Research Article
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Effect of a single session of transcranial direct current stimulation combined with virtual reality training on functional mobility in children with cerebral palsy: A randomized, controlled, double-blind trial.

Efeitos de uma única sessão de estimulação transcraniana por corrente contínua associada ao treino de mobilidade com realidade virtual sobre a mobilidade funcional de crianças com paralisia cerebral: ensaio clinico randomizado, controlado, duplo cego.

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Abstract
Introduction:Abnormal postural control in children with cerebral palsy (CP) exerts a negative impact on activities of daily living. The Timed UpandGo (TUG) test is a valid, reliable test for the evaluation of functional mobility in children with CP. Objective:The aim of the present study was to determine the effects of a single session of transcranial direct current stimulation (tDCS) over the primary motor cortex combined with mobility training using a virtual reality system on functional mobility in children with CP. Method: The sample was composed of 12 children with CP aged 4 to 12 years, who were randomly allocated to an experimental group (virtual reality training + active tDCS) and control group (virtual reality training + placebo tDCS). Evaluations involved the TUG test performed 20 minutes before the intervention as well as immediately after the intervention. The paired t-test was used for the intra-group comparisons and both the unpaired t-test and Levene's test were used for the intergroup comparisons, with a p-value < 0.05 indicative of statistical significance. Results: The data were expressed as mean and standard deviation. In the control group, the time needed to complete the TUG was 14.40 ± 5.79 s before the intervention 13.81 ± 5.18 s after the test (p=0.279). In the experimental group, the time needed to complete the TUG went from 15.73 ± 5.77 s before the test to 13.96 ± 5.48 s after the test(p=0.004). However, no statistically significant difference was found in the inter-group analysis (p=0.853). Conclusion: The findings suggest that tDCSfavors an increase in gait velocity in children with cerebral palsy.
Keywords: cerebral palsy, child, physical therapy, cerebral cortex, electrical stimulation, functionality, Timed Up&Go, TUG.

Resumo
Introdução: Controle postural anormal em crianças com paralisia cerebral (PC) exerce um impacto negativo sobre as atividades da vida diária. O teste cronometrado Timed Up and Go (TUG) é um teste válido e confiável para a avaliação da mobilidade funcional em crianças com PC. Objetivo: A finalidade do presente estudo foi determinar os efeitos de uma única sessão de estimulação transcraniana por corrente contínua (ETCC) sobre o córtex motor primário combinado com treinamento de mobilidade usando um sistema de realidade virtual sobre a mobilidade funcional em crianças com PC. Metódo: A amostra foi composta de 12 crianças com PC com idades entre 4 e 12 anos, que foram distribuídos aleatoriamente em um grupo experimental (treinamento de realidade virtual + ETCC ativa) e grupo controle (formação de realidade virtual + ETCC placebo). As avaliações envolveram a TUG realizadas 20 minutos antes da intervenção, bem como imediatamente após a intervenção. O teste t pareado foi utilizado para as comparações intra-grupo e foram utilizados tanto o teste t não pareado e teste de Levene para as comparações entre os grupos, com um valor de p <0,05 indicativo de significância estatística. Resultados: Os dados foram expressos em média e desvio padrão. No grupo controle, o tempo necessário para completar o TUG foi 14,40 ± 5,79 s antes da intervenção e 13,81 ± 5,18 s após o teste (p = 0,279). No grupo experimental, o tempo necessário para completar o TUG foi de 15,73 ± 5,77 s antes do ensaio para 13,96 ± 5,48 s após o teste (p = 0,004). No entanto, não houve diferença estatisticamente significativa foi encontrada na análise inter-grupo (p = 0,853). Conclusão: As descobertas sugerem que ETCC propicia o aumento da velocidade da marcha em crianças com paralisia cerebral.
Palavra chave: paralisia cerebral, crianças, fisioterapia, córtex cerebral, estimulação elétrica, Timed Up&Go, TUG.

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INTRODUCTION

Cerebral palsy (CP) is defined as a group of permanent movement and posture disorders often accompanied by secondary musculoskeletal problems.(1,2)The prevalence rate is 1.5 to 2.5 individuals for every 1000 live births, with minimal differences among western nations.(3)Spastic CPis the most common type. Seventy-eight percent of children with spastic CPexhibit clinical signs, the most classic of which is spastic hypertonia, which encompasses a set of symptoms, such as an increase in deep tendon reflexes, increased muscle tone, tremors, weakness and an abnormal gait pattern.(4)Poor postural control in children with CP exerts a negative impact on the performance of activities of daily living.(5)

The gold standard for rehabilitation for children with CP is intensive physical therapy, which achieves divergent results. A number of techniques have been employed to improve motor control and the gait pattern in such children,(6,7)such as treadmill training as well as mobility and balance training using a virtual reality system. It is important to develop novel therapeutic modalities that can be used in combination with motor training.(8)

Transcranial direct current stimulation (tDCS) is a non-invasive technique that has generated interest among researchers and physiotherapists due to significant improvements achieved in individuals with brain lesions following short periods of cerebral stimulation.(8,9)This low-cost device is easy to administer, is well-tolerated by patients and has minimal adverse effects,(10)making it a promising method when combined with physiotherapeutic modalities that can potentiate neuroplastic changes.(8)

Training with a virtual reality system offers the user a multidimensional, multisensory experience in a virtual environment.(11-13)Video games with virtual reality have been gaining ground in the rehabilitation process, especially in the field of physical therapy.

A number of tools are used to evaluate mobility as well as both static and dynamic balance in children with CP, such as the Timed Up and Go (TUG) test. This widely used, easily understood assessment tool is valid and reliable for the evaluation of functional mobility in children with CP.(14)With the availability of trained professionals for the use of tDCSand virtual reality as a form of motor training, the present investigation employed the TUG test to evaluate the effects of the combined use of these therapeutic modalities on functional mobility in children with CP.

The aim of the present study was to determine the effects of a single session of transcranial direct current stimulation (tDCS) over the primary motor cortex combined with mobility training using a virtual reality system on functional mobility in children with CP.

METHODS

A cross-sectional, randomized, placebo-controlled, double-blind clinical trial was conducted after approval from the Human Research Ethics Committee of University Nove de Julho (Brazil) under process number 69803/2012. The study was conducted in compliance with the ethical standards established by the Declaration of Helsinki and is registered with the Brazilian Registry of Clinical Trials under process number RBR-9B5DH7. All parents/guardians agreed to the participation of the children by signing a statement of informed consent.

The study took place at the Movement Analysis Lab, University Nove de Julho, Sao Paulo, Brazil, from March 2013 to July 2014. Twenty children with CP were recruited from specialized outpatient clinics and the physical therapy clinics of the university. The following were the inclusion criteria: levels I, II of the Gross Motor Function Classification System (GMFCS); independent gait for at least 12 months; age between four and twelve years; and degree of comprehension compatible with the execution of the procedures. The following were the exclusion criteria: history of surgery or neurolytic block in the previous 12 months; orthopedic deformities; epilepsy; metal implants in the skull or hearing aids. All children who met the eligibility criteria (n = 12) were submitted to an initial evaluation and were randomly allocated to an experimental group (virtual reality training combined with active tDCS) or control group (virtual reality training combined with placebo tDCS). Numbered opaque envelopes were employed to ensure the concealment of the allocation. Each envelop contained a card stipulating to which group the child was allocated.

Evaluation

The evaluations were performed on the same day as the training sessions. The entire protocol lasted a maximum of 1.5 hours. The researcher in charge of the evaluationswas blinded to the objectives of the study and did not take part in the interventions. For the evaluation of functional mobility, the TUG test was performed 20 minutes before and immediately after the single session of tDCS(active or placebo) combined with virtual reality training.

The TUGtest quantifies functional mobility based on the time (in seconds) required for an individual to stand up from a standardized chair without arm rests, walk three meters, turn around, walk back to the chair and sit down again. A shorter time indicates better functional ability.17Each child was instructed to perform the test upon the command "go" at a safe, self-selected walking pace as fast as possible without running.The height of the chair was adjusted so that the subject's knees and hips were flexed 90 degrees when sitting with the feet resting on the floor. All children wore regular shoes or braces (ankle-foot orthosis or foot orthosis). Children with level III CP used gait-assistance devices for the test. The task was performed 3 times.(15-17)If the subject "ran," retesting was necessary. The time to complete the task was recorded in seconds.

Intervention

The child first received an explanation of the procedures and remained at rest for 20 minutes. Two raters were in charge of the procedures to ensure blinding and the reliability of the results. Rater 1 was in charge of placing the electrodes and the administration of tDCS (active or placebo). Rater 2 supervised the virtual reality mobility training. Both the child and Rater 2 were blinded to the allocation to the different groups.

tDCS

The intervention consisted of a single session of tDCS using two sponge (non-metallic) electrodes (5 x 5 cm) moistened with saline solution. The anodal electrode was positioned over the primary motor cortex, following the 10-20 International Electroencephalogram System, and the cathode was positioned in the supra-orbital region on the contralateral side.[18] In the experimental group, a 1-mA current was applied over the primary motor cortex for 20 minutes as the children performed the virtual reality mobility training. The device has a knob that allows the operator to control the intensity of the current. 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 children the initial sensation of the 1 mA current, but no stimulation was administered during the rest of the virtual reality training. This is considered a valid control procedure in studies involving tDCS.

Virtual reality mobility training

Mobility training with virtual reality was performed for 20 minutes with simultaneous tDCS (active or placebo). The children used their habitual braces and gait-assistance devices, when necessary. The braces were placed by the physiotherapist and an assessment of the gait-assistance device was performed and adjustments were made when necessary to achieve the proper size.

Mobility training with virtual reality wasperformed using the XBOX 360™ with Kinect™ (motion sensor) for mobility training. The Your Shape: Fitness Evolved 2012™ was selected for aerobic exercises (walking and walking with obstacles). The child was instructed to stand at a distance of two to three meters in front of the motion sensor for the estimate of height and calculation of the body mass index. Training was performed in a specific room of the Human Movement Analysis Laboratory of the university measuring 250 X 400 cm. A screen measuring 200 X 150 cm was projected on the wall and stereo speakers were used to provide adequate visual and auditory stimuli.[19]

Study design

The flowchart for the present randomized, controlled, double-blind, analytical, cross-sectional, clinical trial is presented in Figure 1, in compliance with the CONSORT statement.

Statistical analysis

The Kolmogorov-Simonov test was used to determine whether the data adhered to the Gaussian curve. Parametric variables were expressed as mean and standard deviation values with respective 95% confidence intervals. The paired t-test was used for the intra-group comparisons (before and after intervention). The unpaired t-test was used for the inter-group comparison (virtual reality training with and without tDCS. A p-value< 0.05 was considered indicative of statistical significance. The Statistical Package for the Social Sciences (SPSS v.19.0) was used to organize and tabulate the data.

RESULTS

In the control group, the time needed to complete the TUG was 14.40 ± 5.79 s before the intervention

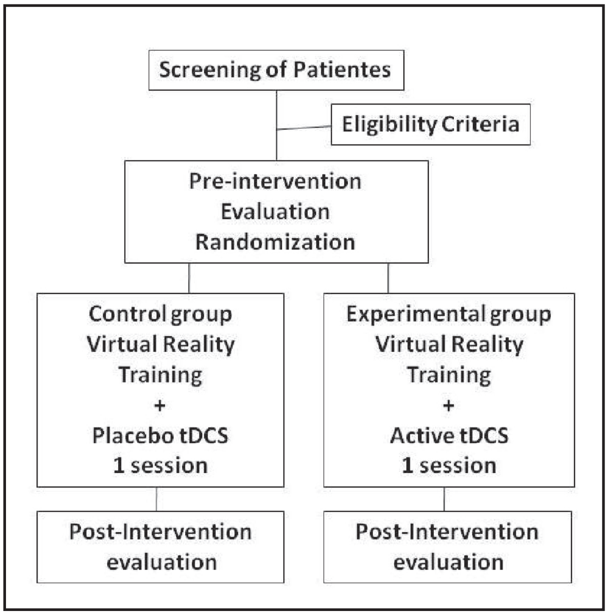

Figure 1. Flowchart of study
Legend: tDCS – transcranial direct current stimulation over primary motor cortex

Table 1. Mean and standard deviation values for time in seconds needed to complete the TUG test before and immediately following the intervention

	Before	After	p-value
Control Group	14.40 ± 5.79	13.81 ± 5.18	0.279
Experimental Group	15.73 ± 5.77	13.96 ± 5.48	0.004

13.81 ± 5.18 s after the test (p = 0.279). In the experimental group, the time needed to complete the TUG went from 15.73 ± 5.77 s before the test to 13.96 ± 5.48 s after the test (p = 0.004)(Table 1). However, no statistically significant difference was found in the inter-group analysis (p = 0.853).

DISCUSSION

The main finding of the present study was that tDCS seems to favor an increase in gait velocity in children with CP, as demonstrated by the faster TUG test after the intervention in the experimental group.

In a study by Williams et al.,[16] time was recorded from the moment the child left the seat rather than on the instruction "go" and stopped as soon as the child's bottom touched the seat. Thus, only the time of movement was measured. However, the TUG allows the evaluation of basic mobilityand includes a set of movements, not just walking time. In the present study, the original method proposed by Podsiadlo and Richardson[15]was employed to record the time and represent the functional ability. The same method was also used by Habib and Westcott.[20]Moreover, the test was performed three times during each evaluation to increase the reliability of the results, as proposed in the literature.

Iatridou et al.[21]determined the reliability of the TUG in 20 children with CP. The intraclass correlation coefficient of the three measures was 0.998(p< 0.001), demonstrating a very low degree of variation. In a study involving 26 children with CP classified on Levels I, II and II, Gan et al.[22]report the following mean times for three performances of the TUG: Level I:8.4 ± 1.2 seconds; Level II: 13.2 ± 4.6 seconds; Level III 50.3 ± 38.4 seconds; and Levels I, II and III: 26 ± 30.4 seconds.

In the present investigation, a significant difference in time on the TUG was only found in the intra-group analysis of the experimental group, which is in agreement with data described in the literature.Tarakci et al.[5]conducted a study involving children with CP using a 40-minute training protocol with the aid of Nintendo Wi™ twice a week for 12 weeks and found a significant mean reduction in the time needed to complete the TUG test from 18.26 ± 4.22 seconds to 14.57 ± 5.39 seconds.

In a cross-sectional study involving 35 children classified on Levels I, II and III of the GMFCS, Chrysagis et al[14]investigated the correlation and validation of different functional evaluation tests. The authors found a strong correlation between the Gross Motor Function Measure-88 (dimensions D and E) and the TUG, for which mean times were 18.34 ± 9.66 seconds for all groups, 10.00 ± 2.05 seconds for Level I, 16.59 ± 7.14 seconds for Level II and 27.55 ± 9.05 seconds for Level III.

In a cross-sectional study involving 39 children with CP, Maanum et al.[2]employed the GMFCS, Functional Mobility Scale, Six-Minute Walk Test and TUG test. Following multivariate regression analysis, the TUGwas found to be a strong predictor of walking capacity in adolescents with CP and was strongly correlated with the Six-Minute Walk Test.

Katz et al.[23]compared the TUG results of children having suffered head trauma (n=15),children with CP(n=15) and children with typical development (n=30) and found longer times need to complete the task among the children with brain lesions (head trauma: 9.4± 3.0 seconds; CP: 9.8± 3.6 seconds) in comparison to those with typical development (5.8± 3.6 seconds).In a five-week clinical trial involving 10 children with CP allocated to an experimental group that received instructions to perform exercises at home (n = 5) and a control group that underwent conventional physical therapy (n = 5), Salem and Godwin[24]found a significant reduction in the time needed to complete the TUG in the experimental group.

In a study involving 19 children with CP and 19 children with typical development, Calley et al.[25]report that the TUG test has a high degree of test-retest reliability. The children with CP required a longer time to complete the test than those with typical development. Moreover, a weak correlation was found between the TUG and the Pediatric Activity Card Sort, whereas a moderate negative correlation was found between the TUG and Six-Minute Walk Test.

In a study involving 13 children with CP submitted to a training protocol and evaluated on four separate occasions, McNee et al.[26]found no significant intra-group differences in the time required to complete the TUG test among any of the evaluations.

CONCLUSION

The findings of the present study suggest that tDCS favors an increase in gait velocity in children with cerebral palsy.

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