Effect of transcranial direct current stimulation on functional walking capacity in children with cerebral palsy

Efeito da estimulação transcraniana por corrente contínua na capacidade funcional de caminhar em crianças com paralisia cerebral

Efecto de la estimulación transcranial por corriente directa sobre la capacidad funcional para caminar en niños con parálisis cerebral

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Caio Aparecido de Paschoal Castro
Master in Health Sciences
Institution: Santa Casa de São Paulo
Address: São Paulo – São Paulo, Brasil
E-mail: caio.paschoal11@hotmail.com

Natália de Almeida Carvalho Duarte
PhD in Human Movement and Rehabilitation
Institution: Universidade Evangélica de Goiás (UNIEVANGÉLICA)
Address: Anápolis – Goiás, Brasil
E-mail: natycarvalho_fisio@hotmail.com

Amanda Queiróga
Graduated in Physiotherapy
Institution: Centro de Neuroestimulação Pediátrica (CENEPE REAB)
Address: São Paulo – São Paulo, Brasil
E-mail: amanda.queiroga@yahoo.com.br

Veronica Unzueta
Graduated in Speech Therapy
Institution: Centro de Neuroestimulação Pediátrica (CENEPE REAB)
Address: São Paulo – São Paulo, Brasil
E-mail: vero.palenqueunzueta@gmail.com

André Luís dos Santos Silva
PhD in Physiotherapy
Institution: Instituto Brasileiro de Fisioterapia Vestibular e Equilíbrio
Address: São Paulo – São Paulo, Brasil
E-mail: fisioterapiavestibular@gmail.com
ABSTRACT
To investigate the effects of a single session of anodal transcranial direct current stimulation (atDCS) over the primary motor cortex (M1) or left temporal cortex (LTC) during treadmill training (TT) on functional walking capacity in children with cerebral palsy (CP). Seventeen children underwent TT combined with tDCS over M1, tDCS over the LTC and sham stimulation. The Six-Minute Walk Test was performed before, immediately after and 20 minutes after each intervention. TT combined with atDCS over the LTC resulted in a better performance in terms of heart rate, respiratory rate and perception of respiratory and physical effort. TT combined with tDCS over M1 and the LTC achieved similar results for gait speed and distance travelled on the test. Anodal tDCS can be considered a promising intervention for functional walking capacity in children with CP.

Keywords: cerebral palsy, child, transcranial direct current stimulation, treadmill training, mobility, physical fitness.
Palavras-chave: paralisia cerebral, criança, estimulação transcraniana por corrente contínua, treinamento em esteira, mobilidade, condicionamento físico.

RESUMEN
Investigar los efectos de una única sesión de estimulación transcranial de corriente directa anódica (tDCS) sobre la corteza motora primaria (M1) o la corteza temporal izquierda (LTC) durante el entrenamiento en tapiz rodante (TT) sobre la capacidad funcional para caminar en niños con parálisis cerebral (PC). Diecisiete niños se sometieron a TT combinado con tDCS en el M1, tDCS en el LTC y estimulación simulada. La prueba de marcha de seis minutos se realizó antes, inmediatamente después y 20 minutos después de cada intervención. El TT combinado con tDCS sobre el LTC dio lugar a un mejor rendimiento en términos de frecuencia cardíaca, frecuencia respiratoria y percepción del esfuerzo respiratorio y físico. El TT combinado con tDCS sobre el M1 y el LTC obtuvo resultados similares para la velocidad de la marcha y la distancia recorrida en la prueba. La tDCS anodal puede considerarse una intervención prometedora para la capacidad funcional de la marcha en niños con parálisis cerebral.

Palabras clave: parálisis cerebral, niño, estimulación transcranial por corriente directa, entrenamiento en cinta rodante, movilidad, acondicionamiento físico.

1 INTRODUCTION

Children and adolescents with cerebral palsy (CP) have lower levels of physical functioning (Verschuren et al., 2016; Verschuren; Takken, 2010). Neuromuscular disorders resulting from brain lesions at an early age have negative repercussions with regards to functional capacity and participation in routine physical activities (Bjornson et al., 2007; Carlon et al., 2013). The Gross Motor Function Classification System (GMFCS) categorizes children with CP on five levels based on self-initiated movements. The physical activity and functional capacity levels defined by this system correlate negatively with motor function (Lauruschkus et al., 2013; Rosenbaum et al., 2007). While children classified on level I can participate in a wide variety of activities, children with greater motor impairment, such as those classified as levels IV and V, have limited options for participating in physical activities (Nooijen et al., 2014; Rosenbaum et al., 2007) [6,7].

Approximately 90% of children with CP have impaired gait due to abnormal cortical excitability, excessive muscle weakness, altered joint kinematics and impaired postural reactions (Grecco et al., 2013a, 2014b). The sum of these neuromotor aspects directly interferes with the ability to participate in physical activities (Butler; Scianni; Ada, 2010; Hjalmarsson et al., 2020).
Low aerobic endurance in this population may be attributed to the diminished recruitment of motor units during dynamic activities, the reduced oxidative capacity of paretic muscles and low overall endurance, with increased energy expenditure during the performance of daily activities and submaximal exercises (Hjalmarsson et al., 2020; Verschuren et al., 2016). These aspects have negative repercussions for functional walking capacity in this population (the maximum distance that the children can walk in a given period of time).

Treatment possibilities for such patients include treadmill training, which is recommended to improve motor control due to the positive impacts on gait speed, muscle strength, postural control and gross motor functions (De Almeida Carvalho Duarte et al., 2014; Grecco et al., 2013b). This therapeutic intervention improves motor learning through cyclic repetition and the activation of brain connectivity areas (Armstrong et al., 2019; Zwicker; Mayson, 2010). Treadmill training can have additional effects on functional walking capacity (Smania et al., 2011; Zwicker; Mayson, 2010).

Another therapeutic resource that has become prominent is transcranial direct current stimulation (tDCS), which is a noninvasive neuromodulatory brain stimulation technique that consists of applying a polarized single-phase low-intensity electrical current to areas of the brain and can either enhance or hinder neuronal depolarization below the application site (Burton et al., 2009; Kurz; Wilson, 2011). Anodal tDCS improves neuronal depolarization and is frequently used for locomotor training, especially when combined with treadmill training. This is a safe neuromodulatory technique that is easy to administer and has minimal adverse effects, which facilitates its use on children and adolescents with CP (Auvichayapat; Auvichayapat, 2011; Bikson et al., 2016; Grecco et al., 2016; Thibaut et al., 2013).

Anodal tDCS over the primary motor cortex combined with treadmill training increases the activation of this brain structure, thereby enhancing the effects of motor training (Grecco et al., 2014c). Specific studies on the effects of anodal tDCS over the primary motor cortex showed promising results with regards to gait, gross motor function and balance in children with spastic CP (Collange Grecco et al., 2015; De Almeida Carvalho Duarte et al., 2014; Grecco et al., 2014b, 2017). Recent studies have analyzed the use of anodal tDCS over the left temporal lobe in adults without brain lesions, targeting the left insular lobe during aerobic training. The justification for this modality is based on the functions of the region, such as pleasure processing (left insula) as well as baroreflex and blood pressure functions (parasympathetic autonomic nervous system).
which may enhance tolerance for physical activity and improve functional capacity (Okano et al., 2015, 2017).

However, no studies were found on the effects of anodal tDCS over the left temporal lobe during treadmill training in children with CP. Similarly, no studies were found comparing the effects of anodal tDCS over the primary motor cortex and left temporal lobe in the pediatric population during treadmill training.

Our hypothesis was that the anodal tDCS over the primary motor cortex would momentarily optimize the effects of treadmill training on gait variables, especially walking speed, whereas anodal tDCS over the left temporal lobe would mainly impact cardiorespiratory aspects during the functional walking capacity test and both interventions would achieve better effects compared to sham stimulation. The aim of the present study was to determine the immediate effects of a session of treadmill training combined with tDCS over the primary motor cortex or left temporal cortex on functional walking capacity (gait speed, distance travelled and cardiorespiratory variables) in children with spastic diplegic CP during the execution of the Six-Minute Walk Test (6MWT) compared to the results obtained with sham stimulation.

2 MATERIALS AND METHODS

Study design: A randomized, sham-controlled, double-blind, crossover, clinical trial was conducted. This study was registered in the Brazilian Registry of Clinical Trials (registration number: RBR-4mw25f) and received approval from the Human Research Ethics Committee of Irmandade da Santa Casa de Misericórdia de São Paulo (certificate number: 3918721). The guardians of the participants signed a statement of informed consent and the participants agreed to participate by signing a term of assent. The children were accompanied by their legal guardians throughout all evaluation and intervention procedures. The evaluation and intervention setting was welcoming and prepared to make the child as comfortable as possible. At any time, the child could enter into contact with the ombudsman, who was an impartial individual that could provide information if the participant or guardian had any questions about the study.
2.1 PARTICIPANTS

Seventeen children with CP were screened at the XXXXXX in the city of XXX, XXX. The inclusion criteria were: a) a diagnosis of spastic cerebral palsy; b) functional classification on Levels I, II or III of the Gross Motor Function Classification System (GMFCS) (PALISANO et al., 1997); c) age between seven and 12 years; d) degree of understanding and cooperation compatible with the execution of the proposed activities; e) statement of informed consent signed by a legal guardian and statement of informed assent signed by the participant. The exclusion criteria were a) having been submitted to surgical procedures or neurolytic block in the 12 months prior to the onset of the training sessions; b) orthopedic deformities with indication for surgery; c) epilepsy; d) metal implants in skull or hearing aids; e) intellectual disorder that would limit the execution of the intellectual activities proposed in the study.

2.2 RANDOMIZATION AND ALLOCATION

Children who met the eligibility criteria were randomly allocated to the three single-session interventions using a block randomization method. Randomization was performed in blocks and stratified based on GMFCS level (I-II or III) (PALISANO et al., 1997). For each stratum, the allocation sequence was generated and the results were placed in sequentially numbered sealed opaque envelopes. After the pre-intervention evaluation, the participant was allocated to one of the interventions by opening an envelope. This process was performed by a member of the team who was not involved in the recruiting or development of the study. Figure 1 displays the flowchart of the study.
2.3 EVALUATIONS

The participants were evaluated before, immediately after and 20 minutes after each of the three interventions. The evaluation consisted of the Six-Minute Walk Test (6MWT) and the measurement of all variables of interest.

2.4 OUTCOMES

The 6MWT was performed following the guidelines of the American Thoracic Society. This test quantifies mobility through the distance in meters travelled in six minutes. The participants were instructed to walk at a self-selected pace without running along a 30-meter track and were permitted to vary the pace and take rest breaks. The participants performed the test using their orthoses and respective walking aids (walkers or crutches), if necessary (Enright, 2003).
At the beginning and end of the test, heart rate (HR), blood pressure (BP), respiratory rate (RR), peripheral oxygen saturation (SpO2) and the psychophysiological sensation of exertion (dyspnea and lower limb muscle fatigue using the ten-point Modified BORG scale) were measured. HR, SpO2 and perceived exertion were also collected in the third minute of the test. Distance walked and speed during the 6MWT were measured using a wireless portable G-Walk inertial sensor (G-Sensor, BTS, Bioengineering SpA, Italy), which furnishes linear acceleration along three orthogonal axes (anteroposterior, mid-lateral and vertical). The G-Sensor is composed of a wireless network of inertial sensors for human motion analysis. Acceleration data were transmitted via Bluetooth to a computer and processed using a proprietary software (BTS G-Studio, version 2.6.12.0). The sensor was connected to a strap and attached over the intervertebral space between the fourth and fifth lumbar vertebrae to capture the gait variables.

2.5 INTERVENTION

Three types of single-session interventions were performed involving treadmill training combined with tDCS (anodal over the primary motor cortex, anodal over the left temporal cortex and sham stimulation) with a one-week wash-out period between interventions. Each session lasted 20 minutes.

**Treadmill training:** Gait training was performed on a Inbramed treadmill (Milenium ATL model, RS, Brazil). The training speed was established based on the child’s performance in each session. The ideal speed was considered the maximum velocity the child was able to walk while performing adequate support of the feet at initial contact and during the entire support phase of gait. The speed was gradually increased in the first two minutes of the session, remained constant for most of the session and gradually decreased in the last two minutes. During training, the children used their habitual braces, which were duly placed by the physiotherapist. The therapist remained behind the participants, facilitating gait training if necessary and ensuring both the safety of the intervention and the best possible movement kinematics. Throughout treadmill training, the therapist in charge also provided verbal commands to the participant to improve the execution of gait (Grecco et al., 2013b, 2014b).

**Transcranial direct current stimulation:** The tDCS device (Soterix Medical Inc., USA) involved two sponge surface (non-metallic) electrodes (5 x 7 cm) moistened in saline solution.
Electrode positioning was defined based on the International 10–20 Electroencephalogram System (Homan; Herman; Purdy, 1987):

a) Anodal tDCS over the primary motor cortex: the anode was positioned over the motor cortex with the central area properly positioned over Cz. The cathode was positioned over the right shoulder;

b) Anodal tDCS over the left temporal cortex: the anode was positioned over the left temporal cortex with the central area properly positioned over T3. The cathode was positioned over the right shoulder;

c) Sham tDCS: electrodes positioned as described for primary motor cortex stimulation.

For active tDCS, the current was gradually increased until reaching 1 mA in 30 seconds, maintained at this intensity during the 20 minutes of treadmill training and gradually diminished in the final 30 seconds. For sham stimulation, the electrodes were positioned and the device was switched on for the first 30 seconds, giving the child the initial sensation of the current; however, no stimulation was administered the remaining time. This is considered a valid control procedure in studies involving tDCS.

2.6 STATISTICAL ANALYSIS

The Shapiro-Wilk test demonstrated normal distribution of the variables. Thus, data were expressed as mean and standard deviation or 95% confidence interval. The effects of anodal tDCS combined with treadmill training were analyzed using repeated-measures analysis of variance followed by Tukey's test for multiple comparisons. The dependent variables were distance travelled, gait speed, HR, RR, oxygen saturation, systolic and diastolic BP, subjective perception of respiratory and physical exertion during the 6MWT. The fixed independent variables were evaluation time (baseline, post-intervention and follow-up) and group (anodal tDCS over the primary motor cortex, anodal tDCS over the left temporal cortex and sham stimulation). A p-value < 0.05 was considered indicative of a statistically significant difference. The effect size (Cohen’s d) was calculated from the differences between the baseline and post-intervention evaluations comparing treadmill training combined with tDCS over the left temporal cortex to the other interventions. The data were organized and tabulated using the SPSS software v. 22.0.
3 RESULTS

A total of 38 children with CP were screened, 17 of whom were eligible and randomly allocated to perform the three interventions. Twenty-one did not meet the inclusion criteria: 11 due to orthopedic deformities, three for being in the postoperative period of surgery, four have having been submitted to neurolytic block (botulinum toxin), one for having a cochlear implant and two declined to participate. The 17 children concluded all the stages of the study (no dropouts).

No moderate or severe adverse effects were observed during the study. Sixteen children reported tolerable tingling during the anodal tDCS session and one child reported no perception of the current during the intervention. No adverse effects were reported by the participants or guardians between sessions. With regard to successful blinding, 14 participants could not correctly state the type of stimulation (active or sham) that they had received at the end of the first intervention phase. After the children had undergone all three interventions, however, 16 could identify the sham tDCS session. Table 1 presents the anthropometric characteristics and functional classification of the children studied as well as the outcome measures at the initial evaluation.

<table>
<thead>
<tr>
<th>Table 1. Anthropometric characteristics, functional classification and outcome measures at initial evaluation.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (female/male)a</td>
</tr>
<tr>
<td>GMFCS (II/III) a</td>
</tr>
<tr>
<td>Age (years) b</td>
</tr>
<tr>
<td>Body mass (kg) b</td>
</tr>
<tr>
<td>Height (cm) b</td>
</tr>
<tr>
<td>Body mass index (kg/m²) b</td>
</tr>
<tr>
<td>Medications (yes/no) a</td>
</tr>
<tr>
<td>Anticonvulsant (yes/no) a</td>
</tr>
<tr>
<td>Muscle relaxant (yes/no) a</td>
</tr>
</tbody>
</table>

a Numbers indicate frequency (n) of children. bData expressed as mean ± standard deviation. GMFCS: Gross Motor Function Classification System. Source: Table of the author.

3.1 OUTCOME MEASURES - SIX-MINUTE WALK TEST

Table 2 displays the mean and standard deviation values for the variables of interest during the 6MWT before, after and 20 minutes after the three interventions (anodal tDCS over the primary motor cortex, anodal tDCS over the left temporal cortex and sham stimulation).
Distance: The distance travelled on the 6MWT was not altered significantly at the evaluation conducted immediately after the intervention sessions. However, a significant difference was found at the evaluation conducted 20 minutes after the end of the intervention sessions. The mean difference in the distance travelled after treadmill training + tDCS of the motor cortex and treadmill training + sham stimulation was 6.2 meters (95% confidence interval [CI]: -6.5 to 3.9; d = 0.08) and after treadmill training + tDCS over the left temporal cortex and treadmill training + sham stimulation was 7.5 meters (95%CI: 2.2 to 12.7; d = 0.09), demonstrating an increase in the distance travelled on the test after active tDCS.

Speed: The administration of active tDCS during treadmill training did not result in a significant difference compared to sham stimulation immediately after the end of the intervention sessions on speed during the execution of the 6MWT. However, the results of the evaluation conducted 20 minutes after the end of sessions demonstrated an increase in speed after tDCS over the primary motor cortex, with a mean difference of 0.03 (95%CI: 0.001 to 0.06; d = 0.18), and after tDCS over the left temporal cortex, with a mean difference of 0.5 (95%CI: 0.02 to 0.09; d = 0.3).

Heart rate: tDCS over the left temporal cortex resulted a lower HR during the execution of the 6MWT at both the evaluations immediately after and 20 minutes after the end of the sessions in comparison to tDCS over the primary motor cortex (mean difference [MD]: -12.4 bpm, 95%CI: -16.8 to -8.0, d = 0.03; and MD: -15.3 bpm, 95%CI: -19.7 to -10.9, d = 0.02) and in comparison to sham stimulation (MD: -14.1, 95%CI: -18.5 to -9.7, d = 0.02; MD: -13.9, 95%CI: -18.3 to -9.5, d = 0.02). Considering the importance of HR recovery (two minutes after the 6MWT), this variable was analyzed statistically. The multiple comparison test revealed no significant difference in HR recovery between tDCS over the motor cortex and sham stimulation (p = 0.793). However, a significantly lower HR two minutes after the 6MWT was found in the group submitted to tDCS over the left temporal cortex compared to both tDCS over the motor cortex (p < 0.001, d = 1.81) and sham stimulation (p < 0.001, d = 1.83). Figure 2 shows the mean and standard deviation values before, immediately after, two minutes after (recovery) the 6MWT and at follow-up considering the three interventions.
Figure 2. Mean and standard deviation HR before, immediately after, two minutes after 6MWT at a follow-up considering three interventions analyzed (treadmill training + tDCS over primary motor cortex, treadmill training + tDCS over left temporal cortex and treadmill training + sham stimulation).

* Significant difference between anodal tDCS over motor cortex and over left temporal cortex. # Significant difference between anodal tDCS over left temporal cortex and sham stimulation.

Source: Image of the author.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Anodal tDCS over primary motor cortex</th>
<th>Anodal tDCS over left temporal cortex</th>
<th>Sham tDCS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
<td>Follow-up</td>
</tr>
<tr>
<td>Distance (m)</td>
<td>222.7(184.0-261.4)</td>
<td>236.2(197.6-274.9)</td>
<td>232.4(192.3-272.6)**</td>
</tr>
<tr>
<td>Speed (m/s)</td>
<td>0.57(0.48-0.67)</td>
<td>0.64(0.52-0.74)</td>
<td>0.62(0.53-0.73)**</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>139.8(133.3-146.3)</td>
<td>142.0(135.9-148.1)</td>
<td>130.1(135.5-149.6)</td>
</tr>
<tr>
<td>RR (bpm)</td>
<td>34.5(32.6-36.0)</td>
<td>33.5(32.2-34.9)</td>
<td>34.6(32.8-36.4)</td>
</tr>
<tr>
<td>SpO2 (%)</td>
<td>98.1(97.8-98.5)</td>
<td>98.4(98.1-98.6)</td>
<td>98.3(98.1-98.5)</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>121.9(116.7-127.1)</td>
<td>121.4(116.3-126.4)</td>
<td>122.1(118.0-126.2)</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>74.0(71.3-76.8)</td>
<td>74.2(71.7-76.7)</td>
<td>74.2(71.4-77.1)</td>
</tr>
<tr>
<td>BORG Fatigue</td>
<td>8.8(8.3-9.4)</td>
<td>9.5(9.2-9.9)</td>
<td>9.1(8.6-9.6)</td>
</tr>
<tr>
<td>BORG Respiratory</td>
<td>8.9(7.2-8.6)</td>
<td>8.4(8.0-8.9)</td>
<td>8.2(7.8-8.7)</td>
</tr>
</tbody>
</table>

tDCS: transcranial direct current stimulation; HR: heart rate, bpm: beats per minute; RR: respiratory rate, bpm: breaths per minute; SpO2: peripheral oxygen saturation; SBP: systolic blood pressure; DBP: diastolic blood pressure. * Significant difference between anodal tDCS over left temporal cortex and sham tDCS. ** Significant difference between anodal tDCS over motor cortex and sham tDCS. # Significant difference between anodal tDCS over left temporal cortex and anodal tDCS over motor cortex.

Source: Table of the author.
Respiratory rate: Specifically, anodal tDCS over the left temporal cortex achieved a better result compared to both stimulation over the motor cortex (MD: -2.8, 95%CI: -4.4 to -1.1, d = 0.56) and sham stimulation (MD: -2.3, 95%CI: -3.9 to -0.7, d = 0.62) at the evaluations after the interventions (p < 0.05 for all analyses).

Peripheral oxygen saturation: No significant difference was found at the evaluations conducted after the three interventions (p > 0.05 for all analyses).

Blood pressure: The analysis showed a difference in the measures at the initial evaluation prior to the intervention between sham stimulation (mean lower systolic BP) and the active stimulations. No differences were found in the measures obtained with anodal tDCS over the motor cortex and sham stimulation (p = 0.612) at the evaluations after the interventions, whereas significant differences were found between anodal tDCS over the motor cortex and left temporal cortex (MD: -8.5, 95%CI: -12.3 to -4.8, p < 0.001, d = 0.64) as well as between tDCS over the left temporal cortex and sham stimulation (MD: -4.7, 95%CI: -8.4 to -0.9, p = 0.010, d = 0.49). The three interventions differed from each other at the follow-up evaluation (p < 0.05 for all analyses). For diastolic BP, analysis of variance revealed no significant difference between interventions.

Perception of exertion: The subjective perception of exertion was measured using the BORG scale. The analysis revealed lower perceived respiratory exertion after tDCS over the left temporal cortex compared to both tDCS over the motor cortex (MD: -1.5, 95%CI: -1.9 to 1.0, p < 0.001, d = 1.58) and sham stimulation (MD: -1.5, 95%CI: -2.0 to -1.1, p < 0.001, d = 1.52). These results were maintained at the follow-up evaluation. No significant differences in the results were found between tDCS over the motor cortex and sham stimulation at any evaluation time (p > 0.05 for all analyses). Likewise, the analysis revealed that the subjective perception of physical exertion was lower after tDCS over the left temporal cortex compared to both tDCS over the motor cortex (MD: -0.9, 95%CI: -1.4 to -0.3, d = 0.88) and sham stimulation (MD: -1.8, 95%CI: -2.4 to -1.3, d = 1.53) (p < 0.001 for all analyses).

4 DISCUSSION

The main objective of the present study was to determine whether a 20-minute session of anodal tDCS over the primary motor cortex and left temporal cortex during treadmill training
would have effects on gait speed, distance travelled and cardiorespiratory variables during the execution of the 6MWT in children with spastic diplegic CP categorized on GMFCS levels II and III. The central hypothesis of the study was that the treadmill training combined with anodal tDCS would have better effects on the performance of children during the execution of the 6MWT compared to sham stimulation, but that these effects would present a certain selectivity related to the area of the brain to which anodal stimulation was administered. Anodal tDCS over the primary motor cortex was believed to have greater effects on gait speed and distance travelled, whereas anodal tDCS over the left temporal cortex would result in greater effects on cardiorespiratory variables, such as HR, RR, blood pressure and the perception of exertion. This hypothesis was formulated considering previous findings described in the literature involving anodal tDCS administered over the primary motor cortex in children with spastic CP and anodal tDCS over the left temporal cortex on physical fitness variables (Montenegro et al., 2011; Okano et al., 2017). However, this hypothesis was only partially confirmed, as anodal tDCS over the left temporal cortex achieved better results for most of the cardiorespiratory variables.

Previous studies on the effects of tDCS in children with spastic CP using mobility as the outcome analyzed the effects of anodal stimulation over the primary motor cortex. Promising results were described in these studies, especially with regards to gait speed and gross motor function (De Almeida Carvalho Duarte et al., 2014; Grecco et al., 2014c, 2014a, 2014b). A study that analyzed the effects of anodal tDCS over the primary motor cortex during 20 minutes of rest (children seated without performing any type of motor training) reported that the children with spastic CP who composed the active group presented an increase in mean gait speed immediately after the application, with loss of this effect 20 minutes after the intervention (Grecco et al., 2014a). In a randomized controlled clinical trial analyzing the effects of ten treadmill training sessions combined with anodal tDCS over the primary motor cortex also in children with spastic CP on GMFCS levels I to III, greater effects on the outcomes, such as the distance walked on the 6MWT and gait speed, were found compared to treadmill training combined with sham stimulation and these results remained at the follow-up evaluation one month after the intervention (Grecco et al., 2014b).

The results of the present investigation are not in complete agreement with previous evidence. No difference in the gait speed and the distance travelled on the 6MWT were found
between the three interventions immediately after application. However, the mean distance travelled 20 minutes after active tDCS (primary motor cortex and left temporal cortex) and gait speed were greater than the values found for sham stimulation. These results hinder a more in-depth discussion on the possible selective effect of the area of the brain stimulated on these mobility variables. However, it is plausible that anodal tDCS can optimize the effects of treadmill training on these variables in children with spastic CP compared to the sham situation. Further studies are needed to continue the analysis of the effects of anodal stimulation over these two important areas of the brain and broaden knowledge on the specific effects obtained with the facilitation of cortical excitability in each area, assisting in individual therapeutic planning for each child.

One of the aspects not analyzed in this study but that could contribute to the understanding of the effect of tDCS over these areas of the brain is the frequency and duration that the child remained at rest during the 6MWT. The execution of this test involves the possibility that the participant may request rest periods, followed by the return to walking until time ends (six minutes). To gain a better understanding of the results, after the statistical analysis, we reviewed the notes of the evaluators and found that the children asked for rest periods more often after tDCS over the primary cortex motor compared to tDCS over the left temporal cortex. Specifically, seven children (three on level II of the GMFCS and four on level III of the GMFCS) needed to rest during the execution of the test after tDCS over the cortex motor, remaining a mean of 86.6 ± 26.0 seconds seated. In contrast, only three children classified on level III of the GMFCS asked to stop and sit during the execution of the 6MWT after tDCS over the left temporal cortex, remaining a mean of 67.1 ± 16.3 seconds seated.

Anodal tDCS over the left temporal cortex is reported to have the potential to increase tolerance to physical activities due to its indirect effects on the parasympathetic and insular systems (Montenegro et al., 2011; Okano et al., 2015). Although previous evidence is related to the effects found in adults and no studies were found addressing the stimulation of this cortex in children with brain lesions, the results of the present study can be considered promising for the physical rehabilitation of children. In a general context, anodal stimulation over the left temporal cortex resulted in the greater control of the cardiorespiratory variables (HR, RR and systolic BP) as well as the perception of physical and respiratory exertion. No differences were found in the means of these variables between tDCS over the motor cortex and sham stimulation. These
results suggest that tDCS over the left temporal cortex can increase tolerance to motor training in children with spastic CP, providing greater possibilities for improving the cardiorespiratory endurance and functional walking capacity of this population during the rehabilitation process.

It has been increasingly clear in the clinical field and scientific literature that children and adolescents with CP have two important aspects that influence the activity and participation: motor control and cardiorespiratory endurance (Bjornson et al., 2007; Franki et al., 2012). Several therapeutic strategies have been used to improve motor control, whereas interventions focused on improving the cardiorespiratory endurance (or training tolerance) are scarce. The greatest difficulty observed in clinical practice refers to the control of cardiorespiratory aspects and perceived exertion. Children have significant difficulty in performing motor training at aerobic levels with relatively low levels of physical exertion, which limits the development of physical fitness (Craig, 2003; Montenegro et al., 2011). If tDCS over the left temporal cortex can actually provide the effects obtained in this study, it may be considered a therapeutic resource to be combined with treadmill training, thereby increasing the possibility of obtaining effects on gait and cardiorespiratory endurance in this population.

The results of the present study must be considered preliminary and no definitive conclusions can be drawn. However, the findings are promising and can assist future studies in broadening knowledge on the specific effects of tDCS administered to different areas of the cerebral cortex. This study has two aspects that can be considered limitations with regards to definitive conclusions: 1) As a crossover study, all design biases were assumed. Additionally, there is always the possibility that the effect of one intervention influences the effect of the subsequent intervention; and 2) the study involved the analysis of a single intervention session for each modality studied. The literature has shown that a single session cannot trigger a significant clinical effect, for which ten treatment sessions (five sessions per week over two consecutive weeks) are needed. Thus, randomized, controlled, parallel, double-blind, clinical trials should be developed with ten treadmill training sessions combined with tDCS over the left temporal cortex, primary motor cortex and sham stimulation.

Based on the immediate effects described in the present study, anodal tDCS over the left temporal cortex and primary motor cortex during treadmill training are promising tools for promoting an improvement in functional walking capacity in children with spastic diplegic CP. TDCS over the left temporal cortex apparently has the potential to influence cardiorespiratory
variables and the perception of exertion during the execution of the 6MWT. The authors emphasize the need for future studies with a larger number of participants and intervention sessions to confirm the results.

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