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

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Introduction

Most children with cerebral palsy have compromised gait.[1,2] Gait rehabilitation for such individuals has been focused on improving muscle strength and diminishing spasticity.[3] However, the main causes of motor impairment seem to be related to a lack of neural organisation.[4–7] The abnormal gait pattern is directly attributable to damage to the central nervous system.[8] Indeed, children with cerebral palsy experience a reduction in nervous system activation during the execution of movements[6,7] owing to lower motor excitability[9] as well as the inadequate processing of corticospinal and somatosensory circuits.[10]

Different therapies have been tested with the aim of improving functional reorganisation in individuals with neurological disorders.[11,12] In this vein, virtual reality allows an immersive, interactive, three-dimensional, multisensory experience.[13–16] Using a movement detection system, the individual needs to plan and execute movements while the game offers feedback in real time on the performance and progression of the exercises.[17–19] Motor learning is strengthened by practice and feedback,[20] which are both offered through motor training involving virtual reality.[12]

Transcranial direct current stimulation (tDCS) is a potential method for enhancing motor learning. This non-invasive form of brain stimulation involves the delivery of a weak electrical current through two electrodes to modulate motor cortex excitability and enhance neuroplasticity, which may be the mechanism underlying motor learning.[21] The literature reports promising results regarding the combined use of tDCS, motor training and virtual reality.[22,23] However, the effects of anodal tDCS over the primary motor cortex during gait training with virtual reality in children with cerebral palsy remain unclear.

Gait is the result of a complex, bilateral, neurological process involving different areas of the brain.[24] It is therefore of interest to study the effect of anodal tDCS over the primary motor cortex bilaterally.[25] However, the safety of tDCS in children with neurological injuries has not been established owing to the small number of studies on this topic,[26,27] which raises questions regarding possible adverse effects. The authors of the present study consider it valid to determine first whether there is a positive effect of unilateral anodal tDCS over the primary motor cortex in children with cerebral palsy without significant side-effects. Moreover, as part of the corticospinal tract, fibres do not intersect at the level of the brainstem,[28] unilateral stimulation could provide results in both lower limbs.

We hypothesise that anodal tDCS over the primary motor cortex can enhance the effects of gait training with virtual reality on gait, gross motor function and independence in children with spastic diparetic cerebral palsy. This hypothesis is based on

the results of previous studies demonstrating that anodal tDCS over primary motor cortex can regulate corticospinal excitability,[29–31] as well as improved performance and motor learning when stimulation is applied during a motor training programme.[32–35]

The primary aim of the present study was to compare the effects of anodal vs. sham tDCS during gait training with virtual reality on gait pattern, gross motor function, functional performance and cortex excitability in children with spastic diparetic cerebral palsy. The secondary aim was to determine whether the effects would be maintained one month after the end of the intervention.

Materials and methods

The present study received approval from the Human Research Ethics Committee of Universidade Nove de Julho, Brazil, under process number 69803/2012 and was conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Written informed consent was obtained from the parents or legal guardians. The study is registered with the Brazilian Registry of Clinical Trials under process number RBR-9B5DH7. A randomized, controlled, double-blind, clinical trial was conducted.

Participants

Participants were recruited and selected for eligibility using the following inclusion criteria: diagnosis of spastic diparetic cerebral palsy, classification on levels II or III of the Gross Motor Function Classification System,[36] independent gait for at least 12 months, age between five and ten years and degree of comprehension compatible with the execution of the procedures. The diagnosis of spastic diparetic cerebral palsy was confirmed by physical examination. Spastic diparesis was defined as motor impairment and more evident spasticity in the lower limbs when compared with other regions of the body. Magnetic resonance imaging of the brain was used to confirm the bilateral injury. The following were the exclusion criteria: history of surgery or neurolytic block (botulinum toxin and phenol) in the previous 12 months, orthopaedic deformities, epilepsy, metal implants in the skull, use of hearing aids and use of anticonvulsant or muscle relaxant drugs. The participants did not take any medications throughout the study.

The children were randomly allocated to an experimental group (gait training with virtual reality and anodal tDCS) and control group (gait training with virtual reality and sham tDCS). A block randomization approach was employed. The allocation sequence was concealed from the researchers in sequentially numbered, sealed, opaque envelopes. Following the initial evaluation, each participant was allocated to one of the groups by opening an envelope. This process was performed by a member of the research team who was not involved in the recruitment process or other aspects of the study.

Primary outcome measures

Gait analysis was performed using the SMART-D 140® system (BTS Engineering, Italy) with eight infrared cameras, the SMART-D INTEGRATED WORKSTATION® with 32 analogue channels and a synchronised video system. After the determination of the anthropometric measures (height, weight, lower limb length, distance between the femoral condyles or diameter of the knee, distance between the malleoli or diameter of the ankle, distance between the anterior iliac spines and thickness of the pelvis), passive markers were placed at specific reference points directly on the skin for the evaluation of the kinematics of each segment of the body. The markers were placed over C7 and the sacrum as well as bilaterally over the acromion, anterosuperior iliac spine, greater trochanter, femoral epicondyle, femoral wand, tibial head, tibial wand, lateral malleolus, lateral aspect of the foot at the fifth metatarsal head and at the heel (only for static offset measurements), as described by Davis et al.[37] The Davis marker set was chosen as the protocol of choice to acquire the movement of lower limbs and trunk based on Ferrari et al.[38] After the child was familiarised with the process, at least six trials were performed along a 10-metre catwalk at a pace self-selected by each child. Three consistent trials of each lower limb were considered for analysis. All readings were performed by the same experienced researcher to ensure the reliability of the data collection. In the present study, only

spatiotemporal and kinematic gait variables were identified and computed. The following spatiotemporal parameters were analysed.

- Velocity (m/s): Mean velocity of progression.
- Cadence: Number of steps in a time unit (steps/minute).
- Stride length (m): Longitudinal distance between successive points of heel contact of the same foot.
- Step length (m): Longitudinal distance between the point of initial contact of one foot and the point of initial contact of the contralateral foot.
- Step width (m): Distance between the rear end of the right and left heel centre lines along the mediolateral axis.
- Stance phase: Percentage of gait cycle that begins with initial contact and ends at toe-off of the same limb.

All kinematic gait analysis graphs were normalised as a percentage of the gait cycle, producing kinematic plots of the pelvis, hip, knee and ankle for each cycle. The Gait Profile Score was calculated according to the procedure implemented by Baker et al.[39] The gait profile score represents the root mean square (RMS) difference between a particular gait trial and averaged data from individuals with no gait pathology and summarises the overall deviation in kinematic gait data relative to normative data.[39] The overall gait profile score is based upon 15 clinically important kinematic variables (pelvic anterior/posterior, pelvic up/down obliquity, left-side rotation, hip flexion, abduction, internal rotation, knee flexion, dorsiflexion and foot progression for the left and right sides). In the analysis, a gait profile score was determined for each side based on all nine gait variable scores. A higher gait profile score value denotes a less physiological gait pattern. In the literature, the gait profile score has been used to quantify gait alterations in different adverse health conditions in both children and adults.[39–45]

Secondary outcome measures

The Gross Motor Function Measure-88 allows a quantitative assessment of gross motor function in individuals with cerebral palsy. This measure is made up of 88 items distributed among five subscales: (1) lying down and rolling; (2) sitting; (3) crawling and kneeling; (4) standing; and (5) walking, running and jumping. The items of each subscale receive a score of 0 to 3 points, with higher scores denoting a better performance.[46,47] In the present study, dimensions D and E were used.

The Pediatric Evaluation Disability Inventory (PEDI) quantitatively measures functional performance. The first part of the questionnaire was used in the present study, which assesses skills in the child's repertoire grouped into three functional categories: self-care (73 items), mobility (59 items) and social function (65 items). The score is totalled per category.[48,49] The three functional categories were selected to investigate whether the effects of the intervention on gait would increase the independence and participation of the child in activities involving all these functions rather than mobility alone.

Motor cortex excitability was measured using a magnetic stimulator (MAGSTIM Bistim²) with a figure-eight coil. Responses to stimuli applied to motor cortices were recorded in the abductor muscle of the thumb and the quadriceps muscle contralateral to the stimulated side. These measures were performed for the right and left motor cortex. The motor evoked potential was evaluated with the muscles at rest. The motor threshold was measured in each region assessed. Given the lack of more conclusive safety data for children, we did not exceed an intensity of 80% of the output of the machine. The motor evoked potential was set to an intensity of 110% of the motor threshold. Motor evoked potential responses were filtered and amplified using surface electromyography. The signals were transferred to a personal computer for offline analysis of the amplitude of the motor evoked potential. Ten individual measures of motor evoked potential were performed and the mean was used for the statistical analysis. The motor evoked potential evaluations were performed before and after the interventions as well as at the one-month follow-up.

A questionnaire based on previously reported adverse events[50] was administered after each session to assess safety. Moreover, the researcher in charge of the tDCS sessions asked the children and their guardians about the occurrence of any adverse effects.

Intervention

The experimental group performed gait training involving virtual reality with the application of anodal tDCS over the primary motor cortex of the contralateral hemisphere to lower limb with greater motor impairment. The control group performed gait training involving virtual reality with sham tDCS. Five weekly 20-minute sessions were conducted over two consecutive weeks (total: 10 sessions).

Mobility training with virtual reality

Gait training with virtual reality was performed using the Kinect program (Xbox 360 and the game Your Shape: Fitness Evolved 2012 run the world, Microsoft, USA) in a room containing only the virtual reality equipment with no outside influences. The equipment has an infrared camera sensor that recognises movements without the need for a control device. The walking activities of the Kinect sports program were used, in which the participant is required to walk at intercalated slow and fast paces. The selected game consists of a race track. With the camera positioned, the child started the game walking slowly and was offered specific tasks to increase the velocity for a specific period of a time. Visual and audio feedback was provided when the activity was not performed adequately in the virtual reality environment. The activity was practiced for 20 minutes with the participant using his/her habitual braces and gait-assistance device. The application of tDCS was synchronised with the beginning and end of the activity.

Transcranial direct current stimulation

A transcranial stimulation device (Soterix Medical Inc., USA) was employed using two sponge (non-metallic) electrodes (5 × 5 cm) moistened with saline solution. The anodal electrode was positioned over the primary motor cortex contralateral to the lower limb with greater motor impairment, following the 10–20 International Electroencephalogram System,[51] and the cathode was positioned in the supraorbital region on the contralateral side. As the study involved children with bilateral brain lesions, the goal was to determine whether unilateral stimulation could achieve an improvement in motor function. During the initial evaluation, each child was asked which lower limb exhibited greater difficulty during gait. The primary motor cortex responsible for the control of this limb was selected for stimulation. A current of 1 mA current was applied as the child performed 20 minutes of gait training with virtual reality. In the first ten seconds, stimulation was gradually increased until reaching 1 mA and gradually diminished in the last ten seconds of the session. In the control group, the electrodes were positioned at the same sites and the device was switched on for 30 seconds, giving the child the initial sensation of the current, but no stimulation was administered the rest of the session. This is considered a valid control procedure in studies involving tDCS.[52]

Statistical analysis

Intention to treat analysis was employed when necessary, with the data from the previous evaluation repeated to substitute missing data. The Kolmogorov-Sirmonov test demonstrated normal data distribution. Thus, parametric tests were performed and the data were expressed as mean and standard deviation. Two-way analysis of variance (ANOVA) was used to compare the effects of stimulation during motor training on the main outcome variables and the Bonferroni correction for multiple comparisons was employed as the post hoc test. The dependent variables were spatiotemporal gait parameters, gait profile score, gait variable scores, gross motor function (dimensions D and E), functional performance (self-care, mobility and social function) and motor evoked potential. The independent fixed variables were treatment (baseline, posttreatment and follow-up), group (anodal tDCS and sham tDCS) and group–treatment interaction. The frequency of adverse events was recorded. A p-value <0.05 indicated a statistically significant result. The data were organised and tabulated using the Statistical Package for Social Sciences (v.19.0).

Results

A total of 31 children with cerebral palsy were screened, 20 of whom were eligible for participation in the study and were randomly allocated to the two groups. All children completed all ten training sessions. One child in the experimental

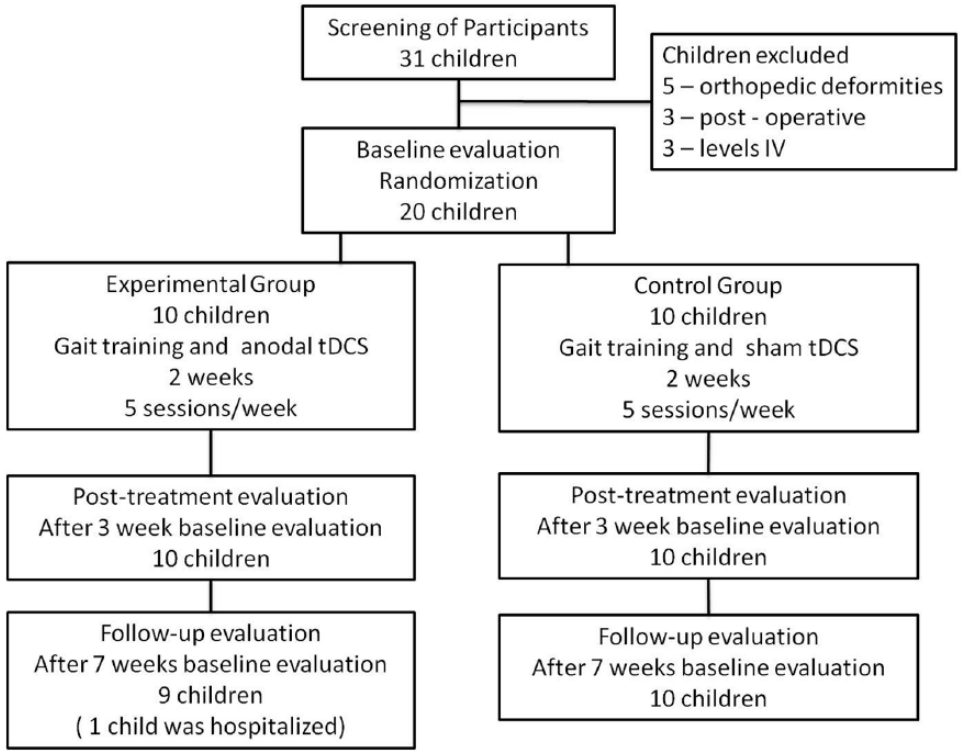

Figure 1. Flowchart of study based on Consolidated Standards of Reporting Trials (CONSORT).
tDCS: transcranial direct current stimulation.

group did not undergo the follow-up evaluation owing to respiratory problems and hospitalisation (Figure 1). Table 1 displays the anthropometric characteristics and functional classification of the children studied. No statistically significant differences between groups were found at baseline regarding anthropometric variables, age or variables related to the outcomes ($p > 0.05$). No child experienced any serious adverse event throughout the study. Four (40%) children reported mild tingling with anodal tDCS.

Primary outcome

Gait analysis. A significant time × group interaction was found for two gait-related outcomes: velocity and cadence. For velocity, the interaction effect ($F_{(2,18)} = 45.7$, $P < 0.001$) as well as the main effects of group ($F_{(1,9)} = 4.6$, $P = 0.035$) and time ($F_{(2,18)} = 5.6$, $P = 0.012$) were significant. Similar results were found for cadence: interaction term ($F_{(2,18)} = 52.4$, $P < 0.001$), main effect of group ($F_{(1,9)} = 12.5$, $P = 0.006$) and main effect of time ($F_{(2,18)} = 26.6$, $P < 0.001$). The post hoc analysis for these two variables demonstrated better results in the experimental group in comparison with the control group at the posttreatment evaluation (velocity: $P = 0.001$; cadence: $P < 0.001$) and follow-up evaluation (velocity: $P = 0.012$; cadence: $P = 0.007$). No significant differences were found regarding the other gait-related variables (gait profile score and gait variable scores) ($P > 0.05$). Table 2 displays the mean and standard deviation of the results of the three-dimensional gait analysis at the different evaluation times (baseline, post-treatment and follow-up).

Table 1. Anthropometric characteristics and functional classification of children studied.

	Groups	
	Experimental $n = 10$	Control $n = 10$
Gender (female/male)[a]	4/6	5/5
GMFCS (II/III)[a]	3/7	4/6
Age (years)[b]	8.2 (1.6)	8.8 (1.1)
Body mass (kg)[b]	25.7 (3.6)	26.1 (4.6)
Stature (cm)[b]	125.2 (10.8)	126.3 (12.3)
Body mass index (kg^2/m)#	16.2 (3.7)	17.1 (5.2)

[a]Numbers indicate frequency (n) of children in each group.
[b]Data expressed as mean (standard deviation).
GMFCS: Gross Motor Functional Classification System.

Table 2. Mean and standard deviation of spatiotemporal variables, Gait Profile Score and Gait Variation Scores at baseline evaluation, posttreatment evaluation and follow-up evaluation in experimental and control groups.

	Experimental group			Control group		
	Baseline	Posttreatment	Follow-up	Baseline	Posttreatment	Follow-up
Velocity (m)	0.63 (0.17)	0.85 (0.11)[a,b]	0.73 (0.15)[a,b]	0.61 (0.15)	0.70 (0.14)[a]	0.64 (0.14)
Cadence (step\minute)	92.4 (14.1)	116.8 (8.7)[a,b]	101.8 (12.4)	92.6 (10.4)	99.7 (8.2)	95.8 (8.9)
Stride length (m)	0.67 (0.16)	0.78 (0.18)	0.71 (0.12)	0.67 (0.16)	0.71 (0.13)	0.69 (0.15)
Step length (m)	0.37 (0.09)	0.38 (0.07)	0.36 (0.08)	0.41 (0.09)	0.41 (0.08)	0.42 (0.08)
Step width (m)	0.18 (0.04)	0.17 (0.03)	0.17 (0.02)	0.19 (0.04)	0.18 (0.05)	0.18 (0.03)
Stance phase (%)	62.3 (6.3)	58.6 (3.2)	59.9 (4.7)	61.9 (4.2)	60.4 (4.8)	61.1 (4.4)
GPS (°)	11.9 (1.9)	10.9 (2.1)	11.5 (1.4)	12.1 (1.3)	11.6 (1.4)	11.7 (1.0)
GVS pelvic obliquity (°)	3.8 (1.9)	2.8 (0.8)	3.0 (0.9)	2.4 (0.9)	3.2 (1.6)	4.1 (1.6)
GVS pelvic tilt (°)	7.6 (5.2)	3.5 (1.7)	3.9 (1.8)	7.3 (5.0)	7.9 (6.5)	6.9 (4.8)
GVS pelvic rotation (°)	4.2 (1.1)	4.5 (1.8)	3.2 (0.2)	5.5 (1.1)	4.7 (0.9)	4.7 (1.4)
GVS hip ab-adduction (°)	9.3 (8.3)	3.8 (1.5)	4.8 (1.1)	8.1 (4.8)	11.7 (5.7)	7.9 (4.6)
GVS hip flex-extension (°)	7.3 (3.3)	8.4 (5.6)	7.4 (4.6)	9.5 (5.1)	6.9 (3.6)	6.5 (2.4)
GVS hip rotation (°)	19.6 (11.1)	15.1 (0.5)	18.1 (8.0)	21.6 (12.6)	20.4 (10.7)	21.6 (11.7)
GVS knee flex-extension (°)	11.8 (4.4)	10.1 (3.8)	17.2 (4.5)	14.9 (9.3)	19.6 (9.3)	16.7 (6.0)
GVS ankle dorsi-plantarflex (°)	5.4 (2.8)	5.8 (0.7)	6.9 (3.1)	6.8 (2.8)	6.9 (4.0)	6.4 (2.6)
GVS foot progression (°)	11.6 (9.4)	10.3 (4.6)	13.8 (1.9)	12.8 (7.2)	10.3 (5.0)	11.0 (3.4)

[a]ANOVA $P < 0.05$ posttreatment and follow-up different from baseline.
[b]ANOVA $P < 0.05$ experimental group different from control group.
GPS: Gait Profile Score; GVS: Gait Variation Score.

Table 3. Mean and standard deviation of gross motor function, functional performance (self-care, mobility and social function) and motor evoked potential at baseline evaluation, posttreatment evaluation and follow-up evaluation in experimental and control groups.

	Experimental group			Control group		
	Baseline	Posttreatment	Follow-up	Baseline	Posttreatment	Follow-up
Gross motor function measure D	59.7 (9.2)	76.1 (13.2)[a,b]	76.2 (12.8)[a,b]	58.9 (10.4)	69.1 (9.3)	61.7 (8.5)
Gross motor function measure E	59.0 (10.9)	79.1 (8.5)[a,b]	78.1 (8.6)[a,b]	60.3 (10.1)	69.9 (11.4)[a]	65.5 (9.5)
Mobility	34.3 (5.9)	45.7 (5.3)[a,b]	44.9 (5.5)[a,b]	34.4 (8.3)	37.7 (7.7)	36.9 (8.3)
Self-care	37.5 (7.1)	43.6 (7.5)	44.4 (8.3)	38.2 (8.8)	39.0 (8.0)	38.6 (8.3)
Social function	49.8 (3.8)	50.8 (3.9)	50.7 (3.7)	48.6 (5.2)	49.2 (4.6)	49.3 (5.3)
Motor evoked potential (mV)	1.5 (0.5)	2.4 (0.3)[a,b]	1.8 (0.4)[b]	1.6 (0.5)	1.5 (0.4)	1.5 (0.4)

[a]ANOVA $P < 0.05$ posttreatment and follow-up different from baseline.
[b]ANOVA $P < 0.05$ experimental group different from control group.

Secondary outcomes

Gross motor function. Gross motor was evaluated using dimensions D (standing) and E (walking, running and jumping) of the Gross Motor Function Measure-88. Significant interaction effects were found for dimension D ($F_{(2,18)}=8.3$, $P=0.002$) and dimension E ($F_{(2,18)}=26.7$, $P \leq 0.001$). Moreover, significant effects of group (dimension D: $F_{(2,18)}=48.6$, $P=0.001$; dimension E: $F_{(2,18)}=98.7$, $P<0.001$) and time (dimension D: $F_{(2,18)}=32.6$, $P=0.001$; dimension E: $F_{(1,9)}=6.3$, $P<0.033$) were found. The post-hoc test demonstrated a significant increase in motor function in the posttreatment evaluation (dimension D: $P=0.032$; dimension E: $P=0.001$) and follow-up evaluation (dimension D: $P=0.031$; dimension E: $P=0.002$) after anodal tDCS combined with virtual reality training. Moreover, a significant improvement in dimension E was found at the posttreatment evaluation in the group submitted to sham tDCS combined with virtual reality training ($P=0.05$) (Table 3).

Functional independence. Table 3 displays the PEDI results on self-care, mobility and social function. For mobility, the interaction effect ($F_{(2,18)}=8.5$, $P=0.002$) and the main effect of group ($F_{(2,18)}=27.8$, $P<0.001$) were significant. The post-hoc test demonstrated a significant increase in mobility following anodal tDCS combined with virtual reality training in the posttreatment evaluation ($P=0.014$) and follow-up evaluation ($P=0.029$). The same did not occur following sham tDCS ($P>0.05$). No significant differences were found regarding self-care or social function ($P>0.05$).

Motor cortex excitability. For motor cortex excitability, the time × group interaction ($F_{(2,18)}=17.9$, $P<0.001$) as well as the main effect of group ($F_{(1,9)}=4.9$, $P=0.05$) and time ($F_{(2,18)}=7.9$, $P=0.003$) were significant. The post hoc analysis demonstrated an increase in motor evoked potential in the posttreatment evaluation following anodal tDCS combined with virtual reality training ($P=0.002$), but this effect did not remain through to the follow-up evaluation ($P>0.05$ in comparison with baseline). No significant changes in motor evoked potential occurred in the control group ($P>0.05$) (Table 3).

Discussion

The aim of the present study was to analyse the effects of anodal and sham tDCS over the primary motor cortex in children with cerebral palsy during gait training involving a virtual reality environment. The experimental group (motor training

with anodal tDCS) demonstrated positive effects regarding spatiotemporal gait variables (velocity and cadence), gross motor function (dimensions D and E of the Gross Motor Functional Measure-88) and mobility. Furthermore, anodal tDCS led to a significant change in motor cortex plasticity, as evidenced by the increase in the amplitude of the motor evoked potential.

As virtual reality training was performed at the same frequency, duration and intensity in both groups, the findings demonstrate that the differences in the results were owing to tDCS (anodal vs. sham tDCS). Apparently, anodal tDCS over the primary motor cortex contralateral to lower limb with greater motor impairment potentiated and maintained the effects of motor training. Analysing the results of this pilot study, both groups demonstrated the effects of motor training on velocity, cadence, gross motor and functional mobility, but these effects were greater in the experimental group. Moreover, only the experimental group demonstrated a change in motor evoked potential after motor training. This finding suggests that anodal tDCS enhances spontaneous neuronal firing.

Three-dimensional gait analysis is considered a very specific procedure that allows the comparative evaluation of the lower limbs. The statistical analysis of the results revealed no significant differences in the gait variable scores between the right and left legs before and after treatment in either group. These results are important, as one might expect asymmetry following unilateral stimulation of the primary motor cortex in children with bilateral lesions and spastic diparesis. It is possible that unilateral anodal tDCS did not cause asymmetry owing to indirect effects in cortex regions distant from the stimulated region, as has been demonstrated in previous studies involving neurophysiological measures.[53–55] Moreover, a portion of the corticospinal tract fibres ascends ipsilaterally. Thus, unilateral stimulation may result in bilateral effects. Further studies are needed to test this hypothesis using neurophysiological measures, such as electroencephalogram, which allows the analysis cortex activity in specific areas and provides a comparison between hemispheres.

During 'virtual walking', gait movements (joint flexion and extension) are simulated. However, no specific training of the full gait cycle is offered, as occurs with conventional gait training on the ground or treadmill training. Thus, no training of the swing and stance phases was performed in the present study to achieve better joint alignment and propulsion of the body. This aspect should be investigated further. If the functional effect is directly dependent on the motor task being trained, training in an inappropriate manner may result in pathologic motor learning and a possible adverse effect. Indeed, when compared with other treatments involving anodal tDCS over the motor cortex, the results are fundamentally different. For instance, anodal tDCS combined with treadmill training (repetitive training of the gait cycle) leads to a significant improvement in gait pattern (kinematics), but no improvement in gross motor function.[27]

Few studies are found in the literature on virtual reality for gait training in children with cerebral palsy. The use of this resource in neurological rehabilitation is relatively recent and employed to train motor functions of the upper limbs in the majority of studies.[42,43] However, promising results have been published in recent years regarding improvements in balance, gross motor function and gait.[14–17,20,44,45] There are no guidelines established yet on the ideal protocol for motor improvements, but virtual reality may offer benefits when combined with motor training with or without robotic resources.[44,45] It is likely that the benefits of virtual reality in children with cerebral palsy can be explained by the repetitive training of a task with variability (different situations and levels of difficulty) and feedback offered by the system. While no previous studies have addressed this issue in children with cerebral palsy, two studies involving stroke survivors report interesting results with the combination of motor training of the upper limbs with virtual reality and tDCS.[22,23] The results with and without tDCS were similar, as occurred in the present study. However, an increased effect on certain variables was found, such as a reduction in spasticity.

The main limitations of the present study were the small sample size and the electrode set up employed. Future studies should involve a larger

sample size. For example, considering the effects obtained regarding gait velocity and cadence, an alpha of 0.05 and a power of 80%, 51 children would be required in each study group (experimental and control) to confirm the results of anodal tDCS combined with reality virtual. Moreover, it is likely that no significant differences between groups were found regarding gait pattern, self-care or social function owing to the small sample size. We believe that a larger study could detect specific effects of the intervention. Further studies should involve different tDCS protocols, such as bilateral anodal stimulation of the primary motor cortex for spastic diparesis, as well as different motor training activities to determine the best method for optimising gait in children with cerebral palsy. Bilateral stimulation of the primary motor cortex (C3 and C4) with the cathode electrode positioned in cephalic (for instance Oz) or extracephalic (deltoid muscle) regions should be tested considering the bilateral representation of gait. A third limitation of the present study is related to the topography of the motor impairment. Therefore, future studies should include children with different conditions, such as hemiparesis and quadriparsis.

Clinical messages

- In children with diparetic cerebral palsy, transcranial direct current stimulation combined with virtual reality for gait training led to improvements in gait velocity, cadence, gross motor function and independent mobility.
- Transcranial direct current stimulation increased cortex excitability in comparison with sham stimulation.

Conflict of interest

The authors declare no conflicts of interest.

Ethical approval

Received approval from the Human Research Ethics Committee of the university Nove de Julho, São Paulo, Brazil, under protocol number 69803/2012.

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