Scoping review

# The use of transcranial direct current stimulation in individuals with cerebral palsy: a scoping review

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**ABSTRACT | BACKGROUND:** Cerebral palsy (CP) is a neurodevelopmental condition that begins in early childhood and persists throughout life, causing limitations in daily activities and social participation. Neuromodulatory interventions using non-invasive brain stimulation, like transcranial direct current stimulation (tDCS), have been increasingly investigated, aiming to influence cortical excitability in neurologic conditions, including CP. **OBJECTIVE:** To summarize current evidence for the use of tDCS on individuals with CP. **METHODS:** Using scoping review methodology, the terms "cerebral palsy" and "transcranial direct current stimulation" were screened in PubMed, Cochrane, LILACS, SciELO, PEDro, and Embase databases, searching for clinical trials that applied tDCS interventions into children and adults with CP. Quality assessment of all eligible studies was performed using the PEDro Scale. **RESULTS:** A total of 1773 articles (including duplicates) were found, of which 14 met the predetermined criteria. Two hundred and thirty-three individuals with CP, with ages ranging from 5 to 27 years, participated in these studies. The main therapeutic effects of anodal tDCS were reported on upper limb dysfunctions, balance, and gait. The primary motor cortex was the most frequently applied target. The combined use of tDCS with other motor training techniques, such as constraint-induced movement therapy (CIMT) and treadmill locomotor training, showed better results. **CONCLUSION:** Emerging evidence reveals that the use of tDCS in individuals with CP is safe, feasible, easy to apply, tolerable, and effective when performed according to the recommendations available to date. The tDCS protocols in these studies were partially homogeneous, and sample sizes were generally small. More large-scale longitudinal studies are needed, particularly in individuals with ataxic and dyskinetic CP.

**KEYWORDS:** Cerebral palsy. Transcranial direct current stimulation. Evidence-based medicine. Review.

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## Introduction

Cerebral palsy (CP) is a well-recognized neurodevelopmental condition that begins in early childhood and persists throughout life[1], attributed to non-progressive disturbances that affect fetal or infant brain development, with repercussions on movement and posture, causing limitations in daily activities and social participation.[2] CP is the leading cause of childhood disability, with a prevalence of approximately three per 1000 births.[3]

CP is most often classified as spastic, dyskinetic, or ataxic.[4,5] Dyskinesia and ataxia usually affect all four limbs, whereas spasticity is categorized topographically as hemiplegia (one side affected), diplegia (lower limbs affected more than upper limbs), and quadriplegia (whole-body involvement). However, some experts recommend abandoning these labels and advocate specific classifications such as unilateral or bilateral, which must be accompanied by a description of other components, including motor abnormalities (nature and typology of the motor disorder, and functional motor abilities), accompanying impairments, anatomical and neuro-imaging findings, causation and timing.[2,4]

Over the past 25 years, tremendous progress has been made in understanding CP-associated movement disturbances, its early detection, classification, and how to measure change over time with reliable and valid measurements. Scientific, clinical, and social progress is converging to support the empowerment of individuals with CP and their families, changing the focus of rehabilitation from controlling or eliminating disabilities to achieve better results in activities/participation, thus impacting the quality of life.[6]

The understanding of brain function, injury recovery, and neuroplasticity provided a basis for the development of technologies, which have already been well-studied for decades, and whose applicability in the clinical environment is more recent and is becoming part of neurorehabilitation approaches.[7] Neuromodulatory interventions using non-invasive brain stimulation have been increasingly investigated, aiming to influence cortical excitability in neurologic conditions including stroke, epilepsy, and cerebral palsy.[8]

In contrast to many other neuromodulatory methods, transcranial direct current stimulation (tDCS) has low cost, safety, feasibility, and simple applicability.[9] Its application involves placing two conductive-rubber electrodes wrapped in saline-soaked sponges on the scalp, held in place by a rubber band. A low-intensity direct current, often 1 to 2 mA, is delivered to cortical areas from the device. This current has the effect of spontaneously modulating neural networks. The primary mechanism of action is an alteration in resting membrane neuronal potential. The application can be performed by anodic or cathodic stimulation, which corresponds to the positive and negative terminals of the battery that operates the device.[10]

Individuals with CP may benefit from the neuromodulatory effects of tDCS as it presents an attractive adjunct to physical therapy to improve motor function.[11,12] Studies suggest that tDCS has a potentiating effect on motor training, providing additional targeted stimulation to the motor cortex; thus, specific brain networks would be activated by a task, for example, during rehabilitation training. The tDCS may be combined with basically any other therapeutic intervention, with motor training, cognitive or behavioral interventions in a significant way.[7,11-14]

Despite the reported promising results, the literature still lacks a scoping review covering the reported methods, outcomes, and potential therapeutic applications in individuals with CP across different age ranges. This review aims to fill this gap, summarizing current evidence by reporting, comparing, and discussing studies that used tDCS in individuals with CP. Moreover, this review provides recommendations for future studies in the field to facilitate their development and comparison.

## Method

We systematically performed a scoping review of articles describing the use of tDCS in individuals with CP. The methodology for this review was based on the framework proposed by Arksey and O'Malley[15] and later advanced by others.[16,17] Furthermore, in keeping with the suggestion of Colquhoun et al.[18] for scoping reviews, we followed the relevant aspects of the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols.[19]

PubMed, Cochrane, LILACS, SciELO, PEDro, and Embase databases were searched from inception until February 2021. The following blocks of search terms were used, selected from MeSH (Medical Subject Headings) and DeCS (Health Descriptors). A title search was performed through specific terms combined by "AND" (between term blocks) and "OR" (intra terms), the term blocks and combinations. MeSH [(Cerebral Palsy)] AND MeSH [(transcranial direct current stimulation)] were used for these databases (Table 1).

**Table 1.** Description of search terms according to population and intervention of interest

| | **Search terms** |
|---|---|
| **Population** | MeSH [(Cerebral Palsy)or(Cerebral Palsy, Dystonic-Rigid)or(Cerebral Palsies, Dystonic-Rigid)or(Cerebral Palsy, Dystonic Rigid)or(Dystonic-Rigid Cerebral Palsies)or(Dystonic-Rigid Cerebral Palsy)or(Cerebral Palsy, Mixed) or(Mixed Cerebral Palsies)or(Mixed Cerebral Palsy)or(Cerebral Palsy, Monoplegic, Infantile)or(Monoplegic Infantile Cerebral Palsy)or(Infantile Cerebral Palsy, Monoplegic)or(Cerebral Palsy, Quadriplegic, Infantile) or(Quadriplegic Infantile Cerebral Palsy)or(Infantile Cerebral Palsy, Quadriplegic)or(Cerebral Palsy, Rolandic Type)or(Rolandic Type Cerebral Palsy)or(Cerebral Palsy, Congenital)or(Congenital Cerebral Palsy)or(Little Disease)or(Little Disease)or(Spastic Diplegia)or(Diplegias, Spastic)or(Spastic Diplegias)or(Diplegia, Spastic) or(Monoplegic Cerebral Palsy)or(Cerebral Palsies, Monoplegic)or(Cerebral Palsy, Monoplegic)or(Monoplegic Cerebral Palsies)or(Cerebral Palsy, Athetoid)or(Athetoid Cerebral Palsy)or(Cerebral Palsies, Athetoid)or(Cerebral Palsy, Dyskinetic)or(Cerebral Palsies, Dyskinetic)or(Dyskinetic Cerebral Palsy)or(Cerebral Palsy, Atonic)or(Atonic Cerebral Palsy)or(Cerebral Palsy, Hypotonic)or(Hypotonic Cerebral Palsies)or(Hypotonic Cerebral Palsy) or(Cerebral Palsy, Diplegic, Infantile)or(Diplegic Infantile Cerebral Palsy)or(Infantile Cerebral Palsy, Diplegic) or(Cerebral Palsy, Spastic)or(Spastic Cerebral Palsies)or(Spastic Cerebral Palsy) |
| **Intervention of interest** | (tDCS)or(Cathodal Stimulation Transcranial Direct Current Stimulation)or(Cathodal Stimulation tDCS)or(Cathodal Stimulation tDCSs)or(Stimulation tDCS, Cathodal)or(Stimulation tDCSs, Cathodal)or(tDCS, Cathodal Stimulation) or(tDCSs, Cathodal Stimulation)or(Transcranial Random Noise Stimulation)or(Transcranial Alternating Current Stimulation)or(Transcranial Electrical Stimulation)or(Electrical Stimulation, Transcranial)or(Electrical Stimulations, Transcranial)or(Stimulation, Transcranial Electrical)or(Stimulations, Transcranial Electrical) or(Transcranial Electrical Stimulations)or(Anodal Stimulation Transcranial Direct Current Stimulation)or(Anodal Stimulation tDCS)or(Anodal Stimulation tDCSs)or(Stimulation tDCS, Anodal)or(Stimulation tDCSs, Anodal) or(tDCS, Anodal Stimulation)or(tDCSs, Anodal Stimulation)or(Repetitive Transcranial Electrical Stimulation). |

Source: the authors (2023).

Titles and abstracts were screened by the authors to identify potentially eligible studies and exclude duplicates. Full texts of the selected studies were retrieved and independently assessed by each author (disagreements were resolved through discussion with a third author).

### Eligibility criteria

Studies should meet the following criteria: (1) clinical study with data (on the manuscript or upon request) on CP dysfunctions preintervention and postintervention (and active vs. sham conditions, when applicable); (2) participants should have a clinically established CP diagnosis at baseline; and (3) studies that investigated tDCS as a single treatment or associated with another therapy. No restriction on language or year of publication was stipulated. We excluded studies: (1) non-invasive brain stimulation techniques other than tDCS; (2) case reports, systematic reviews, and protocol studies.

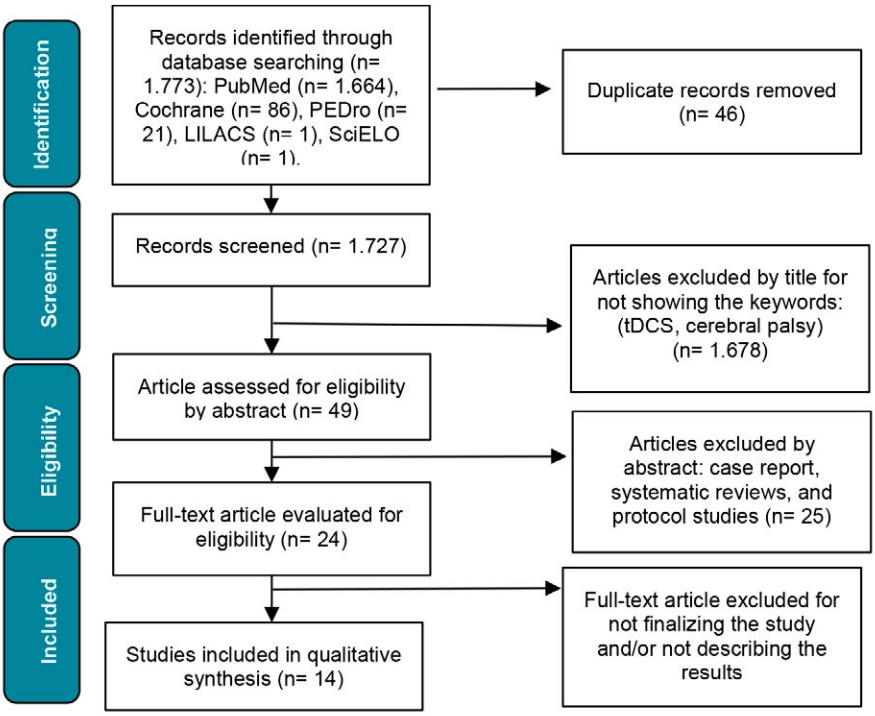
### Quality assessment

A quality assessment was conducted for each included study by using the Physiotherapy Evidence Database (PEDro scale), in order to most effectively identify gaps in the existing body of evidence. The PEDro scale includes 11 specific criteria, graded on a "yes"/"no" scale in which the first item relates to external validity and the other 10 items assess the internal validity of a clinical trial. The first criterion does not count toward the overall score that the paper receives for the quality of its study design. The PEDro scale is marked out of 10; the higher the PEDro score, the higher the assumed "quality" of the trial as assessed by the following cut-points defined by Foley et al.: 9–10, excellent; 6–8, good; 4–5, fair and below 4, poor.[20,21]

## Results

Following the initially determined search criteria, a total of 1773 articles were found in the databases. Forty-six duplicate articles were removed; 1678 articles had titles that did not address the CP condition and the tDCS intervention; 25 studies were case reports, systematic reviews, or protocol studies; and 10 studies were not completed. The details of the process of searching, screening, and selecting articles are described in detail in Flowchart 1.

**Flowchart 1.** Flow chart of the article selection process




Source: the authors (2023).

The study design, sample size, stimulation protocol, and main findings of each study are described in Table 2.

**Table 2.** Summary of the data extraction (to be continued)

| Title | Author / Year | Population | Sample Size | Outcome Measure | Intervention / Range of Total 'n' of Sessions | Side Effect | Effect Size and Confidence Intervals, Summary of Results |
|---|---|---|---|---|---|---|---|
| Changes in spectroscopic biomarkers after transcranial direct current stimulation in children with perinatal stroke[30] | Carlson et al., 2017 | Perinatal stroke | 15 children in the experimental group (7 active tDCS and 8 sham tDCS) and 19 children in the control group with typical development | Relation of metabolite concentration and motor function | Active cathodal tDCS. The cathode was placed over the contralesional M1. The protocol consisted of 20 minutes, during 10 sessions, and an intensity of 1mA. For the first five weekdays, constraint-induced movement therapy (CIMT) was applied with the higher-functioning limb restrained using a soft, removable cast. For the next five weekdays, Hand-arm Intensive Bimanual Therapy was utilized. | No effects | Motor performance improved in both groups, and tDCS was associated with greater achievement of goals. Cathodic tDCS in uninjured M1 showed a decrease in glutamate and creatine. However, no change occurred with the sham tDCS. The concentrations of metabolites in the injured M1 did not change after the intervention. Baseline levels at injured M1 associated with improved clinical response. |
| Effect of a single session of transcranial direct-current stimulation on balance and spatiotemporal gait variables in children with cerebral palsy: A randomized sham-controlled study[22] | Grecco et al., 2014 | Children with spastic CP - GMFCS I, II, or III | 10 children in the experimental group and 10 children in the control group | Gait velocity, cadence, stride length, step length, step width, anteroposterior oscillation, and mediolateral oscillation | The anode was positioned over the M1 of the dominant hemisphere, and the cathode was positioned in the supra-orbital region contralateral to the anode. The current was applied for 20 minutes, during which the children remained seated. For sham stimulation, the electrodes were positioned in the same manner, and the stimulator was switched on for 30 seconds. The protocol consisted of a 20-minute, single-session with an intensity of 1 mA. The children were submitted to 3 evaluations (1 before stimulation, 2 after stimulation, and 3 twenty minutes after stimulation) | Adverse effects were uncommon (three children) and restricted to redness and tingling of the skin in the experimental group. | Reduction in anteroposterior sway with eyes open and eyes closed; reduction in mediolateral sway with eyes open and closed; increase in walking speed, step length, and stride length in the second evaluation. However, results do not last longer than 20 minutes after stimulation. |

**Table 2.** Summary of the data extraction (continuation)

| Title | Author / Year | Population | Sample Size | Outcome Measure | Intervention / Range of Total 'n' of Sessions | Side Effect | Effect Size and Confidence Intervals, Summary of Results |
|---|---|---|---|---|---|---|---|
| Effects of anodal transcranial direct current stimulation combined with virtual reality for improving gait in children with spastic diparetic cerebral palsy: a pilot, randomized, controlled, double-blind, clinical trial[23] | Grecco et al., 2015 | Children with spastic diparetic CP | 10 children in the experimental group and 10 children in the control group | Gait velocity, cadence, stride length, step length, step width, stance phase, Gross Motor Function Measure-88 (dimensions D and E), Pediatric Evaluation Disability Inventory (self-care, mobility, and social function), and motor evoked potential (before and after the interventions as well as at the one-month follow-up) | The anodal electrode was positioned over the M1 contralateral to the lower limb with greater motor impairment, and the cathode was positioned in the supraorbital region on the contralateral side. The protocol consisted of 20 minutes, during 10 sessions, and an intensity of 1mA. A current was applied as the child performed gait training with virtual reality. | Four children reported mild tingling with anodal tDCS | Two variables demonstrated better results in the experimental group in comparison with the control group at the posttreatment evaluation and follow-up evaluation: velocity and cadence; a significant increase in motor function in the posttreatment and follow-up evaluation: dimension D and dimension E; a significant increase in mobility in the posttreatment and follow-up evaluation; demonstrated an increase in motor evoked potential in the posttreatment evaluation. |
| Effect of transcranial direct-current stimulation combined with treadmill training on balance and functional performance in children with cerebral palsy: a double-blind randomized controlled trial[24] | Duarte et al., 2014 | Children with spastic CP - GMFCS I, II, or III | 12 children in the experimental group and 12 children in the control group | Stabilometric analysis, Pediatric Balance Scale (PBS), and Pediatric Evaluation of Disability Inventory (PEDI) | The anodal electrode was positioned over the M1 of the non-dominant hemisphere and the cathode was positioned in the supra-orbital region on the contralateral side. The protocol consisted of 20 minutes, during 10 sessions, and an intensity of 1mA. A current was applied as the children performed gait training. | Three children in the experimental group experienced redness in the supra-orbital region. No other adverse effects were reported, such as behavioral changes, headache, or discomfort. During the sessions, 18 children (12 in the experimental group and 6 in the control group) reported a tingling sensation at the beginning of stimulation, but this sensation either ceased after a few seconds or was not considered bothersome. | The stabilometric evaluation revealed positive effects on the reduction in body sway in the anteroposterior direction with eyes open and eyes closed and mediolateral direction with eyes open and eyes closed. The experimental group maintained these effects on anteroposterior and mediolateral sway with eyes open and closed after the intervention; the effect was maintained at Evaluation 3 only with regard to mediolateral sway with eyes closed. In the PEDI, an increase in the final score was found for mobility and self-care. |

**Table 2.** Summary of the data extraction (continuation)

| Title | Author / Year | Population | Sample Size | Outcome Measure | Intervention / Range of Total 'n' of Sessions | Side Effect | Effect Size and Confidence Intervals, Summary of Results |
|---|---|---|---|---|---|---|---|
| Transcranial direct current stimulation during treadmill training in children with cerebral palsy: a randomized controlled double-blind clinical trial[25] | Grecco et al., 2014 | Children with spastic CP - GMFCS I, II, or III | 12 children in the experimental group and 12 children in the control group | Gait velocity, cadence, stride length, step length, step width, Gait Profile Score (GPS), Six Minutes Walk Test, Gross Motor Function Measure-88 (dimensions D and E), Treadmill test, and motor evoked potential. | The anodal electrode was positioned over the primary motor cortex of the dominant hemisphere, and the cathode was positioned in the supra-orbital region on the contralateral side. The protocol consisted of 20 minutes, during 10 sessions, and an intensity of 1mA. A current was applied as the children performed the treadmill training. | No effects | The experimental group demonstrated improvements in gait velocity, cadence, and GPS at Evaluations 2 and 3. Improvements also occurred regarding the Pelvic Tilt and Hip Ab-Adduction, gait variable scores at Evaluations 2 and 3 as well as Knee Flex-Extension at Evaluation 2; a significant increase in the distance traveled after the intervention at Evaluation 3. In the analysis of MEP of the quadriceps muscle, an effect was found in the experimental group. |
| Transcranial direct current stimulation for children with perinatal stroke and hemiparesis[27] | Kirton et al., 2016 | Children with perinatal stroke and hemiparetic CP | 12 children in the experimental group and 11 children in the control group | Assisting Hand Assessment (AHA), Canadian Occupation Performance Measure (COPM), Melbourne Assessment (MA), Jebsen Taylor Test (JTT), Quality of life (QOL), Daily box and blocks testing (ABIL-HAND-Kids, bilateral grip, and pinch strength. | The cathode electrode was positioned over the mapped contralesional M1 (anode over the contralateral forehead). The protocol consisted of 20 minutes, during 10 sessions, and an intensity of 1mA associated with motor learning therapy. | The most common side effect was itching (39%), which was mild (7) or moderate (2), decreased over sessions; Uncommon side effects included headache (3), mild burning (3), or unpleasant tingling (1). | Across all participants, AHA scores increased from baseline at 1 week. COPM scores achieved ≥2 points in performance and satisfaction. A similar difference was still apparent at 2 months for performance and satisfaction. The increase in mean COPM performance scores from baseline to 2 months was greater in tDCS compared to sham; a similar trend was seen for satisfaction scores from baseline to 2 months. Parents reported that quality-of-life scores were associated with tDCS treatment for school activity. Unaffected grip strength increased at 2 months across all participants with no treatment group effect. The use of tDCS proved to be safe and well tolerated. |
| Effect of transcranial direct current stimulation combined with virtual reality training on balance in children with cerebral palsy: a randomized, controlled, double-blind, clinical trial[26] | Lazzari et al., 2016 | Children with CP - GMFCS I, II, or III | 10 children in the experimental group and 10 children in the control group | Stabilometric analysis, PBS, and Time Up and Go Test | The anodal electrode was positioned over the M1, and the cathode was positioned in the supraorbital region on the contralateral side. The protocol consisted of 20 minutes, during 10 sessions, and an intensity of 1mA associated with virtual reality. | No effects | The experimental group demonstrated improvements in PBS at Evaluation 2, and the effect was maintained at Evaluation 3; with the post hoc test demonstrating statistically significant improvements at the post-intervention and follow-up. These analyses demonstrated statistically significant effects favoring the experimental group over the control group with regard to the TUGT, and area of oscillation of the center of pressure when standing on the force plate with eyes open, only at Evaluation 2. |

**Table 2.** Summary of the data extraction (continuation)

| Title | Author / Year | Population | Sample Size | Outcome Measure | Intervention / Range of Total 'n' of Sessions | Side Effect | Effect Size and Confidence Intervals, Summary of Results |
|---|---|---|---|---|---|---|---|
| Effects of a single session of transcranial direct current stimulation on upper limb movements in children with cerebral palsy: a randomized, sham-controlled study[35] | Moura et al., 2017 | Children with hemiparesis spastic CP - MACS I, II, or III | 10 children in the experimental group and 10 children in the control group | Motor training of the paretic upper limb | The anodal electrode was positioned over C3/C4, corresponding to the M1 of the hemisphere contralateral to the motor impairment, and the cathode was positioned over the supraorbital region contralateral to the anode. A current of 1 mA was administered for 20 minutes during the single session. The non-paretic upper limb was constrained with the use of a comfortable neoprene glove during the 20-minute session. | No effects | In the experimental group, significant differences were found during the pre-intervention evaluation with regard to the going phase, adjusting phase, total movement duration, index of curvature, and number of movement units. During the post-intervention evaluation, significant differences remained with regard to the going phase, adjusting phase, total movement duration, and index of curvature. In the control group, significant differences between the paretic and non-paretic sides were found with regard to the going phase, adjusting phase, total movement duration, number of movement units, endpoint error, and adjusting sway index. During the post-intervention evaluation, significant differences were found for the adjusting phase, total movement duration, index of curvature, number of movement units, endpoint error, and adjusting sway index. |
| Reduction of spasticity in cerebral palsy by anodal transcranial direct current stimulation[28] | Aree-uea et al., 2014 | Children with CP with spasticity in the right upper limb | 23 children in the experimental group and 23 children in the control group | Degree of spasticity by using the modified Ashworth Scale (MAS) for the following right upper limb joints, shoulder, elbow, wrist, and fingers. Passive range of motion (PROM) testing was performed on shoulder flexion, shoulder extension, shoulder abduction, shoulder adduction, elbow flexion, wrist flexion, and thumb (carpometacarpal) abduction using the procedures described by Norkin and White. | Five consecutive daily treatments with 1 mA anodal tDCS over the left M1 for 20 minutes each day. | One participant in the active tDCS condition developed a 2 mm diameter erythematous rash, 0.5 mm deep, and mild skin burn at the center under the reference electrode on the third day of stimulation, and mild pruritus. | Significant differences were found during the pre-treatment and post-treatment for spasticity between the treatment condition group in the MAS score: shoulder, wrist and fingers, and there continued to be no significant group differences at the 48-hour assessment point. Showed significant differences in the shoulder abduction PROM score for the active tDCS group at post-treatment. However, this change did not maintain at the 24-hour assessment point, and there continued to be no significant group differences at the 48-hour assessment point. |

**Table 2.** Summary of the data extraction (continuation)

| Title | Author / Year | Population | Sample Size | Outcome Measure | Intervention / Range of Total 'n' of Sessions | Side Effect | Effect Size and Confidence Intervals, Summary of Results |
|---|---|---|---|---|---|---|---|
| Safety and feasibility of transcranial direct current stimulation in pediatric hemiparesis: randomized, controlled preliminary study[29] | Gillick et al., 2015 | Children with hemiparesis | 5 children in the experimental group and 6 children in the control group | Token test of intelligence, Grip-strength dynamometer (hand affected and unaffected), Box and Blocks Test, and Single-pulse TMS. | A bihemispheric tDCS montage was used with ipsilesional-anodal and contralesional-cathodal electrode positioning. The cathode electrode was placed over the M1 hotspot of the non-lesioned hemisphere, and the anode electrode was placed over the M1 hotspot of the lesioned. hemisphere. A current of 0.7mA was administered for 10 minutes during a single session. | Itchiness (n=1), burning (n=1), sleepiness (n=4) and difficulty concentrating (n=2). Upon follow-up testing, only one participant in the control group reported mild sleepiness. | No serious adverse events, including seizure, occurred. For the 11 participants who completed the study, group differences in MEPs and behavioral data did not exceed 2 standard deviations in those receiving the tDCS and those in the control group. The finding in this investigation of the safety and feasibility of using tDCS allows for further investigation of serial tDCS sessions in combination with rehabilitation interventions. |
| Transcranial direct current stimulation and constraint-induced therapy in cerebral palsy: a randomized, blinded, sham-controlled clinical trial[31] | Gillick et al., 2018 | Children and young adults with Unilateral Cerebral Palsy (UCP) | 10 children in the experimental group and 10 children in the control group | Grip strength was measured in both hands, Assisting Hand Assessment (AHA), Canadian Occupational Performance Measure (COPM), and TMS (motor evoked potential). | TDCS electrodes were configured with the cathode positioned on the non-lesioned hemisphere primary motor cortex (M1), and the anode on the contralateral supraorbital prominence. The protocol consisted of 20 minutes, during 10 sessions, and an intensity of 0.7mA combined with CIMT, followed by 100 minutes of CIMT alone in small groups. | The proportion of the group with minor adverse event (MAE) reports included nausea (1), tactile symptoms at the site of stimulation (1), headache (1), dizziness (3), and sleepiness (7), with sleepiness as the most common. The most common reported MAEs during tDCS were headache (5) and tingling (4). | Both groups showed improvement in the AHA score after the intervention; moreover, maintenance of the score was observed at the six-month follow-up. Similar patterns of change were observed in COPM performance for both groups after intervention and at six months thereafter. |
| Cerebellar transcranial direct current stimulation in children with ataxic cerebral palsy: A sham-controlled, crossover, pilot study[34] | Grecco et al., 2016 | Children with ataxic CP | 6 children received active tDCS and sham tDCS | PBS, stabilometric evaluation using a force plate, Timed Up and Go Test, Pediatric Evaluation of Disability Inventory (PEDI). | The anodal electrode was positioned over the cerebellar region, and the cathode was placed over the central supraorbital region. The current was applied over the cerebellar region during the 20 minutes of treadmill training and was gradually increased to 1 mA. | Was reported tolerable tingling (4), pain similar to a stinging sensation (1), and tingling during sham tDCS (3). | It showed significant reductions in anteroposterior and mediolateral oscillations with eyes closed after the intervention and one month later, respectively. Moreover, exclusively in the anteroposterior oscillation, it remained after 3 months. The results obtained through PBS showed a significant difference in follow-up 1 with a higher score in the experimental group one month after the end of the intervention; both types of intervention showed a significant difference in the assessment after the intervention. The experimental intervention resulted in an improvement in functional performance (mobility activities) compared to the control group only in the evaluation after the intervention. |

**Table 2.** Summary of the data extraction (conclusion)

| Title | Author / Year | Population | Sample Size | Outcome Measure | Intervention / Range of Total 'n' of Sessions | Side Effect | Effect Size and Confidence Intervals, Summary of Results |
|---|---|---|---|---|---|---|---|
| Transcranial Direct Current Stimulation (tDCS) in Unilateral Cerebral Palsy: A Pilot Study of Motor Effect[32] | Inguaggiato et al., 2019 | Individuals with UCP | 8 subjects received active tDCS and sham tDCS | Box and Block Test (BBT [dexterity test]), Hand Grip Strength (HGS [isometric strength of the hand]), Safety Questionnaire, Blood Pressure, and Heart Rate. | The anodal electrode was placed over C3 or C4 in order to stimulate the primary motor cortex (M1) of the damaged hemisphere, with the cathode electrode placed over the contralateral supraorbital area. During a single session of active tDCS, a constant current of 1.5 mA was applied for 20 minutes. | Headache, neck pain, scalp pain, burning, tingling, drowsiness, lack of concentration, and feelings changes were reported in the T1 active tDCS group. In the T2 sham tDCS group were reported headache, neck pain, scalp pain, burning, tingling, and drowsiness. In the T2 active tDCS group, headache, drowsiness, and lack of concentration. In the T2 sham tDCS group, headache, neck pain, tingling, and drowsiness. In the T3 active tDCS group, daytime sleepiness, hyperactivity, inattention, irritability, and restlessness. In the T3 sham tDCS group, daytime sleepiness, hyperactivity, inattention, irritability, and restlessness. | Regarding the performance of the hemiplegic hand in the BBT. Post-hoc comparisons showed a significant improvement from baseline only after active tDCS T0 VS T1 and T2. The possible transport effect induced by receiving active stimulation first (tDCS active first VS sham) was verified. These results were maintained for at least 90 minutes. |
| Influence of Combined Transcranial Direct Current Stimulation and Motor Training on Corticospinal Excitability in Children With Unilateral Cerebral Palsy[33] | Nemanich et al., 2019 | Children with UCP | 10 children in the experimental group and 10 children in the control group | Cortical excitability and motor evoked potential | The cathode is positioned over the TMS-derived motor hotspot of the contralesional hemisphere, and the anode is positioned over the contralateral forehead. The intervention consisted of 20 minutes, during 10 consecutive weekdays, and an intensity of 0.7mA, combined with CIMT. | No effects | Although not statistically significant, a comparison between contralesional MEP and ipsilesional MEP was observed in the ipsilesional first dorsal interosseous (FDI) and in the contralesional first dorsal interosseous (FDI). A hypothetical reduction in contralesional excitability was observed in participants in the active group + CIMT. However, the effectiveness of tDCS in modulating corticospinal excitability was not statistically different from the sham group + CIMT. |

Source: the authors (2023).

**Participants/Population**

The 14 articles included in this review were composed by individuals of different ages (five to 27 years), ranging from childhood to adulthood: seven studies were conducted in children[22-26], three in adolescents[27-29], and four in adults.[30-33]

The functional consequences of involvement of the upper and lower extremities were separately classified using objective functional scales, the Gross Motor Function Classification System (GMFCS)[22-26,28,29,34] and the Manual Ability Classification System (MACS).[27,29,31-33,35]

A total of 233 individuals with CP participated in the studies involving the use of tDCS. Ten articles cited in this review performed their interventions on individuals with spastic unilateral CP (n=140). In this same context, five studies were conducted on individuals with spastic bilateral CP (n=93). In some studies, we found an experimental group and a control group with a mixed composition, that is, participants with unilateral and bilateral CP. Ataxic-type CP was addressed in only one study.[34]

**Country/location of studies**

In the current study, there was no use of filters by language, country, and time. The articles included in this review were developed in different locations: seven articles were conducted in Brazil[22-26,34,35], three in the United States[29,31,33], two in Canada[27,30], one in Thailand[28], and one in Italy.[32]

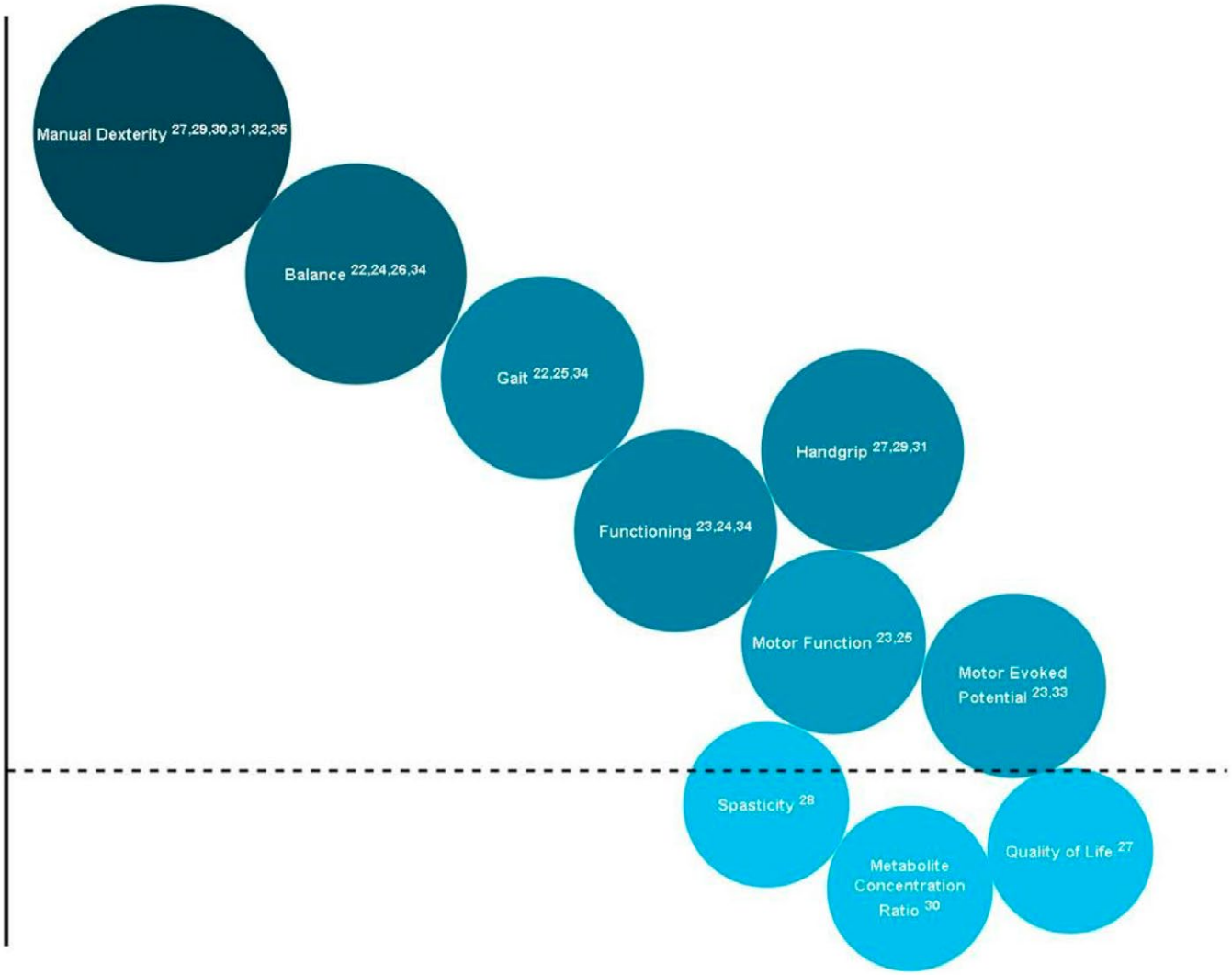
**Studies design**

All studies included in this review were randomized controlled clinical trials. The authors and their colleagues Carlson[30], Duarte[24], Grecco[23,25], Kirton[27], Lazzari[26], Gillick[29], and Aree-uea[28] performed double-blind studies. Inguaggiato et al.[32] and Grecco et al.[34] used the single-blind cross-over study model. The single-blind, randomized, controlled clinical trial model was also used by Grecco et al.[22], Moura et al.[35], Gillick et al.[31], and Nemanich et al.[33]

**Outcomes**

The effects of tDCS were analyzed on different outcomes: manual dexterity (n=6), handgrip (n=4), metabolite concentration ratio (n=1), balance (n=4), gait (n=3), functioning (n=3), motor evoked potential (n=2), motor function (n=2), spasticity (n=1) and quality of life (n=1). (Figure 2)

**Figure 2.** Graphic representation of the main outcomes found in clinical trials with tDCS in cerebral palsy. The larger the circle, the greater the number of clinical trials




Source: the authors (2023).

Regarding upper limb dysfunctions, different aspects were observed. Manual dexterity was assessed using different instruments: Canadian Occupational Performance Measure (COPM)[27,30,31], Hand Support Assessment (AHA)[27,30,31,33], Melbourne Assessment (MA)[27,30], Box and Block Test for Affected Hands (BBT-A) and for Unaffected Hands (BBT-U).[29,30] Baseline motor function, particularly of upper limbs, was correlated with lesioned hemisphere metabolite concentrations preintervention, and these correlations consistently increased in strength following the intervention. The metabolites analyzed were: N-acetyl-aspartate (NAA), involved in neuronal health; choline (Cho), compounds that reflect cell membrane health; creatine (Cre), compounds involved in energy metabolism; myo-Inositol (Ins), which reflects the health of glial cells; and glutamate (Glu), which demonstrates metabolic activity and the concentration of excitatory neurotransmitters.[30] Correlation analyses were also used to test the association between improvement for BBT after active tDCS and age and lesion area (cortical, subcortical, or frontal lobe lesion).[32] In addition, other aspects of manual function were assessed, such as handgrip strength[27,29,31,32], bilateral pinch, fine and gross motor hand function, with Jebsen Taylor Test (JJT), and specific manual ability for children with upper limb impairment with Abil-Hand-Kids.[27]

Static and dynamic balance was assessed in four studies, through body sway or stabilometric analysis[22,24,26,34], Pediatric Balance Scale (PBS)[24,26,34] and Timed Up and Go Test (TUGT).[26]

Gait was analyzed through space-time variables, such as speed, cadence, step length, stride length, step width[22,23,25]; center of mass sway under force platform (anteroposterior and mediolateral with eyes open and eyes closed)[22]; observation and measurement of lower limbs joints position during gait, with Gait Profile Score (GPS)[23,25]; 6-minute walk test and treadmill test.[25]

Functioning and gross motor function were outcomes evaluated using the Pediatric Evaluation of Disability Inventory (PEDI)[23,24,34] and Gross Motor Function Measure (GMFM)[23,25]. The motor evoked potential (MEP) was used to assess the excitability of a neural network for the movement assessed, in addition to all the structures involved in the execution of this movement.[25] The Pediatric PC Quality of Life Inventory was also used.[27] Spasticity and passive range of motion of upper limb joints (goniometry) were evaluated in only one study.[25,28]

**Interventions**

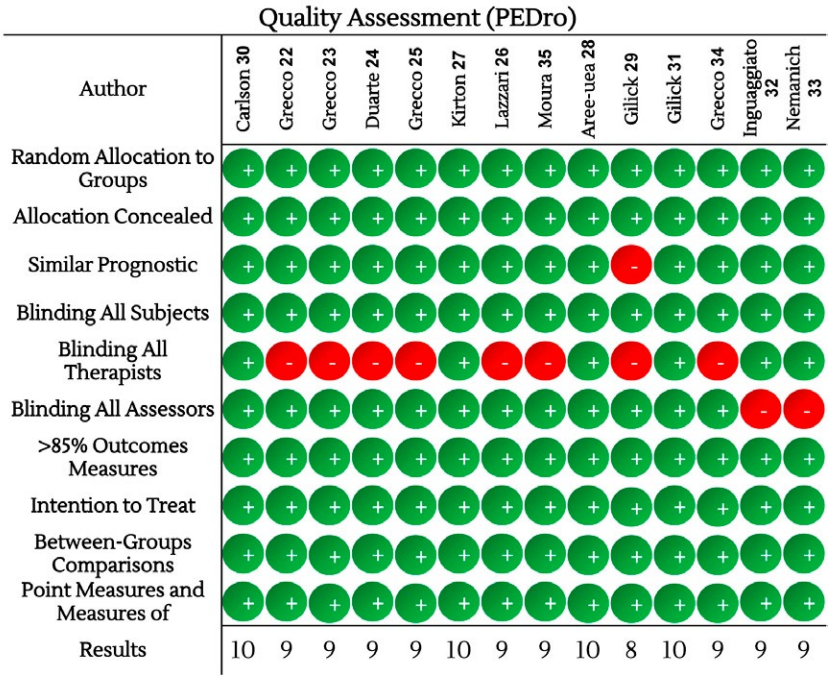
The current intensity applied varied from 0,7[31,33] to 1,5 mA[32], with most studies using 1mA[22-28,30,34,35], and a duration of 20 min, except in one study that used 10 min.[29] Eight studies applied tDCS over repeated sessions ranging from 5[28] to 10[23-27,30,31], and three in a single-session.[22,29,35] All 14 included studies used active tDCS (i.e., anodal tDCS: nine studies[22-26,28,32,34,35], cathodal: four studies[27,30,31,33]; and anodal & cathodal tDCS: one study[29]) in an experimental group. The control group was composed of typically developing children[30], children with CP without tDCS stimulation but maintaining baseline therapy[22,24,26,28,29,32], and/or sham stimulation.[22,23,30–32,34,35] The primary motor cortex, also known as M1 (Cz, C3, and/or C4), was the target chosen in almost all studies except one that stimulated the cerebellum.[34] Regarding the time of tDCS, three studies applied only tDCS, without other associated interventions, while 11 studies applied tDCS online with other therapeutic strategies aimed at motor learning.[22,29,32]

The other therapeutic strategies implemented were: CIMT[30,31,33]; intensive bimanual therapy[30]; virtual reality mobility training protocols[23,26]; treadmill gait training[24,25,34]; goal-directed, peer-supported, after-school motor learning camp[27], functional training of the paretic upper limb[35]; and routine physical therapy.[28]

**Quality assessment**

The studies' quality assessment is shown in Figure 3. The scores obtained for methodological quality ranged from eight to 10 points, ranging from good to excellent methodological quality.

**Figure 3.** Measure of the Methodological Quality of clinical trials according to PEDro scale




Source: the authors (2023).

## Discussion

The results of this systematic review provide evidence from 14 studies with relatively high methodological quality in support of tDCS when applied to selected individuals with CP, although sample sizes were generally small. Participants presented with uni or bilateral spastic CP, varying in GMFCS level from I to IV and MACS level from I to V. However, the majority of participants had unilateral CP, with GMFCS classification ranging from I to III, and the most severe conditions (level V) were less frequent.[28,31,33]

Reflections on the characteristics of this sample should not be limited to the higher frequency of the spastic type (79.2%).[36] Possibly, the characteristics of other associated intervention modalities may also have guided the choice of this population, for example, there may be no safety in performing treadmill gait training in some dyskinetic patients. This argument may also explain the greater inclusion of patients with lower functional levels, despite epidemiological studies indicating a higher frequency of major functional impairments, such as 73.3% classified in GMFCS levels III to V.[36] It was observed that the inclusion criteria of most studies selected participants who walked and presented upper limbs voluntary movement. The ability of free locomotion on a treadmill and Box and Block Testing are examples of this profile. The belief that patients with more severe levels benefit from passive therapies has fallen into disuse with the emergence of new technologies and the evolution of known therapeutic techniques.[14] The use of tDCS in these patients would open a window of opportunity for the improvement of motor skills and for potential discovery, improving control and body alignment in lower postures and allowing more upper limb movements. The possibility of using tDCS in individuals with CP with greater motor impairment is an important attraction for future research.

There is consensus that for motor improvements to be lasting, tDCS must occur in conjunction with training.[37] This may enhance skill acquisition by increasing afferent inputs to the cortex while its intrinsic excitability is being enhanced by tDCS, which has been shown to beneficially enhance the effects on motor outcomes of CIMT[30,31]; intensive bimanual therapy[30]; virtual reality mobility training protocols[23,26]; treadmill gait training[24,25,34]; goal-directed, peer-supported, after-school motor learning camp[27], functional training of the paretic upper limb[35]; and physical therapy training.[28] In contrast, Nemanich et al.[33] were unable to show any additional benefit of tDCS combined with CIMT in neurophysiologic outcomes (motor-evoked potential amplitude or cortical silent period duration). Studies that analyzed the combination of tDCS and motor training showed longer-lasting results in some cases (up to one month after the end of stimulation). The variation in the follow-up time of the studies in this review ranged from 20 minutes to three months. It is also important to note that the three studies[22,29,32] without training association were single-session studies and were particularly interested in analyzing safety.

The absence of adverse events was recorded in five[25,26,30,33,35] of the 14 studies; the remaining studies recorded some mild and transient side effects (e.g., redness, headache, tingling, itchiness, and sleepiness) and were relatively the same as those reported in adults with different health conditions.[38] Safety conclusions in non-invasive neuromodulation studies have been based on the absence of serious adverse effects such as seizures, hearing problems, or pain, and experience with tDCS in children has been limited compared to adults.[8,38] However, only 4% of the >16,000 human studies on non-invasive brain stimulation studied children.[38] Our study adds that the type and magnitude of adverse events reported do not differ between children, adolescents, and adults with CP. We emphasize that although adverse effects are minimal in most studies, some trials do not report them clearly or do not bring this important information to the literature, since from it, we can identify a profile of who developed them and if there are similarities. This will only be possible with the methodological improvement of the reports.

The safety concerns of tDCS application in children are also related to current intensity and age. Conventional current intensities range from 0.1 mA (occasionally used as a sham) to 4.0 mA, with most studies applying 1.0 mA and 2.0 mA.[38] Most of the studies analyzed in this review applied 1.0 mA. Only one study investigated the effect of a single session of anodic tDCS with an intensity of 1.5 mA, with no reports of serious effects.[32] Evidence from relevant animal models indicates that brain injury by tDCS occurs at predicted brain current densities that are over an order of magnitude above those produced by conventional tDCS.[38]

A more specific issue for the use of tDCS in children concerns the age and its relationship with possible effects on brain development. In the present scoping review, age ranged from five to 27 years. The largest prospective pediatric cohort to date supports evidence of compatible safety, feasibility, and tolerability in school-aged children. In their study, 612 tDCS sessions were followed, including 92 children, among which one group stands out for being relatively similar to ours, children with perinatal stroke, whose ages ranged from eight to 18 years.[39] However, there is a study that refers to the safety of transcranial electrical stimulation in children from 2.5 years.[8] This study was found in a review article on the application safety in the pediatric population, but was not found in the databases consulted in our study. In this double-blind crossover clinical trial, in particular, seven children received stimulation at home for 16 weeks, twice a day, with 10-minute sessions and with an intensity of 0.5 mA, and no adverse events were reported.[40]

Although in other therapeutic modalities early intervention is recommended as crucial for individuals with CP, in relation to tDCS, more caution is necessary. As the mature brain and the developing brain differ in anatomy and function, data on the effect of tDCS on the mature brain may not reveal possible side effects of stimulating a developing brain. Further, the atypically developing brain may respond differently from the typically developing brain.[41] In the literature available so far, there is no age limit for starting the use of tDCS, only the reaffirmation that the risks for its use in school-age children are minimal.[38]

Therefore, some considerations should be made when interfering with the brain development process of children through transcranial stimulation, such as: head circumference, the thickness of the skull bones, the synapses functioning, connections and brain networks, knowledge of the detailed description of existing structural changes, structured monitoring of the therapeutic process and the application of tDCS. Dosage modifications may be necessary to ensure safety and efficacy.[38] The understanding of all these peculiarities can enable the early use of this therapeutic resource in the population with CP, expanding the development opportunities of each child.

The tDCS montage, including electrodes location, current intensity, duration, and session's number, was similar in 11 articles[22-27,30,31,33,35] of the 14 included in this review. Although the choice of electrodes placement should be related to the functional complaint and, consequently, the brain region that would generate more effective benefits and changes when activated or inhibited, M1 was the most frequent application target among the studies, even for different outcomes. The most studied outcomes were manual dexterity[27,30-33,35], balance[22,24,26,34], and gait.[22,25,34] Also, regarding tDCS montage, in most studies, the anode was positioned in M1, and the cathode was in the contralateral supraorbital region. Few studies chose to place the cathode in the right deltoid muscle[28], but also without any neurophysiological explanation for this. This raises the question of whether the choice of the therapeutic target would be more related to conclusions of safety and effects in studies with adults than to the particularities of individuals with CP, which consequently would direct a safe choice of research groups to stimulate already known targets. M1 represents a key structure to produce lasting polarity-specific effects on corticospinal excitability and motor learning in humans.[42,43] However, CP is a heterogeneous disease affecting a diverse population. The establishment of participant selection criteria based on lesion location and/or integrity of the corticospinal pathway may assist in determining which patients are most likely to benefit from tDCS.

When analyzing the studies, it is clear that most of them were carried out by the same research groups, and it is relevant to consider their importance for the technique foundation in the world scenario; however, it can lead to a possible publication bias, reducing the evidence strength.[44] The tDCS protocols, samples, and outcomes in these studies were quite similar, which stands out for the difficulty of conducting randomized controlled trials with individuals with CP, since there are many differences in the location and extent of the lesion, motor disorders, associated impairments, previous treatment, and family-related issues.[45]

New studies that address a greater variability of participants, with different functional conditions, in addition to the variation of interventions and outcomes tested, will be necessary for a better understanding of tDCS effects in individuals with CP. The intrinsic difficulties in scientific research in some scenarios are known, where access to equipment, and access of participants to study sites, are extremely difficult and often lead to abandonment or withdrawal from participation, influencing follow-up and the methodological quality of the study. Most of the available literature supporting interventions for children and adolescents with CP originates from high-income countries.[46]

Some limitations of the current study should be pointed out. First, although the focus of this review has been the use of tDCS in individuals with CP, due to the combination of this resource with other intervention modalities, we were faced with the lack of standardization of the terms of motor therapies, or lack of description of the components of the associated interventions, which can make it difficult to interpret the results of some studies. Second, some search terms may not have been included and reduced the number of articles found.

## Conclusion

The main therapeutic effects of anodal tDCS were reported on manual dexterity, balance, and gait. The combined use of tDCS with other motor training techniques, such as CIMT and treadmill locomotor training, showed better results. Emerging evidence reveals that the use of tDCS in individuals with CP is safe, feasible, easy to apply, tolerable, and effective when performed according to the recommendations available to date. The tDCS protocols in the studies were partially homogeneous, and sample sizes were generally small. More large-scale longitudinal studies are needed, particularly in individuals with ataxic and dyskinetic CP.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### Authors' contributions

Freire AC, Santos VN, and Marques JB created the idea that originated the work and elaborated the hypotheses, structured and performed the methods. Goulardins JB and Machado BSS drafted the manuscript. All authors reviewed the manuscript.

### Conflicts of interest

No financial, legal or political conflicts involving third parties (government, companies and private foundations, etc.) were declared for any aspect of the submitted work (including, but not limited to grants and funding, participation in an advisory board, study design, preparation manuscript, statistical analysis, etc.).

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