training and training of intellectual activities) CG:n = 15 sham tDCS + dual task(treadmill gait training and training of intellectual activities)	Anode: over the primary motor cortex that manages the control of the trunk and lower limbs (Cz) Cathode: over the left deltoid muscle	1 mA 20 min	10	1: before the intervention 2: immediately following intervention 3: one mouth follow-up	GMFM TUGT PEDI 6MWT

Table 2 (continued)

Intervention type	Study name	Group condition	Stimulation parameters		Sessions	Measurement time	Outcome measures
			Stimulation site	Stimulation intensity 、duration and frequency			
rTMS	Valle et al.,2007	IG:n = 6, 1 Hz active rTMS n = 5, 5 Hz active rTMS CG:n = 6 sham rTMS	M1(controls the leg on the non-affected hemisphere)	1 Hz:1500 pulses 5 Hz:1500 pulses an intensity of 90% RMT	5	1: before intervention 2: 20 min after intervention	MAS PEDI ROM
	Dadashi et al.,2019	IG:n = 2 rTMS CG:n = 2 sham rTMS	M1 (on the affected hemisphere)	1 Hz frequency 20 min 1200 pulses 4 times per week for 6 weeks an intensity of 100% RMT	24	1: before intervention 2: post-intervention	COP
	Marzbani et al.,2018	IG:n = 2 rTMS + lower limb OT CG:n = 2 sham rTMS + lower limb OT	M1 (controls the leg on the affected hemisphere)	1 Hz frequency 20 min 1200pulses 4 times per week for 3 weeks an intensity of 100% RMT	12	1: before intervention 2: post-intervention	10MWT 6MWT TUGT
	Mahgoub et al.,2021	IG:n = 15 rTMS + ST CG:n = 15 sham rTMS + ST	M1 (controls the leg on the non-affected hemisphere)	10 Hz frequency 15 min 1500 pulses an intensity of 100% RMT	20	1: before intervention 2: 3 months after intervention	Gait parameters
	He Y et al.,2024	IG:n = 15 conventional PT CG:n = 16 sham rTMS + conventional PT	M1 (on the non-affected hemisphere of the head)	1 Hz frequency 20 min 5 times per week for 4 weeks an intensity of 90% RMT	20	1: before intervention 2: post-intervention	10MWT 6MWT GMFM Gait parameters MAS

IG Intervention Group; *CG* Control Group; *VR* Virtual Reality; *NDT* Neurodevelopmental Treatment; *PT* Physical Therapy; *ST* Standard Therapy; *OT* Occupational Therapy; *M1* Primary motor area; *Cz* Central zero; *ROM* Range of Motion; *RMT* Resting Motor Threshold

Table 3 PEDro scores of included studies

Intervention type	Study name	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Total Score
tDCS	Grecco et al.,2015	YES	YES	YES	YES	YES	NO	YES	YES	YES	YES	YES	7
	Fajardo et al.,2022	YES	YES	NO	NO	NO	NO	YES	YES	NO	NO	YES	4
	Grecco et al.,2014a	YES	YES	YES	YES	NO	NO	YES	YES	YES	YES	YES	8
	Elsadany et al.,2019	YES	YES	NO	YES	NO	NO	NO	YES	NO	YES	YES	5
	Radwan et al.,2023	YES	YES	NO	YES	NO	NO	NO	YES	NO	YES	YES	5
	Grecco et al.,2017	YES	YES	YES	NO	NO	NO	YES	NO	NO	YES	YES	5
	Duarte et al.,2014	YES	YES	YES	YES	YES	NO	YES	YES	NO	YES	YES	8
	Lazzari et al.,2017	YES	YES	YES	YES	YES	NO	YES	YES	NO	YES	YES	6
	Grecco et al.,2014b	YES	YES	NO	YES	YES	NO	YES	YES	NO	YES	YES	7
	Lazzari et al.,2015	YES	YES	YES	NO	YES	NO	NO	NO	NO	YES	YES	4
	Grecco et al.,2023	YES	YES	YES	YES	YES	NO	YES	YES	YES	YES	YES	9
	Valle et al.,2007	YES	NO	NO	YES	YES	NO	YES	YES	NO	YES	YES	6
	Dadashi et al.,2019	NO	YES	NO	NO	YES	NO	YES	YES	NO	NO	YES	5
rTMS	Marzbani et al.,2018	YES	YES	NO	NO	YES	NO	YES	YES	NO	YES	YES	6
	Mahgoub et al.,2021	YES	YES	YES	YES	YES	NO	YES	YES	NO	YES	YES	8
	He et al.,2024	YES	YES	NO	YES	NO	NO	YES	YES	YES	YES	YES	7

tDCS: Transcranial direct current stimulation; *rTMS* Repetitive transcranial magnetic stimulation; *PEDro*Physiotherapy Evidence Database; *Q* Question

0.16–1.23, P = 0.01, I^2 = 41%). However, there were no observed changes in cadence, step length, or step width, as illustrated in Fig. 4A. One-month follow-up analysis [45, 48] revealed no sustained improvements were observed in speed, cadence, stride length, step length, or stride width after the tDCS intervention (Fig. 4B). A single study [27] reported that rTMS was superior to sham stimulation in enhancing cadence, speed, and stride length after three months.

Subgroup analyses revealed differential effects of tDCS parameters on gait outcomes in children with CP. Comparative assessment of treatment sessions demonstrated no significant differences between single-session and ten-session protocols in gait velocity or stride length (P > 0.05), suggesting that the number of treatment sessions may not significantly impact the effect size (Fig. 8B). In contrast, stimulation site selection critically influenced therapeutic outcomes: anodal stimulation over central zero (Cz) and dominant hemisphere M1 preferentially enhanced gait velocity (SMD = 0.89–1.98) and stride length (SMD = 0.73–0.76), whereas contralateral M1 stimulation (ipsilateral to the more severely affected limb) selectively improved cadence (SMD = 1.94, 95% CI 0.83–3.04, P < 0.01), as showed in Fig. 9B. No consistent efficacy was observed for step length and step width (P > 0.05) across subgroups. These findings highlight the importance of stimulation site selection in enhancing specific gait parameters in children with CP.

Effect of NIBS on functional abilities Functional abilities post-intervention and one month follow-up were assessed using GMFM-D and GMFM-E, as well as the Mobility and Self-care domains of the PEDI.

Our meta-analysis revealed significant improvements in GMFM-D scores immediately after the intervention (SMD = 0.53, 95% CI 0.12–0.94, P = 0.01, I^2 = 17%), and these improvements were maintained at the one-month follow-up (SMD = 0.59, 95% CI 0.17–1.00, P < 0.05, I^2 = 45%). Analysis from five RCTs [25, 45, 46, 50, 53] demonstrated substantial changes in the GMFM-E scores both post-intervention (SMD = 0.563, 95% CI 0.10–1.16, P = 0.02, I^2 = 53%) and at the one-month follow-up (SMD = 0.47, 95% CI 0.06–0.88, P = 0.03, I^2 = 35%), as depicted in Fig. 5A and B. Heterogeneity analysis of the immediate effects was conducted, with the results presented in Table 5. Subgroup analyses of tDCS protocols demonstrated differential efficacy based on stimulation parameters. Comparison of ten-session versus fifteen-session interventions revealed no statistically significant differences in GMFM score improvements at immediate post-intervention or one-month follow-up (P > 0.05). However, fifteen-session protocols exhibited larger effect sizes with enhanced statistical robustness, suggesting a potential benefit of extended treatment duration (Fig. 8A). Contralateral M1 targeting (ipsilateral to the more severely impaired lower limb) produced sustained improvements in both GMFM-D and GMFM-E domains, with significant differences observed post-intervention (P < 0.05) and maintained at one-month follow-up

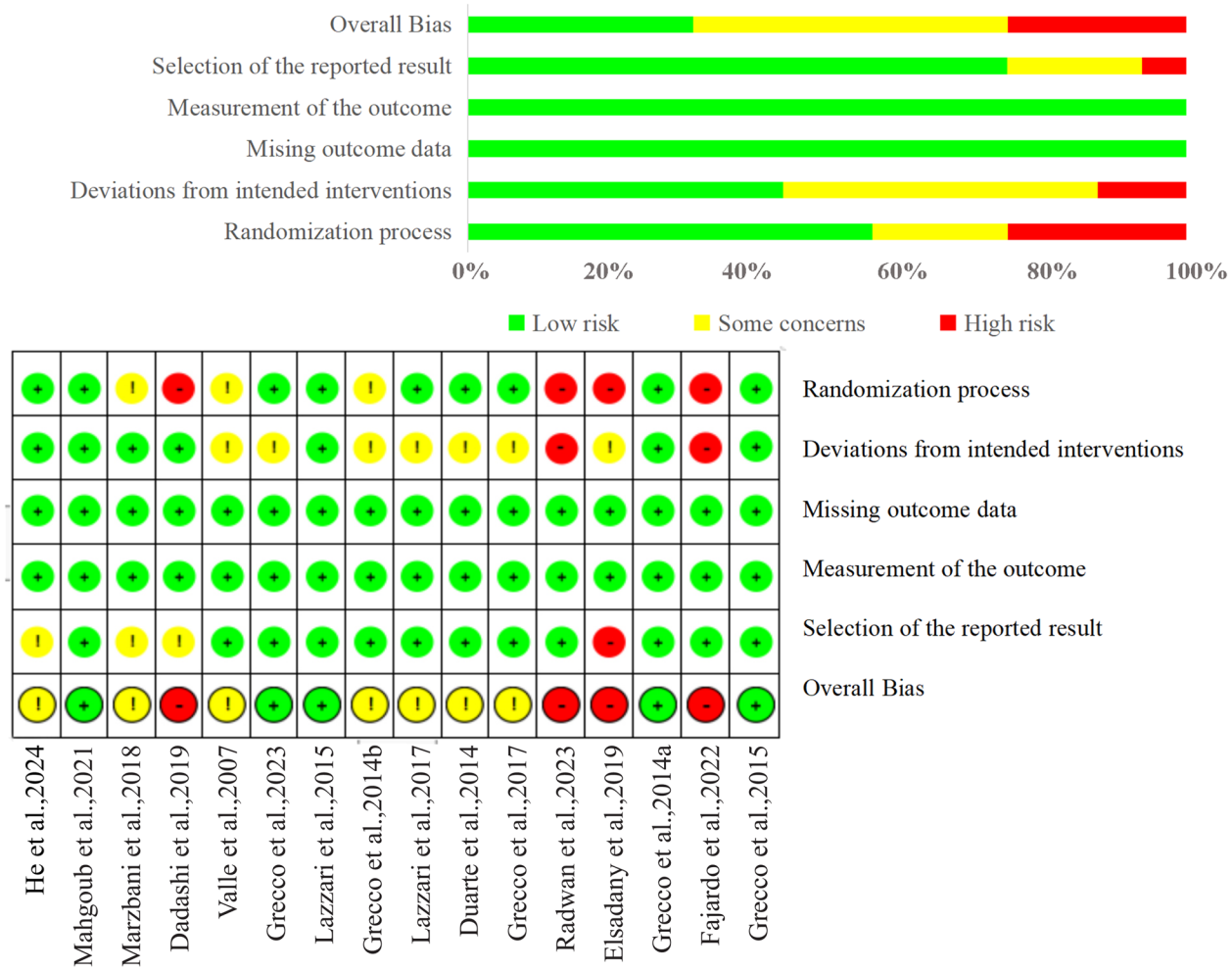

Fig. 2 Risk of Bias Summary for Individual Randomized Controlled Trials (n = 16)

(Fig. 9A). In contrast, dominant hemisphere M1 stimulation failed to demonstrate consistent efficacy across motor domains. These findings underscore the therapeutic superiority of contralateral M1 of the severely impaired side may be a more effective stimulation site for enhancing motor function in children with CP.

In the Mobility domains of PEDI, a meta-analysis of three studies [45–47] showed significant post-intervention improvements (SMD = 0.63, 95% CI 0.10–1.16, P = 0.02, I^2 = 65%) and sustained benefits at the one-month follow-up (SMD = 1.19, 95% CI 0.04–2.35, P = 0.04, I^2 = 80%). High heterogeneity was attributed to one study [46] after sensitivity analysis, as depicted in Table 5.

The Self-care domains of PEDI showed significant effects at the one-month follow-up (SMD = 0.58, 95% CI 0.12–1.05, P = 0.01, I^2 = 0%), but no immediate impact was noted (P > 0.05) [45–47].

Effect of NIBS on balance function

Balance function was evaluated using COP and PBS at two time points: immediately post-intervention and one-month later.

COP parameters indicated no significant static balance changes immediately after tDCS intervention across five studies [47, 49–52] with 82 participants (P > 0.05), regardless of Ground-COP-AP-EO (eyes open), Ground-COP-AP-EC (eyes close), Ground-COP-ML-EO, or Ground-COP-ML-EC (Fig. 6A). High heterogeneity was observed in Ground-AP-EO, Ground-AP-EC and Ground-ML-EC, with I^2 values of 86%, 73%, and 71%, respectively. Excluding one study [50] reduced heterogeneity to 0% for Ground-AP-EO and to 48% for Ground-ML-EC, suggesting it as a source of variability. At the one-month follow-up with three studies [47, 49, 51], similar non-significant findings were reported (Fig. 6B). Although not sufficient for a meta-analysis, a single study [28] provided valuable insights into rTMS's impact

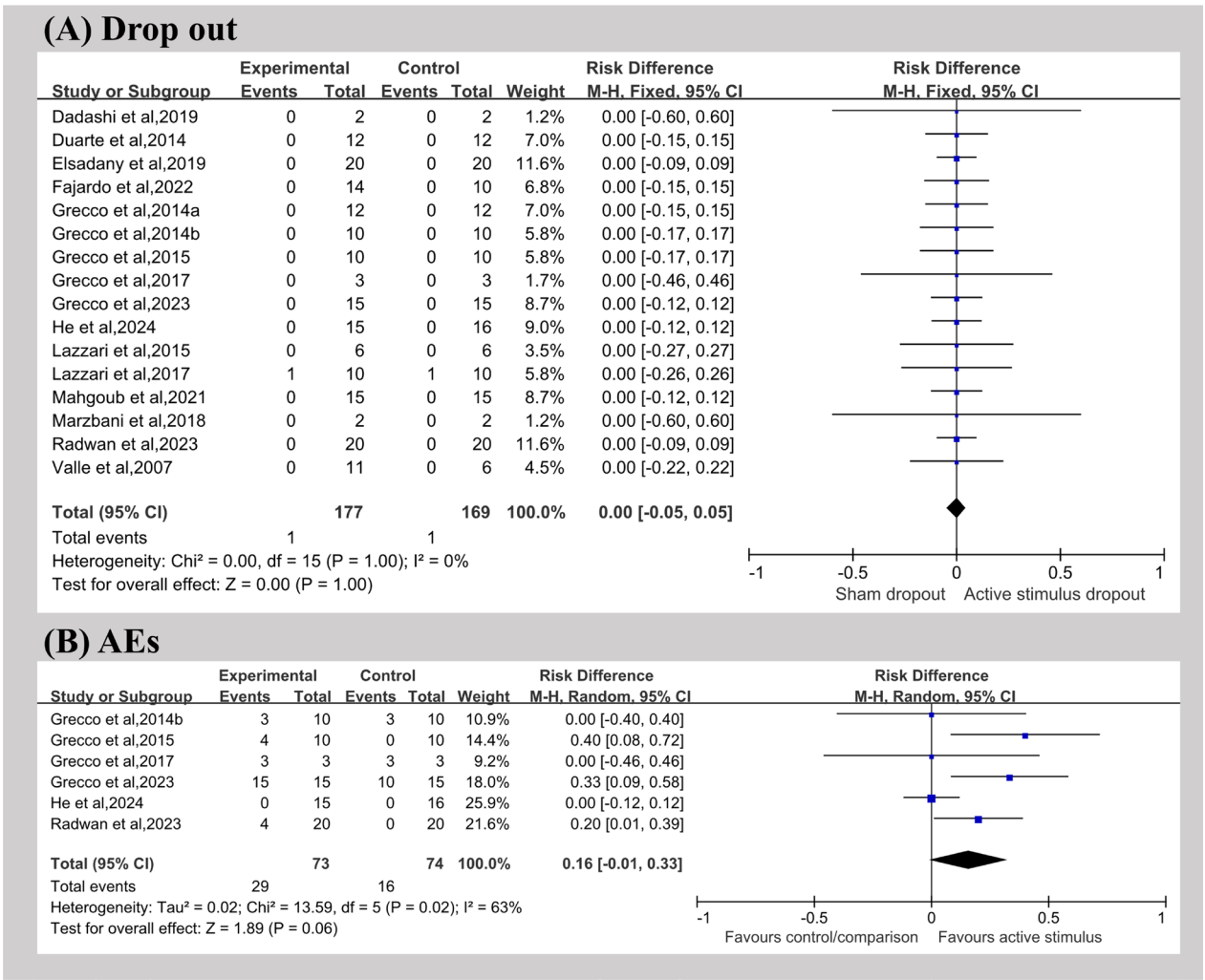

Fig. 3 (A) Forest plot of dropouts in non-invasive brain stimulation (NIBS) trials; (B) Forest plot of adverse events in NIBS trials

Table 4 Treatment-related adverse events in the reviewed studies

Study name	Intervention group (Sample size)	Type of adverse events	Control group (Sample size)	Type of adverse events
Grecco et al.,2015	10	Mild tingling (N = 4)	10	No serious adverse event
Radwan et al.,2023	20	Mild headaches (N = 4)	20	No serious adverse event
Grecco et al.,2017	3	Tingling (N = 3)	3	Tingling (N = 3)
Grecco et al.,2014b	10	Redness and tingling (N = 3)	10	Redness and tingling (N = 3)
Grecco et al.,2023	15	Tingling (N = 12) Redness (N = 15)	15	Ringling (N = 10)
He et al.,2024	15	No serious adverse event	16	No serious adverse event

on balance. It demonstrated that the treatment group showed a significant reduction in oscillations in both the AP and ML directions compared to the sham group, irrespective of visual conditions.

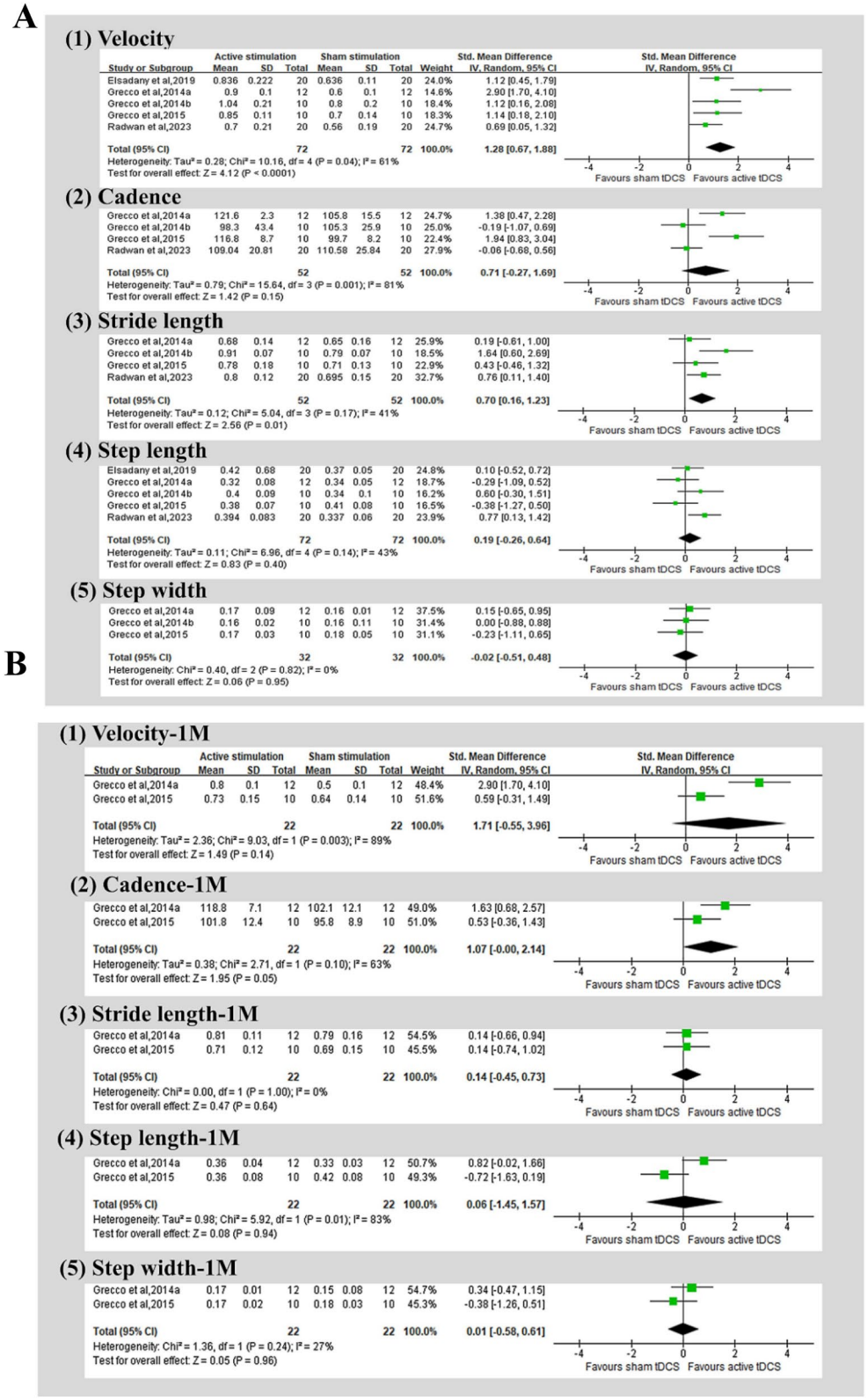

Fig. 4 (A) Forest Plot showing the effect sizes for spatiotemporal gait variables immediately post-intervention; (B) Forest Plot showing the effect sizes spatiotemporal gait variables at the one-month follow-up post-intervention

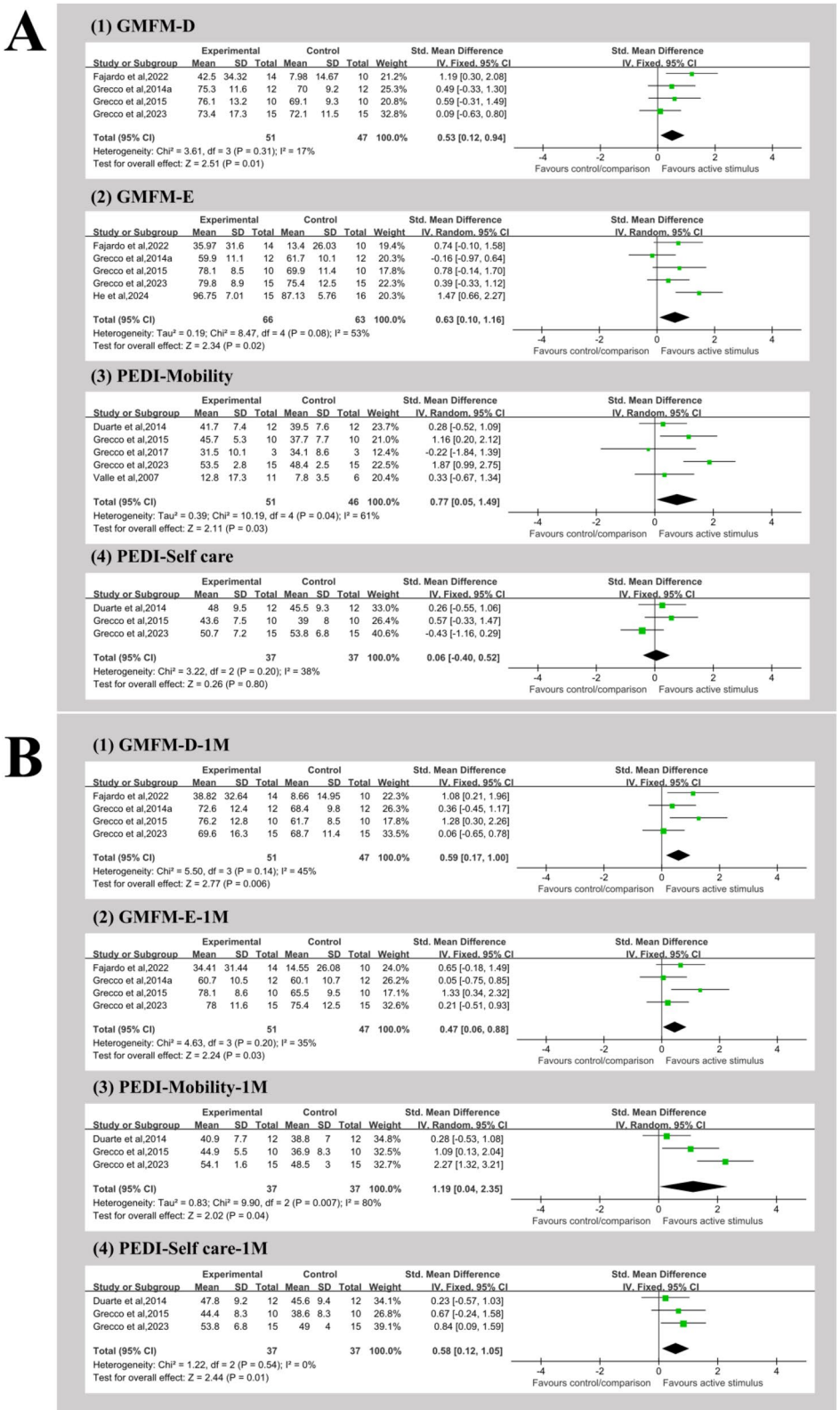

Fig. 5 (A) Forest Plot showing the effect sizes for Gross Motor Function Measure (GMFM) and Pediatric Evaluation of Disability Inventory (PEDI) immediately post-intervention; (B) Forest Plot showing the effect sizes for GMFM, PEDI at the one-month follow-up post-intervention

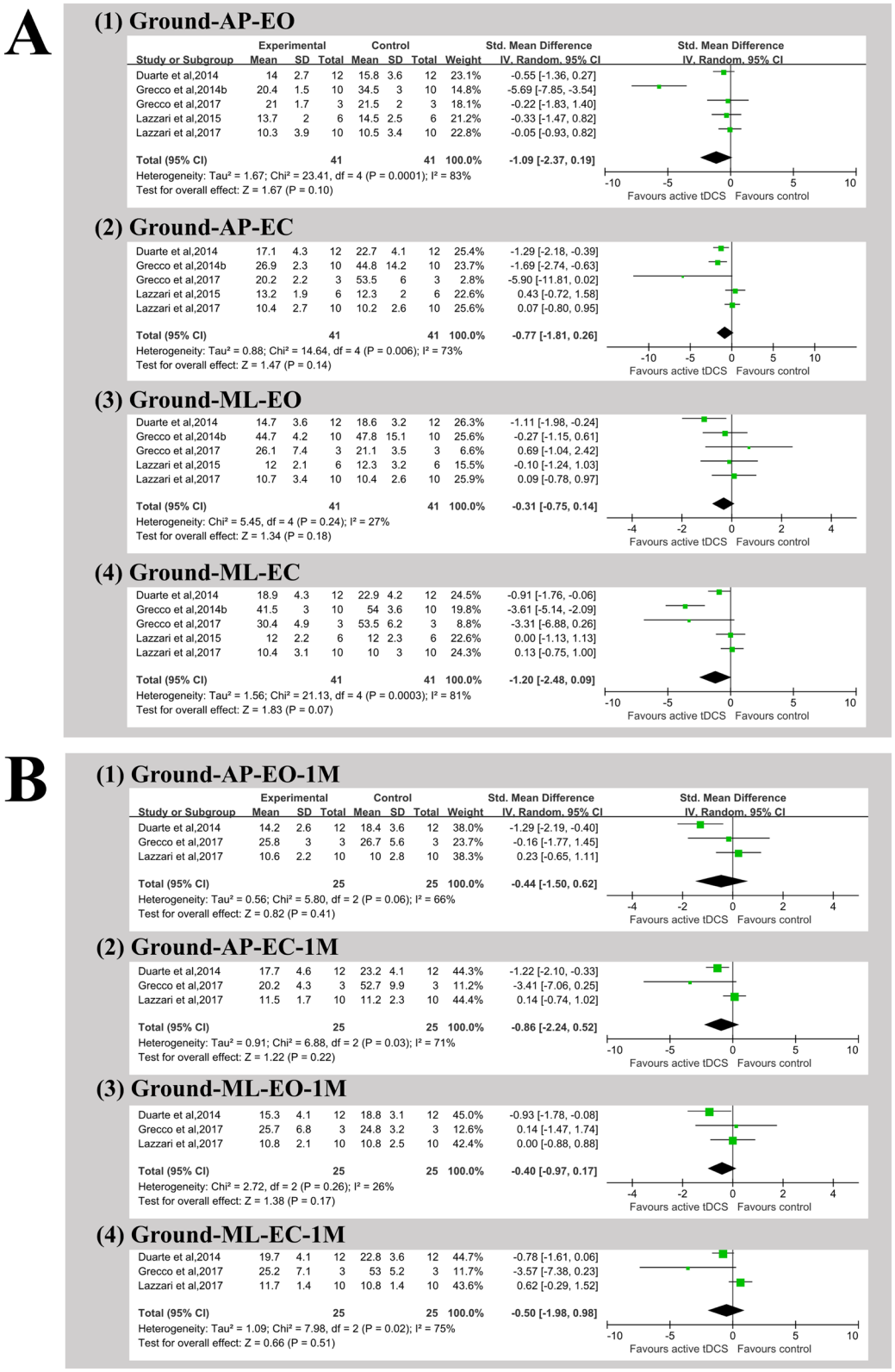

Fig. 6 (A)Forest plot showing the effect sizes for AP and medio-lateral (ML) sway in eyes open (EO) and eyes closed (EC) immediately post-intervention; (B) Forest plot showing the effect sizes for AP and ML sway in EO and EC at the one-month follow-up post-intervention

Table 5 Summary of leave-one-out sensitivity analysis for total studies included in quantitative synthesis

GMFM-E						
Study omitted	Mean [95% CI]	Heterogeneity			Pooled effect size	
		Chi^2	P	I^2(%)	Z	P
Fajardo et al., 2022	0.61 [– 0.06, 1.29]	8.38	0.04	64	1.77	0.08
Grecco et al.,2014a	0.83 [0.37, 1.29]	3.84	0.28	**22**	3.52	< 0.01
Grecco et al.,2015	0.60 [– 0.06, 1.26]	8.33	0.04	64	1.79	0.07
Grecco et al.,2023	0.70 [0.02, 1.39]	7.97	0.05	62	2.01	0.04
He et al.,2024	0.41 [– 0.01, 0.83]	3.19	0.36	**6**	1.91	0.06
PEDI-mobility						
Duarte et al.,2014	0.91 [0.05, 1.77]	7.75	0.05	61	2.08	0.04
Grecco et al.,2015	0.65 [– 0.26, 1.56]	9.6	0.02	69	1.4	0.16
Grecco et al.,2017	0.91 [0.15, 1.67]	8.45	0.04	65	2.34	0.02
Grecco et al.,2023	0.48 [– 0.02, 0.98]	2.95	0.4	**0**	1.89	0.06
Valle et al.,2007	0.87 [– 0.00, 1.75]	9.06	0.03	67	1.95	0.05
PEDI—mobility-1 M						
Duarte et al.,2014	1.68 [0.52, 2.83]	2.96	0.09	66	2.85	< 0.01
Grecco et al.,2015	1.26 [– 0.70, 3.21]	9.90	0.002	90	1.26	0 .21
Grecco et al.,2023	0.64 [– 0.15, 1.43]	1.63	0.2	**39**	1.58	0.11
6MWT						
Grecco et al.,2014a	1.67 [0.68, 2.66]	2.71	0.10	63	3.30	< 0.01
Grecco et al.,2023	1.48 [0.10, 2.87]	5.00	0.03	80	2.10	0.04
He et al.,2024	1.00 [0.43, 1.58]	0.47	0.49	**0**	3.43	< 0.01
Ground—AP-EO						
Duarte et al.,2014	– 1.36 [– 3.23, 0.50]	23.39	< 0.01	87	1.43	0.15
Grecco et al.,2014b	– 0.31 [– 0.81, 0.19]	0.67	0.88	0	1.20	0.23
Grecco et al.,2017	– 1.33 [– 2.87, 0.21]	23.18	< 0.01	87	1.69	0.09
Lazzari et al.,2015	– 1.37 [– 3.04, 0.31]	2.41	< 0.01	87	1.60	0.11
Lazzari et al.,2017	– 1.48 [– 3.23, 0.28]	21.33	< 0.01	86	1.65	0.10
Ground—AP-EC						
Duarte et al.,2014	– 0.65 [– 2.00, 0.70]	12.13	< 0.01	75	0.94	0.35
Grecco et al.,2014b	– 0.49 [– 1.66, 0.68]	10.19	0.02	71	0.82	0.41
Grecco et al.,2017	– 0.63 [– 1.60, 0.34]	11.63	< 0.01	74	1.27	0.20
Lazzari et al.,2015	– 1.12 [– 2.26, 0.03]	10.32	0.02	71	1.92	0.06
Lazzari et al.,2017	– 1.08 [– 2.34, 0.18]	10.56	0.01	72	1.68	0.09
Ground-ML-EC						
Duarte et al.,2014	– 1.41 [– 3.29, 0.47]	20.87	< 0.01	86	1.47	0.14
Grecco et al.,2014b	– 0.43 [– 1.24, 0.38]	5.78	0.12	**48**	1.04	0.30
Grecco et al.,2017	– 0.99 [– 2.32, 0.33]	19.09	< 0.01	84	1.46	0.14
Lazzari et al.,2015	– 1.60 [– 3.24, 0.04]	19.13	< 0.01	84	1.92	0.06
Lazzari et al.,2017	– 1.66 [– 3.28, – 0.04]	15.68	< 0.01	81	2.01	0.04
Ground-AP-EO-1 M						
Duarte et al.,2014	0.14 [– 0.63, 0.91]	0.17	0.68	**0**	0.35	0.72
Grecco et al.,2017	– 0.53 [– 2.02, 0.96]	5.63	0.02	82	0.70	0.49
Lazzari et al.,2017	– 0.93 [– 1.96, 0.10]	1.45	0.23	**31**	1.77	0.08
Ground-AP-EC-1 M						
Duarte et al.,2014	– 1.17 [– 4.53, 2.19]	3.42	0.06	71	0.68	0.49
Grecco et al.,2017	– 0.54 [– 1.87, 0.80]	4.58	0.03	78	0.79	0.43
Lazzari et al.,2017	– 1.56 [– 3.12, – 0.00]	1.30	0.25	**23**	1.96	0.05
Ground-ML-EC-1 M						
Duarte et al.,2014	0.03 [– 0.74, 0.80]	0.02	0.88	**0**	0.08	0.94
Grecco et al.,2017	– 0.48 [– 1.09, 0.13]	2.23	0.14	55	1.54	0.12
Lazzari et al.,2017	– 0.70 [– 1.45, 0.05]	1.32	0.25	**24**		0.07

GMFM-E the E domains of Gross Motor Function Measure; *PEDI* Pediatric Evaluation of Disability Inventory; *1 M* one-month follow-up; *AP* anteroposterior; *ML* mediolateral; *6MWT* 6-min Walk Test; *EC* eye close; *EO* eye open; 95% *CI* 95% confidence interval

A meta-analysis encompassing three articles [47, 49, 51] on tDCS showed no significant difference both immediate (SMD = 0.48, 95% CI − 0.09–1.04, $I^2 = 0\%$) or one-month post-intervention significant changes (SMD = 0.55, 95% CI − 0.03–1.13, $I^2 = 0\%$) in PBS scores. However, there was a trend that suggested this treatment has the potential to produce significant long-term benefits. The analysis exhibited no heterogeneity among the studies [47, 49, 51], as demonstrated in Fig. 7C.

Discussion

Summary of evidence

This systematic review and meta-analysis assess the safety and effectiveness of NIBS, specifically tDCS and rTMS, on mobility and balance of children with CP. The review included 16 studies (11 studies employing tDCS [24–26, 45–52] and five using rTMS [27, 28, 53–55]), totaling 346 children aged 3.17–14 years. Gender distribution across the studies was relatively balanced, with 117 males (55.2%) and 95 females (44.8%) reported in nine articles that detailed this information [24, 25, 27, 45, 48, 49, 51, 53, 55]. Specifically, the male-to-female ratio was 1.1:1 in tDCS studies and 1.2:1 in rTMS studies. For the reporting of GMFCS levels, 11 articles [24–26, 45–52] provided specific information, indicating that the most participants (98.2%) were in mild to moderate motor impairments (levels I-III), with only a few in severe impairment (level IV). This suggests a focus on participants with less severe disabilities. Furthermore, eleven randomized controlled trials (RCTs) using tDCS involved 260 CP children (75.1% of the total sample), predominantly with diplegia (63.1%). Conversely, five studies using rTMS involved 86 CP children (24.9%), mostly with hemiplegia (80.3%). These findings highlight the predominant use of NIBS techniques in children with specific types of CP, emphasizing the need for more research on other subtypes and severity levels.

A meta-analysis was conducted on all 16 studies to evaluate the acceptability and tolerability of NIBS. The meta-analysis revealed no significant difference in dropout rates between the NIBS and control groups, indicating good tolerability of NIBS in children with CP. Adverse events reported were mild to moderate. No serious adverse reactions, such as epilepsy or sleep disorders, were reported. This is consistent with previous findings [21, 22, 56] that NIBS does not increase adverse events in children with CP or brain injury. It should be noted that several studies [24–26, 45, 47–52, 54, 55] excluded patients with epilepsy, potentially limiting the generalizability of the findings. Overall, NIBS appears to be safe for children with CP, though further research is needed for a more comprehensive evaluation of its safety. Additionally, a meta-analysis on 14 studies assessed the effectiveness of NIBS in improving mobility and balance in children with CP. Results showed that NIBS could safely and effectively improve mobility in children with CP, as demonstrated by improvements in 6MWT, key gait parameters (velocity, stride length, GMFM-D and GMFM-E, and the Mobility domains of PEDI scores at post-intervention and one-month follow-up. Notably, two Studies [53, 54] indicated that NIBS, particularly rTMS, significantly enhances 10MWT performance. However, balance, as measured by the COP and PBS, did not exhibit significant changes post-tDCS or at the one-month follow-up.

Overall findings

The mobility function *(6MWT, 10MWT, TUGT, GMFM, Gait parameters)*

NIBS showed a medium to large effect on 6MWT, velocity, and stride length within one month, aligning with previous studies [21] that NIBS can improve mobility after pediatric patients following brain injury. Both rTMS and tDCS are known to enhance synaptic plasticity and modulate cortical excitability, potentially improving motor function [57, 58]. However, the meta-analysis results for the GMFM-D score differ from those reported by Elbanna et al. [21], which may stem from variations in study populations, with Elbanna's research focused solely on post-brain injury patients, encompassing a broader population without isolating CP as a specific subgroup. In contrast, our review is specifically centered on CP, including cases arising from various etiologies such as congenital brain malformations. Additionally, the inclusion of recent studies over the past six years has expanded the sample size, enhancing the reliability and generalizability of the findings [24–30].

Moreover, the impact of NIBS on TUGT scores was mixed, with some studies reporting no significant improvement post-tDCS [46, 49, 51]. The absence of significant improvements in the TUGT scores post-tDCS could be explained by the nature of the test itself. The TUGT primarily assesses functional mobility, which may be less responsive to cortical excitability modulation than more dynamic tests like the 6MWT. Furthermore, the TUGT performance may depend more on balance and coordination than on raw motor output, which may explain the lack of significant changes in TUGT scores after NIBS interventions.

Five studies [24, 26, 45, 47, 50] showed that anodal tDCS improved gait velocity and stride length immediately post-intervention. However, tDCS did not significantly influence step length and width, possibly due to complex interplay of musculoskeletal factors and proprioceptive deficits common in children with CP. These factors can impair the accurate perception and control of limb movements, leading to bilateral limb asymmetry

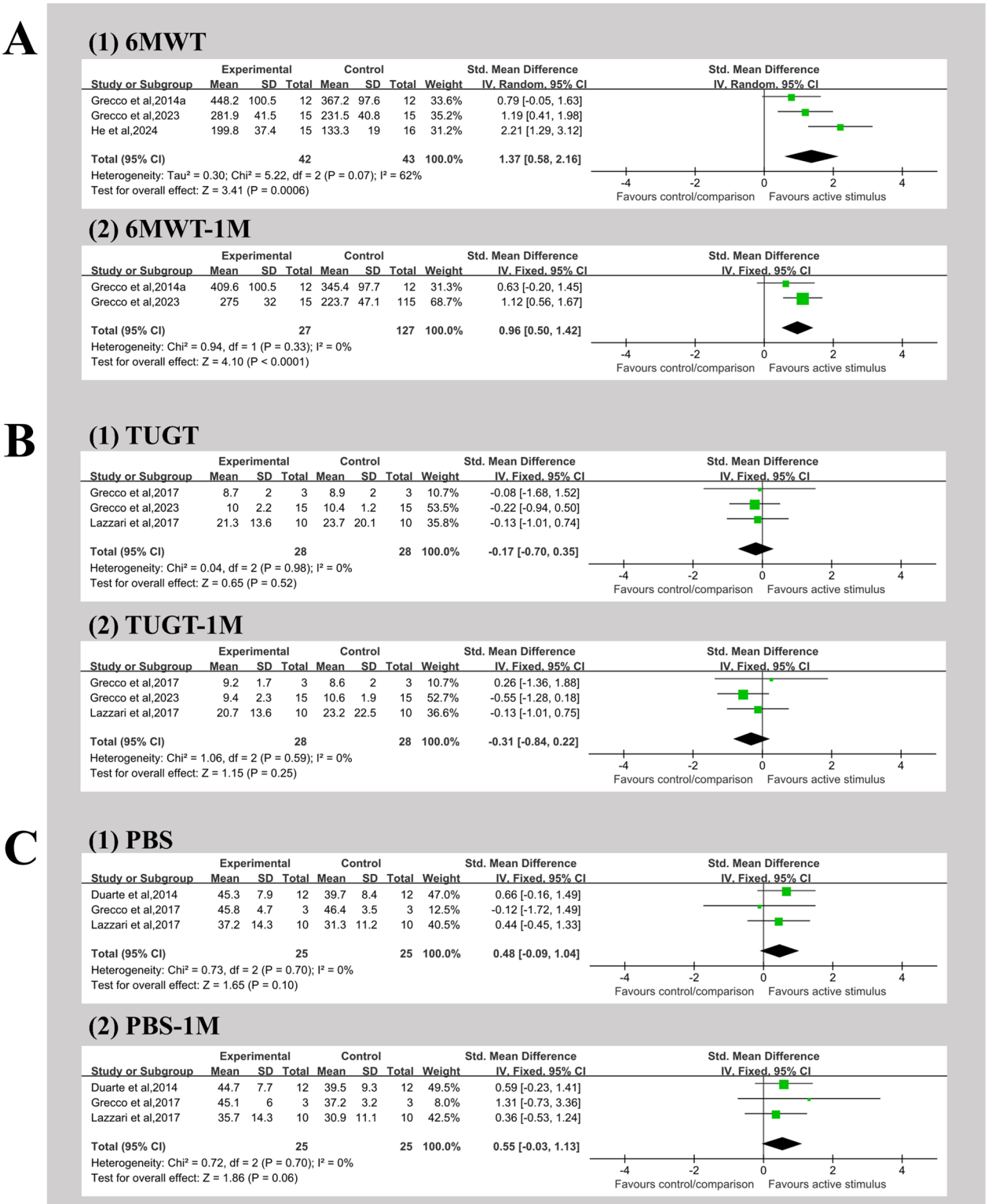

Fig. 7 Forest plot showing the effect sizes from the control between active vs sham NIBS for 6-min Walk Test, Timed Up and Go Test and Pediatric Balance Scale. (A) Result of meta-analysis of 6-min Walk Test immediately post-intervention and one-month follow-up; (B) Result of meta-analysis of Timed Up and Go Test immediately post-intervention and one-month follow-up; (C) Result of meta-analysis of Pediatric Balance Scale immediately post-intervention and one-month follow-up

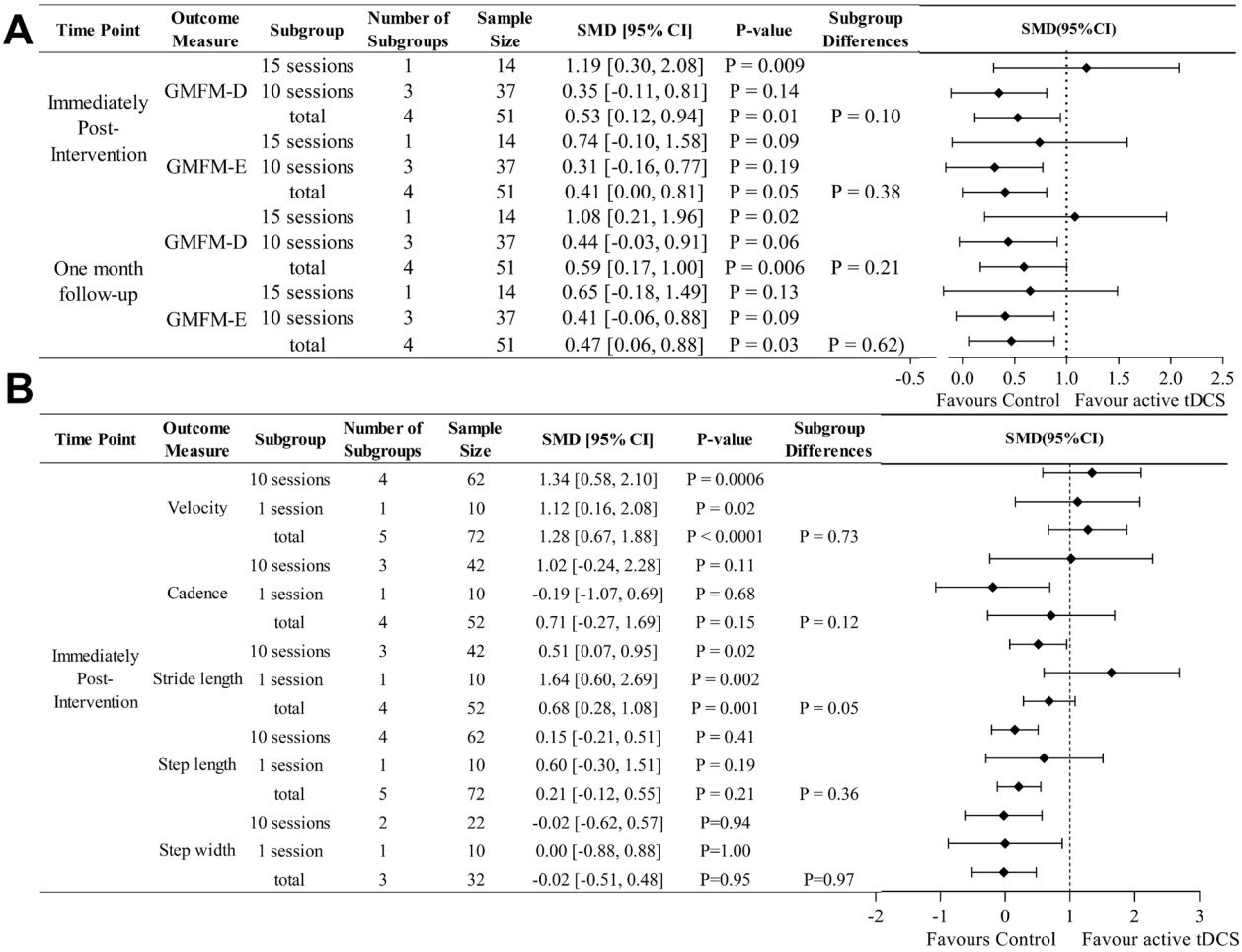

Fig. 8 (A) Forest plot of subgroup analysis on stimulation sessions for GMFM immediately post-tDCS intervention and at the one-month follow-up; (B) Forest plot of subgroup analysis on stimulation sessions for spatiotemporal gait variables immediately post-tDCS intervention

and complicating the expected quantitative relationship between stride length and step length [59]. Electrophysiological studies have reported increased motor-evoked potentials following anodal tDCS, reflecting enhanced cortical excitability [45, 48]. However, whether these changes directly translate into clinically meaningful improvements in gait variables remains debatable. Gait improvement is a multifaceted process that involves the complex interaction of neural, muscular, and biomechanical factors. The studies included in this review suggest that tDCS is often combined with motor training, which likely plays a synergistic role in the observed outcomes [24, 26, 45, 47, 50]. The combined intervention enhances not only cortical excitability but also neuromuscular coordination, proprioception, and motor control, all of which are crucial for effective gait performance. Previous research has indicated that such combined approaches may yield greater improvements in motor function compared to either intervention alone [27, 54].

The NIBS intervention showed significant improvements in the 6MWT, gait speed, and stride length within one month. However, evaluating long-term effects beyond one month is challenging due to limited studies (fewer than two) with follow-up periods ranging from five days to three months. ElasDany et al. [26] found that both tDCS and treadmill interventions positively impacted spatiotemporal gait parameters, gait speed, and step length, with anodal tDCS showing sustained benefits up to 10 weeks. Similarly, Mahgoub et al. [27] demonstrated that combining rTMS with motor exercises significantly improved gait patterns in children with hemiplegic CP compared to physical therapy alone. Thus, NIBS may offer superior and longer-lasting gait improvements. Despite this, evidence suggests that combining NIBS with motor training may enhance neuroplasticity and recovery more effectively than either method alone [60]. Future research should focus on extending follow-up periods, increasing sample sizes, and

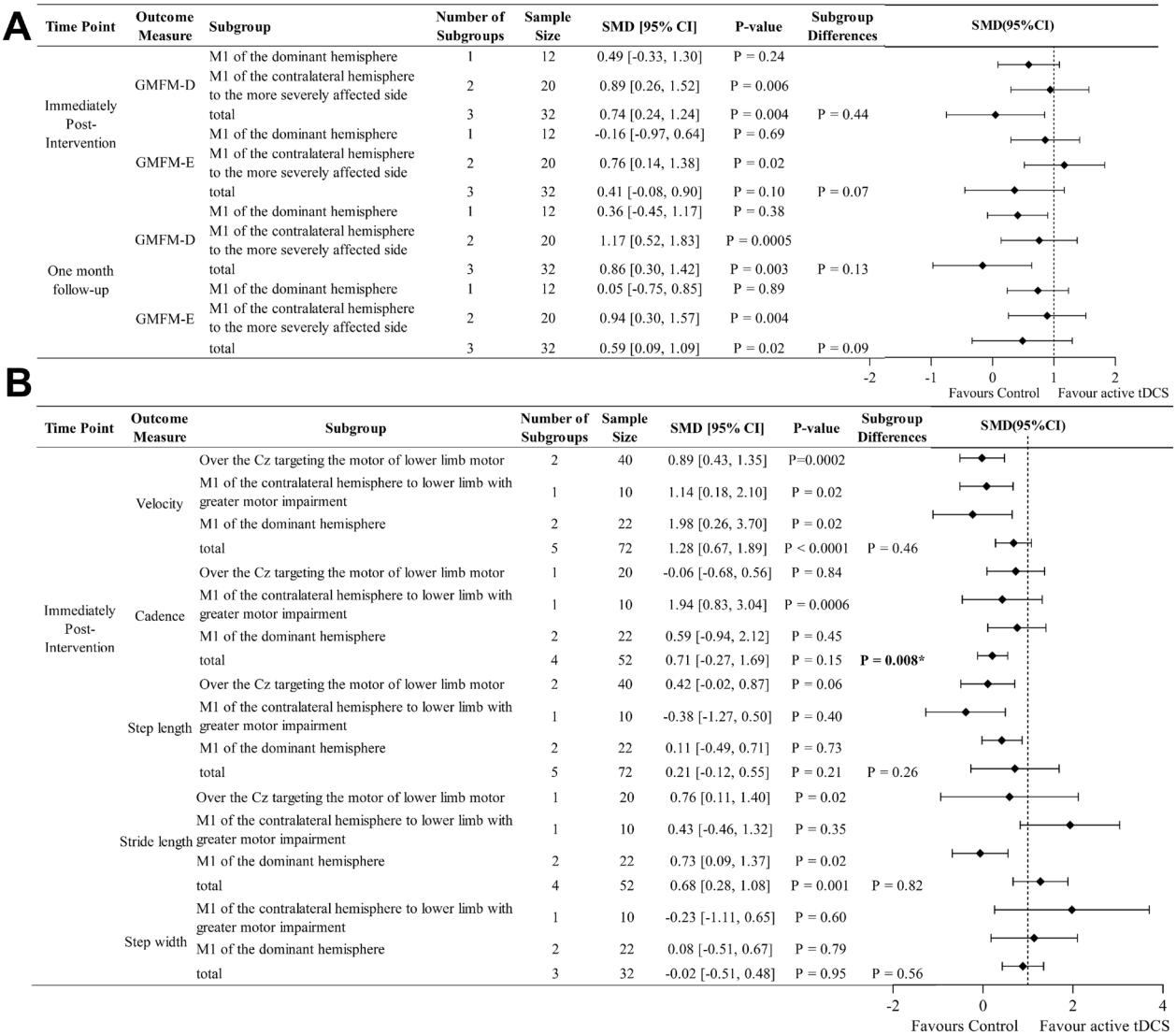

Fig. 9 (A) Forest plot of subgroup analysis on stimulation sites for GMFM immediately post-tDCS intervention and at the one-month follow-up; (B) Forest plot of subgroup analysis on stimulation sites for spatiotemporal gait variables immediately post-tDCS intervention

conducting multicenter RCTs to better understand NIBS's long-term benefits and guide clinical applications.

The balance function *(COP and PBS)*

Regarding balance, the review reveals mixed findings regarding the effect of NIBS techniques on balance in children with CP. Specifically, concerning tDCS, five studies [47–49, 51, 52] found no significant impact of tDCS on COP and PBS scores. This contrasts with positive outcomes reported in earlier reviews [21], suggesting discrepancies that may stem from variations in data extraction methodologies and participant heterogeneity. The divergence from adult stroke rehabilitation literature is also notable. Adult neurorehabilitation literature highlights more pronounced effects when combining tDCS with motor training, which may be related to the difference between developing and developed brain. In contrast, rTMS has shown promise in enhancing balance control among CP children. Dadashi et al. demonstrated improvements in both quantitative and clinical balance measures following a three-week rTMS invention [28]. These results suggest that rTMS might facilitate corticospinal tract functionality and descending pathways, thereby improving balance control. This finding supports the potential of rTMS as a therapeutic tool for hemiplegic CP children, although further research with larger sample sizes is warranted to validate these preliminary observations.

Regarding tDCS targeting sites, most studies in the review targeted the M1, with one exception [49] targeting the cerebellum, which primarily controls balance. This study revealed that anodal tDCS over the cerebellum combined with cycling training improved balance in children with ataxic CP. This underscores the potential of cerebellar tDCS to enhance balance function, particularly in ataxic CP. A planned comparative study aims to evaluate the clinical and functional impacts of tDCS applied to central scalp site versus cerebellum on gait spatiotemporal parameters, functional mobility, balance, gross motor function, and performance. Assessments will be conducted pre-intervention, post-intervention, and at one- and three-months follow-up, providing a longitudinal perspective on treatment efficacy [61].

Sources of heterogeneity and their impact

The sensitivity analysis has provided critical insights into the stability and reliability of our meta-analytic findings. Specifically, it has highlighted significant variability across different outcome measures and identified potential sources of heterogeneity. The mobility domain of PEDI showed improvements both immediately post-tDCS and at the one-month follow-up, but the self-care domain of the PEDI did not, suggesting that NIBS might selectively affect mobility metrics. The meta-analysis examining the effects of NIBS on CP revealed significant improvements in mobility ability, measured by the GMFM-E and 6MWT. However, the analysis showed substantial heterogeneity in the results, primarily driven by rTMS studies. Excluding rTMS studies [53] in the sensitivity analysis reduced the heterogeneity, indicating that tDCS may offer more consistent therapeutic effects in improving motor function in children with CP compared to rTMS. A comprehensive comparison between tDCS and rTMS remains absent in the literature. The limited number of articles makes it challenging to assess the effectiveness and to compare the effects of rTMS and tDCS on mobility and balance in children with CP. Future research should focus on RCTs comparing both techniques to establish optimal treatment protocols.

Significant heterogeneity was observed in both the immediate post-intervention and one-month follow-up assessments of COP parameters. Specifically, high heterogeneity was noted in Ground-ML-EC, Ground-AP-EO, and Ground-AP-EC for both immediate and one-month assessments, whereas Ground-ML-EO did not exhibit significant heterogeneity. Sensitivity analysis identified studies by Grecco et al. and Lazzari et al. as major sources of heterogeneity. [50, 51]. One excluded study [50] conducted only a single tDCS session and examined active versus sham tDCS without combination therapies, while another studies [51] detailed lacked participant information, such as age and CP subtype. Despite excluding these studies, no statistically significant differences were found in COP outcomes, suggesting robust results. Future research should standardize intervention protocols, including session frequency and adjunct therapies, report comprehensive participant characteristics, and explore subgroup effects to improve reliability.

Parameters of NIBS interventions

The effectiveness of interventions is affected by factors like targeted brain regions, stimulation duration, and other parameters related to the stimulation, emphasizing the necessity for tailored stimulation strategies.

Our subgroup analyses demonstrated that the efficacy of tDCS in improving motor function in children with CP is critically influenced by both stimulation site specificity and treatment session. While no statistically significant differences were observed between 10-session and 15-session protocols in GMFM scores (e.g., standing and walking abilities), the 15-session regimen demonstrated larger effect sizes with enhanced clinical significance, suggesting that extended treatment courses may consolidate therapeutic benefits through cumulative neuroplastic adaptations. Stimulation sites further influenced functional outcomes: stimulation of the contralateral M1 region (ipsilateral to the more severely impaired limb) elicited sustained improvements in mobility functions for at least one-month post-intervention, whereas Cz vertex and dominant hemisphere M1 stimulation preferentially enhanced gait velocity and stride length. These findings failed to establish definitive conclusions regarding optimal treatment parameters but highlight the critical role of stimulation site selection in optimizing neuromodulatory interventions for CP-related motor function dysfunction. Subgroup analyses of tDCS stimulation duration and intensity were attempted; however, methodological heterogeneity in outcome assessments (e.g., diverse analysis tools) and uniform stimulation parameters across trials (1 mA intensity, 20-min sessions) limited cross-study comparisons.

Studies [28, 53–55] applied low frequency rTMS to the affected brain side to reduce imbalance in bilateral activity and minimize maladaptive neuroplastic changes caused by unilateral lesions, yet the data [27] is insufficient for comparing outcomes of stimulating the affected versus inhibiting the opposite hemisphere. In our review, pulse numbers ranged from 1200 to 1500, and the number of sessions varied widely ranging from 5 to 24. Research [62, 63] shows that increasing rTMS sessions and pulse counts may improve motor function in children with CP. A moderate increase in session count specifically targets reductions in spasticity. However, recent systematic

reviews on clinical stroke models showed no significant differences in motor recovery based on varying rTMS pulse counts and up to 20 rTMS sessions reported significant results, but those with 5–10 sessions had larger effect sizes, suggesting a potential ceiling effect for rTMS session numbers [29]. Among the five rTMS studies included, three stimulated the unaffected motor cortex, while two targeted the affected hemisphere. Both 1 Hz and 10 Hz rTMS showed advantages over sham stimulation in rhythm, speed, step length, and ankle angle indices. Additionally, 1 Hz rTMS combined with motor training significantly improved lower limb motor function. Dadashi's findings indicate that 3 weeks of 1 Hz rTMS improved balance control in children with CP, highlighting potential of rTMS for enhancing balance [28]. More studies are exploring rTMS to improve upper limb function and reduce spasticity in children with CP [23, 29, 64]. However, few studies have explored its impact on mobility and balance, which limits our ability to conduct robust meta-analysis based on quantitative data. Current limitations, including heterogeneity in stimulation protocols (e.g., duration, intensity,) and outcome assessment timing, hinder definitive meta-analytical conclusions. While rTMS demonstrates potential for enhancing motor function and balance in children with CP, further investigations are needed to validate its efficacy through robust subgroup and meta-analyses. Future studies should prospectively report participant demographics (age, gender, CP subtype, GMFCS level) and NIBS parameters (stimulation site, session number, intensity, frequency) with standardized reporting frameworks. This methodological rigor will facilitate the replication of studies and improve the generalizability of findings.

Limitations

This study has several limitations. Firstly, while significant short-term improvements were observed within one month of NIBS intervention, data on long-lasting effects are limited, with follow-ups ranging from five days to three months. Fewer than two studies have provided long-term data, restricting comprehensive analysis of sustained outcomes. Secondly, the variability in participant age demographics poses a challenge. Developmental differences between children and adolescents may influence the effectiveness of NIBS interventions, underscoring the need for future research to conduct stratified or subgroup analyses to explore age as a potential moderator of intervention outcomes. Lastly, inadequate reporting of stimulation parameters across studies limits the ability to establish optimal guidelines for clinical application. Addressing these limitations in future research will enhance our understanding and clinical utility of NIBS in pediatric populations.

Conclusion

Our findings support the use of NIBS as a safe and feasible tool for enhancing mobility in children with CP, demonstrating both immediate and sustained improvements in gait parameters such as velocity and stride length. However, the impact on balance remains inconclusive, with some evidence suggesting that targeted cerebellar stimulation may offer potential benefits. Future research should focus on extending follow-up periods, increasing sample sizes, and exploring tailored stimulation protocols to better understand the long-term efficacy and optimal application of NIBS in pediatric populations.

Appendix

See Table 6, and 7.

Table 6 Search strategy

	Detail
PubMed N = 38	((((((((((cerebral palsy[MeSH Terms]) OR (Cerebral pals*)) OR (CP)) OR (hemiplegi*)) OR (monoplegi*)) OR (diplegi*)) OR (triplegi*)) OR (quadriplegi*)) OR (tetraplegi*)) AND (((((transcranial magnetic stimulation[MeSH Terms]) OR (transcranial direct current stimulation[MeSH Terms])) OR (((((TMS) OR (transcranial magnetic stimulation*)) OR (rTMS)) OR (repetitive transcranial magnetic stimulation*)) OR (deep transcranial magnetic stimulation*))) OR ((tDCS) OR (transcranial direct current stimulation*))) OR (((NIBS) OR (non-invasive brain stimulation*)) OR (noninvasive brain stimulation*)))) AND ((((((((standing) OR (balance)) OR (mobility)) OR (walking)) OR (lower extremity[MeSH Terms])) OR (lower limb*)) OR (lower extremit*)) OR (motor function)) AND ((humans[Filter]) AND (english[Filter]) AND (allchild[Filter])) Filters: Clinical Trial, Randomized Controlled Trial, Humans, English, Child: birth-18 years
EMBASE N = 80	('cerebral palsy'/exp OR 'cp'/exp OR 'hemiplegi*' OR 'monoplegi*' OR 'diplegi*' OR 'triplegi*' OR 'quadriplegi*' OR 'tetraplegi*') AND ('tms'/exp OR 'transcranial magnetic stimulation*' OR 'rtms' OR 'repetitive transcranial magnetic stimulation*' OR 'deep transcranial magnetic stimulation'/exp OR 'tdcs' OR 'transcranial direct current stimulation*' OR 'nibs' OR 'non-invasive brain stimulation*' OR 'noninvasive brain stimulation*') AND ('balance'/exp OR 'mobility'/exp OR 'standing'/exp OR 'walking'/exp OR 'lower limb*' OR 'lower extremit*' OR 'motor function'/exp) AND ('child'/exp OR 'children'/exp OR 'kid*' OR 'neonate'/exp OR 'infant*') NOT ('adult*' OR 'mice'/exp OR 'mouse'/exp)

Table 6 (continued)

	Detail
Prosquest N = 186	((((("cerebral palsy" OR "CP" OR "hemiplegi*" OR "monoplegi*" OR "diplegi*" OR "triplegi*" OR "quadriplegi*" OR "tetraplegi*") NOT ("apoplexy" OR "autism" OR "ASDs" OR "stroke")) AND (("child" OR "children" OR "kid*" OR "neonate" OR "infant*") NOT ("adult*" OR "mice" OR "mouse")) AND (("TMS" OR "transcranial magnetic stimulation*" OR "rTMS" OR "repetitive transcranial magnetic stimulation*" OR "deep transcranial magnetic stimulation") OR ("tDCS" OR "transcranial direct current stimulation*" NOT ("FES" OR "functional electrical stimulation")) OR ("NIBS" OR "non-invasive brain stimulation*" OR "noninvasive brain stimulation*"))) AND ("standing" OR "balance" OR "mobility" OR "walking" OR "lower extremit*" OR "lower limb*" OR "motor function"))AND (la.exact("ENG") AND stype.exact("Scholarly Journals"))
Scopus N = 85	(TITLE-ABS-KEY ("cerebral palsy" OR "CP" OR "hemiplegi*" OR "monoplegi*" OR "diplegi*" OR "triplegi*" OR "quadriplegi*" OR "tetraplegi*") AND TITLE-ABS-KEY ("TMS" OR "transcranial magnetic stimulation*" OR "rTMS" OR "repetitive transcranial magnetic stimulation*" OR "deep transcranial magnetic stimulation" OR "tDCS" OR "transcranial direct current stimulation*" OR "NIBS" OR "non-invasive brain stimulation*" OR "non-invasive brain stimulation*") AND TITLE-ABS-KEY ("standing" OR "balance" OR "mobility" OR "walking" OR "lower extremit*" OR "lower limb*" OR "motor function") AND TITLE-ABS-KEY ("child" OR "children" OR "kid*" OR "neonate" OR "infant*")) AND (LIMIT-TO (LANGUAGE, "English")) AND (LIMIT-TO (DOCTYPE, "cp") OR LIMIT-TO (DOCTYPE, "ar"))
Web of science N = 98	(TS = "cerebral palsy" OR "CP" OR "hemiplegi*" OR "monoplegi*" OR "diplegi*" OR "triplegi*" OR "quadriplegi*" OR "tetraplegi*" (All Fields) AND "child" OR "children" OR "kid*" OR "neonate" OR "infant*" (All Fields) AND "TMS" OR "transcranial magnetic stimulation*" OR "rTMS" OR "repetitive transcranial magnetic stimulation*" OR "deep transcranial magnetic stimulation" OR "tDCS" OR "transcranial direct current stimulation*" OR "NIBS" OR "non-invasive brain stimulation*" OR "noninvasive brain stimulation*" (All Fields) AND "standing" OR "balance" OR "mobility" OR "walking" OR "lower extremit*" OR "lower limb*" OR "motor function" (All Fields) and Review Article (Exclude – Document Types) and English (Languages))

Table 7 Eligibility criteria

	Inclusion criteria	Exclusion criteria
P-population	Patients with CP (aged 18 years old or younger)	Animal or non-human experiments Be diagnosed with CP when younger than 18 years old but became older than 18 when receiving rehabilitation interventions The children were diagnosed with genetic or chromosomal disorders or congenital nerological illness
I-intervention	NIBS, including transcranial direct current stimulation(tDCS) or repetitive transcranial magnetic stimulation (rTMS)	N/A
C-comparison	Other types of intervention, between-group comparison, within group comparison, pre-post comparison, no treatment, and/or sham-stimulation	N/A
O-outcomes	Outcomes were evaluated using mobility-related measures (e.g., gait analysis, the 6-min Walk Test [6MWT], the 10 m Walk Test [10MWT], Timed Up and Go Test [TUGT], Gross Motor Function Measure [GMFM], and Pediatric Evaluation of Disability Inventory [PEDI]) and balance-related measures (e.g. center of pressure [COP], and the Pediatric Balance Scale [PBS])	N/A
S-study type	Randomized Controlled Trials (RCTs)	Any articles that do not have full-text available. Non-English studies

Abbreviations

AP	Anteroposterior
CP	Cerebral palsy
COP	Center of pressure
Cz	Central zero
GMFCS	Gross Motor Function Classification System
GMFM	Gross Motor Function Measure
ML	Mediolateral
M1	Primary motor cortex
NIBS	Non-invasive brain stimulation
PBS	Pediatric balance scale
PEDI	Pediatric evaluation of disability inventory
PRISMA	Preferred reporting items for systematic reviews and meta-analyses
RCTs	Randomized controlled trials
rTMS	Repetitive transcranial magnetic stimulation
tDCS	Transcranial direct current stimulation
TUGT	Timed Up and Go Test
10MWT	10 Meters Walk Test
6MWT	6-Minute Walk Test

Author contributions

Contributors' Statement Page A conceptualized and designed the study and data collection instruments, collected data, carried out the initial analyses, drafted the initial manuscript, and critically reviewed and revised the manuscript. B conceptualized and designed the study and data collection instruments, collected data, carried out the initial analyses, and critically reviewed and revised the manuscript. C and D conceptualized and designed the study, and critically reviewed and revised the manuscript. E, F, G, H, and I critically reviewed and revised the manuscript. J conceptualized and designed the study, carried out the analyses, and critically reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable.

Competing interests
The authors declare no competing interests.

Consent for publication
Not applicable.

Author details
[1]Department of Rehabilitation, Guangzhou Women and Children's Medical Center, Guangzhou Medical University, Guangzhou 510120, China. [2]Department of Sport Rehabilitation, Shanghai University of Sport, Shanghai 200438, China.

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