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Transcranial Direct-Current Stimulation in Motor Rehabilitation of Children and Adolescents with Cerebral Palsy

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Abstract

Transcranial direct current stimulation (tDCS) is reported to offer considerable benefits to the rehabilitation process of children and adolescents with cerebral palsy (CP), as it modulates cortical activity, enabling the enhancement and prolongation of functional gains achieved with physical therapy. The aim of the present study was to systematize knowledge on tDCS as a treatment option for individuals with CP. A systematic review was performed involving clinical trials published from 2007 to 2017. For such, the Pubmed, Medline, SciELO and LILACS databases were searches for articles using the keywords "cerebral palsy" and "transcranial direct current stimulation" (in English and Portuguese). The Physiotherapy Evidence Database (PEDro) scale was used to evaluate the methodological quality of the studies. Thirty-four articles were preselected, 26 of which were excluded for not the following reasons: population of healthy children or adolescents, diagnosis other than CP, systematic reviews, case reports, cross-sectional studied, pilot studies, therapies involving transcranial magnetic stimulation, other brain stimulation techniques and articles repeated in other databanks. In the eight articles analyzed, tDCS with or without other rehabilitation methods demonstrated a significantly positive impact on functional aspects of children and adolescents with CP. The findings reveal the benefits of using tDCS as a therapeutic tool in this population.

Keyword: Cerebral palsy, Transcranial direct current stimulation, Physical therapy.

Introduction

Cerebral palsy (CP) is defined as a non-progressive neurological condition originating from damage caused to the immature brain in the prenatal, perinatal or postnatal period, with negative repercussions regarding movement and posture [1]. The incidence in the population is approximately 1.5 to 2.5 of every 1000 live births [2].

The classification of CPdepends on the location of the brain damage (pyramidal, extrapyramidal or cerebellar), topography of motor impairment (hemiparesis, diparesis or tetraparesis)and level of gross motor function based on the Gross Motor Function Classification System (GMFCS) [3].

CP causes neuroanatomic and neurophysiologic, resulting in a reduction in glial cells, axonal loss, apoptosis, diminished cortical activity, maladaptive neuroplasticity and significant deficits in the nerve pathways (somatosensory and corticospinal circuits) responsible for the processing and execution of motor actions [5,6].

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A lack of knowledge of the neurophysiopathological mechanisms involved in CP can compromise the applicability and effectiveness of intervention techniques, thereby limiting benefits to the patient. The aim of physiotherapeutic treatments for CP is to minimize the consequences of the disease and promote maximum possible functioning. The following techniques are used for this purpose: early intervention, constraint-induced movement therapy, the Bobath neurodevelopmental method, aquatic physical therapy, equitherapy, TheraTogs, children's Pilates, virtual reality, treadmill training, functional electrical stimulation [7] and transcranial direct current stimulation (tDCS) [8].

TDCS has been highlighted in the scientific literature on CP, especially in studies involving motor rehabilitation. This is a safe, inexpensive form of brain stimulation that involves the administration of a low-intensity monophasic electrical current to the scalp using two silicone-sponge surface electrodes moistened with saline solution [9]. Noninvasive brain stimulation modulates cortical excitability during a functional task performed during therapy. Anodal stimulation facilitates cortical excitability, whereas stimulation with the cathode results in a reduction of the cortical excitability threshold [9].

The benefits of tDCS have piqued the interest of researchers, as this technique is capable of modulating cortical activity, potentiating gains achieved in physical therapy and promoting local neuroplasticity.8 Preliminary studies by Grecco et al. (2014) [8] and Duarte et al. (2014) [10] combining tDCS with treadmill training for children with CP demonstrated significant changes in gait velocity, step cadence and oscillations of the center of pressure (body sway). However, there is a need for further studies on this topic and greater theoretical-practical grounds for the scientific planning of an ideal tDCS protocol and its adaptive effects on the neural physiopathology of CP. Thus, the aim of the present study was to perform a systematic review on the effects of tDCS in the rehabilitation of children and adolescents with CP.

Methods

Searches were conducted in the Pubmed, Medline, SciELO and LILACS databases for articles published in English and Portuguese from 2007 to 2017 using the keywords "cerebral palsy" and "transcranial direct current stimulation". Clinical trials involving tDCS in the rehabilitation of children and adolescents with CP and for which the full text was available were included in the review.

The Physiotherapy Evidence Database (PEDro) scale [11] was used for the appraisal of the methodological quality of the studies. This scale consists of 11 items, 10 of which receive a score. The presence (1 point) or absence (0 points) of each item is used to determine the final score. Studies with a score of seven or more points are considered to be of high methodological quality [11].

Thirty-four articles were preselected, 26 of which were excluded for the following reasons: population of healthy children or adolescents, diagnosis other than CP, systematic review, case report, cross-sectional study, pilot study, therapies involving transcranial magnetic stimulation, other brain stimulation techniques and articles repeated in other databanks (Figure 1).The analysis of the titles and abstracts as well as the appraisal of methodological quality was performed by two independent reviewers.

Results

Thirty-four articles were found, but only eight were selected for the present systematic review (Table 1). Description of studies selected for present systematic review. All articles included in the review received a score of ≥9 points on the PEDro scale, demonstrating high quality in terms of methodological rigor.

Discussion

Available evidence demonstrates the considerable potential of tDCS as a therapeutic tool in the rehabilitation of children and adolescents with CP [8,10,12-17].

Three studies included in the present review combined tDCS with treadmill training [8,10,13] and identified significant improvements in kinematic/spatiotemporal gait variables and static balance. The authors believe that the technique enhanced cortical excitability in motor areas near the injured portion of the brain, which enabled ascending information from the treadmill exercise (repetitive training and synchronization of steps) to reach the cortex, with a better interpretation and subsequent motor response, thereby enhancing motor learning.

Two studies combined tDCS with virtual reality [l3,14] and found important benefits to static balance. The findings suggest that the combination of the two modalities enabled better training of a specific task, as the recurrent sensory (proprioceptive and visual) stimuli were able to reach the

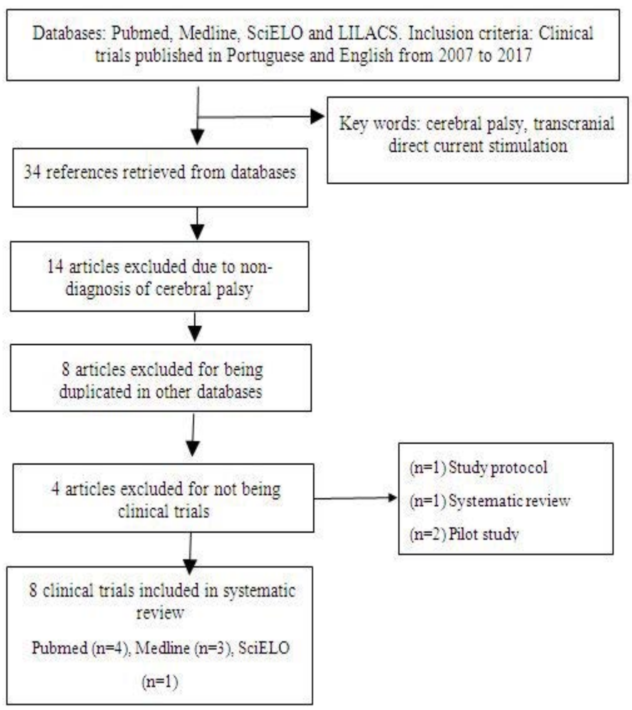

Figure 1: Flowchart of article selection process.

Table 1: Description of studies selected for present systematic review.

Authors/ Year	Type of study	PEDro scale score	Sample	Interventions	Variables analyzed	Outcomes
Kirton *et al.* (2017) [12]	Randomized, controlled, double-blind, clinical trial	10/10	n=24 children and adolescents with diagnosis of CP (6 to 18 years). IG: 12 CG:12	IG: active cathodal tDCS (20min, 1 mA over M1 –non-injured hemisphere) prior to motor training of paretic upper limb. CG: sham cathodal tDCS (30s, 1 mA over M1- non-injured hemisphere) prior to motor training of paretic upper limb. 10 sessions, 5 x week for two consecutive weeks.	Evaluations performed two weeks before the intervention, one week after and at 2-month follow up. Variables analyzed: *Assisting Hand Assessment*, *Canadian Occupational Performance Measure* (COPM), *ABILHAND-Kids, Box and Blocks* for upper limb function, grip strength, pinch strength, and quality of life questionnaire for cerebral palsy.	For IG, performance on COPM increased 2 points after one week and "school activities" item on quality of life questionnaire improved significantly compared to CG. No other variables differed significantly between groups.
Grecco *et al.* (2016) [13]	Randomized, controlled, double-blind, clinical trial	10/10	n = 66 children with diagnosis of CP (7 and 8 years). IG:28 CG:28	IG: active anodal tDCS (20min, 1mA over M1- injured hemisphere) combined with treadmill and 10 min with virtual reality training. CG: sham anodal tDCS (30s, 1mA over M1- injured hemisphere) combined with treadmill and 10 min with virtual reality training. 10 sessions, 5 x week for two consecutive weeks.	Evaluations performed 1 week before the intervention, 1 weekafter the intervention and follow up 4 weeks after last session. Univariate and multivariate logistic regression analyses used to identify clinical, neurological and neuroanatomic predictors associated with response to treatment with tDCS. Variable analyzed: 6-Minute Walk Test, Gross Motor Function Scale (GMFM), gait velocity, 3-dimensional gait analysis and motor evoked potential (MEP).	Presence of ME during initial evaluation and sub cortical injury positively associated with functional results. Logistic regression revealed that present MEP was significant predictor for 6-Minute Walk Test and gait velocity, whereas sub cortical injury was significant predictor of gait kinematics and GMFM.
Lazzari et al. (2016) [16]	Randomized, controlled, double-blind, clinical trial	10/10	n= 20 children with diagnosis of CP (4 to12 years) IG: 10 CG:10	IG: active anodal tDCS (20min, 1mA over M1- injured hemisphere) combined with virtual reality training. CG: sham anodal tDCS (30s, 1mA over M1- injured hemisphere) combined with virtual reality training. 10 sessions, 5 x week for two consecutive weeks.	Evaluations performed before intervention, after intervention and at one-month follow up. Variables analyzed: Static balance (eyes open and closed) using force plate, functional balance using *Pediatric Balance Scale* (PBS) and *Timed Up and Go* (TUG) test.	IG demonstrated significant effects on PBS, TUG and area of oscillation of center of pressure on force plate with eyes open after intervention and at one-month follow up compared to CG.
Grecco et al. (2014) [8]	Randomized, controlled, double-blind, clinical trial	9/10	n= 20 children with diagnosis of CP (6 to 10 years) IG: 10 CG:10	IG: active anodal tDCS (20min, 1mA over M1- injured hemisphere). CG: sham anodal tDCS (30s, 1mA over M1- injured hemisphere). Single session	Evaluations performed before, immediately after and 20 minutes after administration of tDCS. Variables analyzed: Spatiotemporal gait analysis and static balance (eyes open and closed) using force plate.	In IG, tDCS led to significant reduction in anteroposterior sway with eyes open and closed (static balance) and improvements in gait velocity and cadence in comparison to CG, but results were not maintained for more than 20 min after end of stimulation.

Duarte et al. (2014) [10]	Randomized, controlled, double-blind, clinical trial	10/10	n = 24 children with diagnosis of CP (5 to 12 years). IG:12 CG:12	IG: active anodal tDCS (20min, 1mA over M1- injured hemisphere) combined with treadmill training. CG: sham anodal tDCS (30s, 1mA over M1- injured hemisphere) combined with treadmill training. 10 sessions, 5 x week for two consecutive weeks.	Evaluations performed one week before the intervention, one weekafter and at one-month follow up. Variables analyzed: Static balance (stabilometry), PBS.	IG demonstrated better results over CG regarding anteroposterior (eyes open and closed) and mediolateral (eyes closed) sway and PBS, with effects lasting one week and one month after treatment.
Grecco *et al.* (2014) [15]	Randomized, controlled, double-blind, clinical trial	10/10	n= 24 children with diagnosis of CP (7 and 8 years). IG:12 CG:12	IG: active anodal tDCS (20min, 1mA over M1- injured hemisphere) combined with treadmill training. CG: sham anodal tDCS (30s, 1mA over M1- injured hemisphere) combined with treadmill training. 10 sessions, 5 x weeks for two consecutive weeks.	Evaluations performed before and after intervention and at one-month follow up. Variables analyzed: Kinematic and spatiotemporal (velocity, cadence, step length, stride width and support phase) gait variables and cortical excitability (transcranial magnetic stimulation).	IG demonstrated improvements in spatiotemporal (gait velocity, distance traveled and cadence) and kinematic (pelvic tilt, hip abduction, knee flexion and extension) variables and increase in cortical excitability. No significant differences in spatiotemporal or kinematic gait variables found in CG.
Aree-uea *et al.* (2014) [16]	Randomized, controlled, double-blind, clinical trial	10/10	n= 46 adolescents with diagnosis of CP (13 and 14 years). IG:23 CG:23	IG: active anodal tDCS (20min, 10 mA over M1- injured hemisphere). CG: sham anodal tDCS (30s, 10 mA over M1- injured hemisphere). 5 sessions over 5 consecutive days. Both groups maintained physical therapy routine 30 minutes prior to administration of tDCS.	Evaluations performed before and immediately after interventions and at 24-h and 48-h follow up. Variables analyzed: Upper limb spasticity based on passive range of motion and degree of spasticity using Ashworth Scale	In IG, significant reduction in spasticity of upper limb immediately after intervention, with effects lasting up to 48h in comparison to CG.
Young *et al.*(2013) [17]	Randomized, controlled, double-blind, clinical trial	9/10	n= 14 children and adolescents with diagnosis of CP (7 to 19 years). IG:14 *crossover* CG:14	IG: active cathodal tDCS (first 9 min (1mA),20 min pause and additional 9 min of stimulation over de M1- non-injured hemisphere) CG: sham cathodal tDCS (30s, 1mA, over M1- non-injured hemisphere). 2 sessions with one-week crossover interval between sessions.	Evaluations performed before and immediately after interventions. Variables analyzed:	*Barry-Albright Dystonia Scale* and electromyography of muscles of upper extremity. IG demonstrate small difference compared to CG: Reduction in dystonia in some children, but with small effect size. No changes in voluntary motor control.

n: number of individuals; CP: cerebral palsy; IG: intervention group; CG: control group; tDCS: transcranial direct current stimulation; M1: primary motor cortex; MEP: motor evoked potential; COPM:Canadian Occupational Performance Measure; GMFM: Gross Motor Function Scale; PBS: Pediatric Balance Scale; TUG: Timed Up and Go.

cortex due to the modulation of maladaptive neuroplasticity with an increase local synaptic efficiency, thereby potentiating the acquisition of the required movement.

Two studies combined tDCS with specific physical therapy routines [16] and upper limb training.12Both evidenced a better performance and quality of movement in the functions evaluated.

One study included in the present review did not combine tDCS with another form of rehabilitation [18]. However, this study also reports promising results with regard to motor control in children and adolescents with CP, such as small reductions in spasticity.

The age of the children in the studies analyzed ranged from five to 10 years and the age of the adolescents ranged from 12 to 19 years. Previous studies state that tDCS is not indicated for children younger than five years of age due to the period of neuroanatomic development of the brain. The authors argue that the intervention could increase the excitability threshold and exert a negative impact on ongoing neural activities [18].

The number of sessions in the studies ranged from one to ten. A common frequency was five times a week for two weeks with 20 minutes of stimulation per session using a current of 1mA.Regarding the electrode montage, anodal tDCS over the injured motor cortex increased the excitability of the area, whereas cathodal tDCS over the non-injured motor cortex diminished compensatory excitability. Both montages contributed to motor improvements and facilitated the maintenance of the results after the end of the treatment protocol (neuroplastic properties) [8,10,12,14,16].

Research involving tDCSon children and adolescents is in the initial stages (I and II) and important gaps in knowledge exist regarding the effectiveness of the method, combinations with other therapeutic modalities, the ideal administration parameters and outcomes. For non-invasive brain stimulation to be established as a tool indicated in the rehabilitation process, it is necessary to adjust intervention protocols to actual clinical practice, since it is not common for a child with CP to undergo motor physical therapy five times a week.

Further studies with greater theoretical-practical knowledge will enable the ideal tDCS protocols and clarify issues regarding the risks and benefits of modulating a child's developing brain. Transcranial direct current stimulation has advantages over other rehabilitation methods, such as an immediate modulation effect on cortical function with a longer duration, few side effects, ease of application, ease of combining the technique with other physiotherapeutic modalities and low cost. Moreover, this type of intervention is suitable for protocols involving sham stimulation, which enables greater specificity in the results of a study [19].

Conclusion

The present systematic review demonstrated encouraging results with regard to the use of tDCS in the rehabilitation of children and adolescents with cerebral palsy. The effects of the technique (either alone or in combination with other physiotherapeutic modalities) demonstrate important beneficial changes in gait, balance, functional activities and quality of life in a relatively short period of time, with the maintenance of gains even after the end of the treatment sessions. Thus, the findings reveal the benefits of using tDCS as a therapeutic tool in this population. Further studies on this treatment modality should be developed to contribute scientific knowledge on this treatment modality and indicate new perspectives in the field of neurological rehabilitation for children and adolescents.

Competing Interests

The authors declare that no competing interests exist.

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