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Systematic Review

Transcranial Direct Current Stimulation for Improving Spasticity, Gross Motor Functions, Balance and Gait in Spastic Cerebral Palsy: Systematic Review of Clinical Trials.

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ABSTRACT

Context: Cerebral palsy is known as a non-progressive neuromotor disorder that is characterized by abnormalities of muscular tonicity, gross and fine motor skills, balance, posture and gait. Transcranial direct current stimulation (tDCS) has emerged as a rather promising therapeutic tool for the management of the above-mentioned symptoms and to possibly to optimize the rehabilitation strategies.

Purpose: This review study evaluates the effectiveness of tDCS on spasticity, gross motor function, balance, and gait; it also tends to summarize the beneficial protocols of tDCS for spastic cerebral palsy patients.

Methods: Comprehensive searches were performed on three electronic databases including PubMed, PEDro, and Cochrane. The inclusion criteria for considered articles were (1) English-language publications available in full text between 2000 and 2023.(2), The PEDro scale, where a score of at least 5 out of 10 was acceptable, (3) Human studies using the tDCS intervention with control group , and (4) Study design (PICOS) method, where P = spastic CP; I = transcranial direct current stimulation; C = conventional physical Therapy; O = muscle strength, spasticity, , and gait kinematics; and S = RCT.

Results: Nine RCTs were included based on the inclusion criteria. This systematic review showed transcranial direct current stimulation is a non-invasive safe modality, and well-tolerated brain stimulation technique with positive effects on gross motor function, spasticity, balance, muscle strength, and gait. Besides, it can be used in conjunction with different modalities as well as conventional physical therapy.

Conclusion: It can be concluded that transcranial direct current stimulation is a novel, fairly simple, low cost and low risk therapeutic modality that can be easily administered in a clinic as well as at home to produce a significant change in spasticity, balance, gross motor function, and gait.

Keywords: Balance, Cerebral Palsy, Gait, Motor Function, Muscle Strength, Spasticity, Transcranial direct current stimulation.

INTRODUCTION

Cerebral palsy (CP) is a neurological disorder originating from damage to the developing brain during pregnancy or shortly after birth which leads to impaired movement and coordination(1). The word "cerebral" refers to the brain's involvement, and "palsy" pertains to a disorder of movement (2). As one of the most prevalent physical disabilities in childhood, it encompasses a range of motor problems ,such as spasticity, impaired balance, and difficulties in gross motor functions and gait(2).

Cerebral palsy (CP) may represent a permanent movement disorder. It is mainly due to disturbances occurring g in the developing fetal/infant brain(1). CP is a multifactorial disorder, includes prenatal, perinatal, and postnatal factors. The significant risk factor includes premature birth with low birth weight (3). It is characterized by impaired muscle tone (spasticity), movement disorder, limitation of range of motion, contracture, posture impairment, balance and may occasionally be accompanied by disturbances in sensation, perception, cognition, communication, and behavior(4).

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The incidence of CP is estimated to be about 1.6 per 1000 live births in developed countries, making it the most common physical disability in childhood (5). The condition is more common in males than in females, and the risk is higher in premature and low birth-weight infants. Etiological factors include intrauterine exposure to infection or inflammation, maternal health issues such as thyroid disorders and seizures, genetic abnormalities, and perinatal hypoxia-ischemia. However, in many cases, the exact cause remains unknown(6).

Cerebral palsy children are not only affected physical but they are also four times more likely than the children of the same age to develop behavioral and emotional lability. It is important to consider a multidisciplinary or holistic approach while developing the treatment plan for these patients. (7).Depending on the timing and location of the brain damage, different types of CP can be resulted: spastic (the most common type, characterized by stiff muscles and exaggerated reflexes), dyskinetic (marked by fluctuations in muscle tone), and ataxic (characterized by problems with coordination and balance) (8, 9).

Depending on the severity and location of the brain damage, each person's CP symptoms are very different. Variations in muscle tone, such as being either overly stiff or too floppy, exaggerated reflexes or uncontrollable movements, delays in achieving motor skill milestones, are common signs and symptoms. (10).

Despite the many challenges faced by individuals with CP and their families, with early intervention and ongoing treatment, many children with CP can lead fulfilling lives(11). The treatment and management of CP are complex and typically require a multidisciplinary approach, focusing on improving individual capabilities, managing comorbidities, and enhancing quality of life(12).

Recently a considerable focus has been concentrated on transcranial direct current stimulation (tDCS), that has the potential to improve motor performance and increase cortical plasticity in a variety of neurological diseases. (13)

Transcranial Direct Current Stimulation (tDCS) is a type of noninvasive brain stimulation that involves the application of weak electrical currents to the scalp to modulate neuronal activity. It works by using two electrodes (i.e. an anode and a cathode) that deliver a constant low current (usually between 1 to 2 milliamperes) to specific regions of the brain. The underlying principle of tDCS is that the applied current can change the electrical potential across neuronal membranes which in turn, influences the rate at which neurons fire(14-17).

The mechanism of action involves the application of a positive (anodal) or negative (cathodal) current via electrodes positioned on the scalp. Anodal stimulation is generally associated with neuronal depolarization, thus increasing excitability, whereas cathodal stimulation leads to hyperpolarization, decreasing neuronal excitability(17, 18).

If the anode (positive electrode) is placed over a particular brain region, it is believed to make the neurons under the electrode more likely to fire, a process known as 'excitation'. Conversely, placing the cathode (negative electrode) over a region typically makes the neurons less likely to fire, known as 'inhibition'.(14)

However, the exact mechanisms of how tDCS influences brain function are still not fully understood and are an active area of research. It's important to note that the effects of tDCS can be influenced by a variety of factors, including the exact positioning of the electrodes, the duration and intensity of stimulation, and individual differences in brain anatomy and physiology(19)

Transcranial Direct Current Stimulation (tDCS) has been explored as a possible therapeutic modality for children with cerebral palsy (CP). Preliminary research has indicated that it could potentially improve motor function and reduce spasticity in these children (19).

In an RCT conducted by Gillick et al. (2014), it was stated that tDCS seems to be safe, practical, and well-tolerated in the majority of children with hemiparesis. They also concluded that anodal tDCS paired with physical therapy could improve hand function in children with hemiparetic cerebral palsy(20). Similarly, Aree-Uea et al. (2014) showed that anodal tDCS could reduce spasticity in the lower limbs of CP children(21).

Further expanding on the current body of knowledge, several studies have explored the effects of tDCS on various aspects of motor function in CP children. In a study by Lazzari et al. (2015), anodal tDCS was shown to induce a significant improvement in gait symmetry and step length in children with CP(22). This aligns with findings by Grecco et al. (2014), suggesting improvements in gross motor function following tDCS application(23).

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A meta-analysis conducted by Elsner et al. (2016) included five trials with a total of 60 participants, concluding that tDCS might have a positive effect on gait speed and gross motor function in children with CP (24). However, the authors emphasized the need for more well-designed trials, given the low number of included studies and significant risk of bias.

While these studies suggest the potential of tDCS to improve various motor outcomes in children with CP, it is noteworthy that the responses to tDCS can be influenced by individual differences in brain structure and anatomy. This emphasizes the need for personalized approaches in tDCS protocols, taking into account factors like age, type, and severity of CP, and baseline brain activity(3).

Given the increasing interest in tDCS as a potential treatment modality for motor function in CP and the variability in the current literature, it is critical to conduct a systematic review of RCTs investigating the impact of tDCS on spasticity, gross motor functions, balance and gait in spastic CP. A systematic review will help to summarize the current evidence, identify gaps in knowledge, and provide recommendations for future research. It will also contribute to refining treatment protocols for tDCS in the context of CP, potentially leading to enhanced patient outcomes.

MATERIAL AND METHODS

Eligibility criteria

From January 2000 to August 2023, only randomized control trials were used in the research for this review.(i) Studies including Humans using the Patient-Intervention-Comparison-Outcomes-Study design (PICOS) method (25) where P = spastic cerebral palsy; I = transcranial direct current stimulation; C = conventional/traditional physical therapy program; O = spasticity, muscle strength, gross motor function, , balance, and gait; and S = randomized controlled trials, (2) English-language publications (3) Available in Full Text (4) The PEDro scale, where a score of at least 5 out of 10 is acceptable.

Search Strategy and Quality assessment

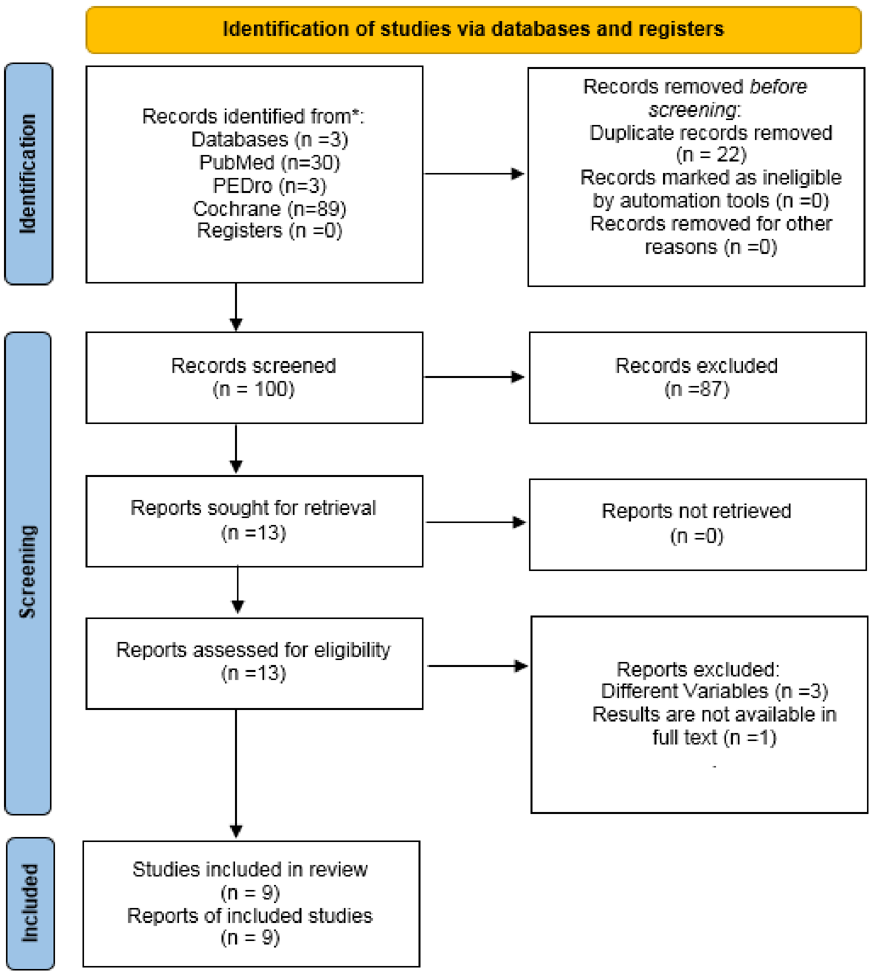

Fig No. 1 Preferred reporting items for systematic reviews and meta-analysis (PRISM) : flow-chart

An extensive and thorough search was executed using the three electronic databases PubMed, PEDro, and Cochrane from the above-mentioned duration. Two of authors who worked independently, selected and extracted papers and data, respectively, that met the criteria for inclusion. In the event of a dispute between the two reviewers, a third reviewer resolved the matter. The review structure shown in figure 1 was designed using the Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines. The search strategy was created by employing Boolean operators to relate the best scientific key terms to the review objectives as shown in Table 1.

Critical Appraisal of the selected researches was done using the PEDro scale as shown in Table 2.The PEDro scale, which consists of 11 elements covering external validity (item 1), internal validity (items 2 to 9), and statistical reporting (items 10 to 11)(26). The scoring was as follows: 0–3 = Poor, 4-5 = Fair, 6–8 = Good, and 9–10 = Excellent.

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Table No. 1 Search Strategy used in PubMed

Sr No	Search Terms
1	Transcranial direct current stimulation
2	Transcranial Direct Current Stimulation OR tDCS OR Noninvasive brain stimulation OR Cathodal Stimulation Transcranial Direct Current Stimulation OR Cathodal tDCS OR Anodal Stimulation Transcranial Direct Current Stimulation OR Anodal tDCS OR tDCS electrode montage
3	≠1 OR ≠ 2
4	Cerebral Palsy
5	Cerebral Palsy OR Little's Disease OR Spastic Cerebral Palsy OR spastic hemiplegia OR spastic hemiplegic OR spastic diplegia OR Spastic diplegic OR Dyskinetic Cerebral Palsy OR Congenital Cerebral Palsy OR spasticity OR Clasp-Knife Spasticity OR hypertonicity
6	≠4 OR ≠ 5
7	Balance
8	Balance OR Posture Equilibrium OR Postural Equilibrium OR Postural Balance OR Postural Control OR Musculoskeletal Equilibrium OR Gait OR walking OR gross motor function OR motor function OR lower extremity function OR fine motor function OR Manual dexterity
9	≠7 OR ≠ 8
10	≠3 AND ≠ 6 AND ≠8
11	#10 AND [humans]/limit AND [English]/lim /RCT/lim/full text/lim/ {2000-2023}/py.

Table No. 2 Summary of PEDro score of included studies

Study	2	3	4	5	6	7	8	9	10	11	Total Score	Quality Status
Aree-uea B (2014)	Y	N	Y	Y	N	Y	Y	Y	Y	Y	8	Good
De-Almeida (2014)	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	9	Good
Ferreira-SB (2014)	Y	Y	N	Y	N	Y	N	N	Y	Y	6	Good
Grecco LA (2014)	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	9	Good
Grecco LA (2014)	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8	Good
Lazzari RD (2017)	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	9	Good
Gillick B (2018)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	10	Good
Nemanich ST (2019)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	10	Good
Radwan A (2023)	Y	Y	Y	N	N	N	Y	Y	Y	Y	7	Good

Abbreviations: Y: Criteria Satisfied, N: Criteria not satisfied

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RESULTS

Based on the aforementioned inclusion criteria, 122 studies (PubMed=30, PEDro=3, and Cochrane=89) were found. The following stage was to eliminate the duplicate studies, of which 22 were found and removed. One hundred studies were completed during the screening's initial phase. In phase 2, only 13 studies were sought for retrieval and given a thorough examination. Four studies were eliminated in the second step of screening due to various factors like different variables other than search terms (n = 3), and the results were not mentioned in the full-text article (n = 1) Table 3. 9 shows the studies were considered in this systematic review. The features of the studies are displayed in Table 4 after each study's characteristics were examined in terms of selection, performance, and other biases.

Table No 3: Reasons for exclusion of studies following assessment of the full text.

Study	Exclusion Reason
Moura RCF (2017)	Different variables other than the search terms
Cole L (2018)	Different variables other than the search terms
Cole (2018)	Different variables other than the search terms
Almeida (2018)	Results are not available in the full-text article

Table No. 4 Characteristics of studies included

Study/Authors name	Study Design	Patient/Population	Interventions	Outcome Measures
Aree-uea B (2014)	Randomized Clinical Trial	46 Spastic Cerebral Palsy Children 8-18 Years	Group A (Active group): tDCS via surface sponge electrodes (35 cm2), current 1 mA for 20 min Anode: Left M1 or the C3 Cathode (reference)electrode: on the right shoulder. Group B (Sham Group): same as an active group but the current discontinued for 30 sec.	Degree of Spasticity (MAS) Passive Range of motion\(PROM)
De-alemida (2014)	Double Blind Randomized Controlled Trial	24 Spastic Cerebral Palsy Children 5-10 Years	I: Treadmill training+ Active tDCS C: Treadmill training+ Placebo tDCS 5 sessions/ week for 2 weeks tDCS (5*5 cm electrode) 1mA for 20 min Anode: PMA Cathode: Supraorbital region for the contralateral side	Stabilometric analysis (balance in the form of COP) , (PBS) , (PEDI)
Fereera-sb (2014)	Double-blinded Randomized Controlled Trial	12 Cerebral Palsy Children 4-12 Years	I: Virtual training+ Active tDCS C: Virtual training+ Placebo tDCS Mobility training with virtual reality was performed using the XBOX 360TM with KinectTM (motion sensor) for mobility training tDCS (5*5 cm electrode) 1mA for 20 min Anode: PMA Cathode: Supraorbital region for the contralateral side	Functional mobility Through time up and go test (TUG)
Grecco (2014)	Double-blind Randomized Controlled Trial	24 Spastic Diparetic Cerebral Palsy Children 5-10 Years	I: Treadmill training+ Active tDCS C: Treadmill training +Placebo tDCS tDCS (5*5 cm electrode) 1mA for 20 min	Spatiotemporal variables

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			Anode: over the PMA Cathode: Supraorbital region for the contralateral side 10 Sessions: 5 time/week for 2 weeks	Gait kinematics (velocity, cadence stride length, step length, step width, stance phase.)
Grecco LA (2014)	Randomized Controlled Study	20 Spastic Cerebral Palsy Children 6-10 Years	I: Active tDCS C: Placebo tDCS One session/ 1mA for 20 min Anode: over the PMA of the dominant hemisphere Cathode: Supraorbital region contralateral to the anode.	Spatiotemporal gait variables (gait velocity, cadence, step length, stride length and step width)
Lazarii (2017)	Double Blind Randomized Controlled	20 Cerebral Palsy Children 4-12 Years	I: Mobility Training with VR+ Active tDCS C: Mobility Training with VR+ Sham tDCS tDCS (5*5 cm electrode) 1mA for 20 min Anode: PMA Cathode: Supraorbital region for the contralateral side	Stabiliometric Evaluation (COP), (PBS) Timed Up and Go Test (TUG)
Gillick (2018)	Randomized Controlled Experiment	20 Unilateral Cerebral Palsy Children 7-21 Years	I: Active tDCS +CIMT C: Sham tDCS + CIMT 10 sessions for 20 min followed by 100 minutes of CIMT alone Anode: Contralateral supraorbital prominence Cathode: non-lesioned hemisphere primary motor cortex (M1)	Adverse effect Grip strength Behavioral outcome
Nemanich (2019)	Randomized Controlled Experiment	20 unilateral cerebral palsy children 7-21 years	I: Active tDCS +CIMT C: Sham tDCS +CIMT 10 sessions for 20 min, Active tDCS +CIMT group received 0.7Ma while 30-s to 1-min ramp-up phase for the control group, followed by 100 minutes of CIMT Anode: Contralateral forehead Cathode: contralateral hemisphere	Motor evoke-potential Cortical silent period Hand function safety
Radwan (2023)	Randomized Clinical Trial	40 Bilateral Spastic CP children 7-12 years	I: tDCS + PT program C: Virtual Reality + PT program Total 10 sessions, 5 sessions/ week for 2 consecutive weeks tDCS 1mA for 20 min Anode: Midline of the skull Cz, corresponding to motor areas of lower limbs Cathode: over inion	Spatiotemporal and kinetic gait parameters (velocity, cadence, step length, stride length, stance time, and swing time, while kinetic parameters included maximum force and maximum peak pressure.)

tDCS: Transcranial Direct current Stimulation, TUG: Time up and Go test, CIMT: Constraint Induced Movement Therapy, COP: Centre of pressure, PBS: Pediatric balance scale, VR: Virtual Reality, PMA: Primary Motor Cortex Area, PEDI: Pediatric Evaluation of Disability Inventory

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DISCUSSION

The findings of this systematic review provide valuable insights into the potential of transcranial direct current stimulation (tDCS) as a non-invasive therapeutic tool for individuals with spastic cerebral palsy (CP). Cerebral palsy, characterized by neuromotor impairments affecting muscle tone, motor skills, balance, posture, and gait, poses significant challenges for affected individuals and their families(27). While traditional rehabilitation strategies have been instrumental in managing CP symptoms. (28) One notable aspect highlighted in this review is the safety and tolerability of tDCS. The finding that tDCS is a non-invasive and well-tolerated brain stimulation technique is consistent with existing literature(29). This suggests that tDCS can be administered without significant discomfort or adverse effects, making it an attractive option for individuals with CP, including children.(30) The positive effects of tDCS on gross motor function observed in the reviewed studies align with previous research demonstrating the potential of tDCS to enhance motor learning and motor recovery in various neurological conditions. These effects may be attributed to the modulation of cortical excitability and plasticity induced by tDCS[(31)]. The ability of tDCS to facilitate motor improvements in CP patients is particularly promising, as it addresses a core aspect of their functional limitations.

Another important finding of this review is the favorable influence of tDCS on spasticity and muscle strength. Spasticity is a common and often challenging symptom in CP, impacting movement and overall functional independence. The observed reduction in spasticity with tDCS is consistent with studies in other neuromuscular conditions(32) suggesting that tDCS may offer a novel approach to spasticity management in CP. The improvement in balance and gait kinematics associated with tDCS is particularly relevant for individuals with CP, as these factors significantly affect mobility and quality of life. Balance deficits are common in CP and can lead to falls and injuries. Gait abnormalities further compound the challenges faced by individuals with CP in daily activities. The positive impact of tDCS on these parameters underscores its potential to enhance functional outcomes.

One of the key takeaways from this review is the recognition that the positive effects of transcranial direct current stimulation (tDCS) need not replace traditional or conventional physical therapy; rather, they can be harmoniously integrated into existing rehabilitation programs. This integration serves as a beacon of hope for individuals living with spastic cerebral palsy (CP) as it holds the potential to amplify the benefits derived from conventional interventions.

A noteworthy perspective underscored by this finding is the concept of a multimodal rehabilitation approach. Multimodal rehabilitation, in essence, is a holistic strategy that brings together diverse therapeutic modalities, each contributing its unique strengths to optimize patient outcomes. In the context of CP management, it means that tDCS can be seen as a complementary component of a broader rehabilitation strategy(33). The rationale lies in the potential synergy that can be harnessed when combining tDCS with conventional physical therapy. While tDCS addresses specific aspects of neuroplasticity and neuromotor function at the cortical level, traditional physical therapy encompasses a broader spectrum of interventions, including exercises, stretching, mobility training, and functional activities. By integrating tDCS into this ecosystem of care, we may unlock enhanced learning, adaptation, and functional improvements.

For example, during a conventional physical therapy session, exercises aimed at improving gait or muscle strength can be synchronized with tDCS sessions that target specific cortical areas associated with motor control. This synchronized approach has the potential to amplify the brain's receptivity to therapeutic interventions and may lead to more pronounced and enduring benefits.

An additional dimension of significance lies in the feasibility, safety, and accessibility of tDCS. The review highlights that tDCS is a non-invasive, safe, and cost-effective modality. Its adaptability for use in both clinical and home settings is particularly relevant in the current healthcare landscape. Telehealth and home-based interventions have gained prominence, especially considering situations where individuals may have limited access to specialized care(34).

The study by Aree-uea B (2014) contributes valuable insights to this discussion. It specifically addresses spastic cerebral palsy in children aged 8-18 years and examines the impact of tDCS on spasticity and passive range of motion. The systematic review's findings on tDCS positively affecting gross motor function and spasticity align with the outcomes of this trial. This alignment reinforces the notion that tDCS may hold promise as a complementary therapy for spastic cerebral palsy.(35)

In this context, tDCS's potential for home-based application can bridge geographical gaps, ensuring that individuals with CP, regardless of their location, can access and benefit from this intervention. This aligns with a broader trend in healthcare, recognizing the importance of patient-centered care and the empowerment of individuals to actively participate in their rehabilitation process.(36)

As we move forward, it is crucial to continue exploring the optimal ways to integrate tDCS into conventional CP rehabilitation programs. This involves the development of standardized protocols, guidance on session frequency and duration, and the identification of the most appropriate patient profiles that stand to gain the most from this multimodal approach. Additionally, long-term studies are needed to assess the durability of the benefits derived from this complementary strategy.

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While the findings are promising, it is essential to acknowledge the limitations of this review. The number of included studies is relatively small, and further research is warranted to confirm the observed effects of tDCS in larger and more diverse CP populations. Additionally, the long-term effects and optimal treatment protocols for tDCS in CP should be explored. In conclusion, the evidence presented in this systematic review supports the potential of transcranial direct current stimulation as a valuable adjunctive therapy for individuals with spastic cerebral palsy. Its safety, positive effects on motor function, spasticity, balance, muscle strength, and gait kinematics make it a compelling option for clinicians and researchers in the field of pediatric rehabilitation. Further studies and clinical trials are needed to establish standardized protocols and confirm the long-term benefits of tDCS in the management of cerebral palsy.

CONCLUSION

Transcranial Direct current Stimulation conjunct with conventional physical therapy and other modes of neurorehabilitation can cause a reduction in spasticity, enhance fine and gross motor function, and improve balance and gait in children with spastic cerebral palsy. Therefore, it is regarded as a safe, feasible, cost-effective, easy home-based adjunct neuro-modulatory modality.

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