

Case Study

Transcranial Direct Current Stimulation Combined with Treadmill Gait Training in Delayed Neuro-psychomotor Development

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Abstract. [Purpose] The aim of the present study was to describe the results of transcranial direct current stimulation combined with treadmill training in a child with delayed neuro-psychomotor development. [Subject and Methods] Transcranial direct current stimulation (intensity: 1 mA) was applied over the primary motor cortex for 20 minutes during simultaneous treadmill training (2.5 km/h) in ten sessions. [Results] Clinically significant improvement was found in motor development (fine motor subscale, 23 to 25; gross motor subscale, 32 to 41). Reductions in mean oscillation of the center of pressure were found in the anteroposterior (239.2 to 146.5 mm) and mediolateral (177.4 to 149.2 mm) directions. Increases occurred in cadence (106 to 123 steps/minute), step length (0.16 to 0.23 m), step width (0.09 to 0.14 m) and gait velocity with support (0.3 to 0.7 m/s). [Conclusion] After treatment, the child was able to initiate the standing position for the first time and walk without support.

Key words: Child, Gait, Motor cortex, Electrical stimulation

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INTRODUCTION

Rehabilitation in children with delayed neuro-psychomotor development has been the focus of a number of scientific studies^{1, 2)}. When such delays are caused by a neurological lesion, the rehabilitation team seeks methods to train subjects in specific tasks with the aim of optimizing the reorganization of the cerebral cortex and improving motor skills. In some cases, motor improvement reaches a plateau during therapy, with a reduction in or even an absence of further motor gains. Thus, novel interventions have been investigated for the pediatric population with the aim of maximizing motor improvement during therapy.

A number of studies have demonstrated the positive effects of treadmill training in children with gait impairment^{1, 3, 4)}. Despite the small amount of evidence regarding the use of treadmill training on children under six years of age, systematic reviews have reported encouraging results, with improvements in gait velocity, muscle strength and gross motor function¹⁾.

Although motor training alone is effective in improving motor function, recent evidence suggests that children with decreased excitability of the motor cortex exhibit poorer motor development⁵⁾. In this context, the use of techniques that can enhance cortical excitability in a noninvasive manner, such as the use of noninvasive brain stimulation (NIBS), may improve outcomes in children undergoing motor rehabilitation. Noninvasive brain stimulation has been recently explored for motor rehabilitation in subjects with brain lesions⁶⁾. Transcranial direct current stimulation (tDCS) is a noninvasive brain stimulation method that employs a weak electrical current through the scalp to modulate the excitability of underlying cortical areas⁶⁻⁸⁾. During tDCS, the current flows from the electrodes and penetrates the skull, reaching the cortex. Although most of the current dissipates in other tissues between the skin and brain, a sufficient amount reaches the cortical structures, altering the membrane potential of the cells located in this region^{9, 10)}. Cortical modulation is dependent on the polarity of the current. tDCS allows two types of stimulation: anodal stimulation, which increases cortical excitability and facilitates the depolarization of the neuronal membrane, or cathodal stimulation, which has an inhibitory effect, with the hyperpolarization of the neuronal membrane^{11, 12)}.

tDCS is a portable, low-cost alternative therapy with considerable potential to optimize motor learning in the neurorehabilitation process. In a recent study reviewing

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the use of NIBS for motor recovery in adults, the authors concluded that use of NIBS is consistently associated with significant motor improvements in stroke patients¹³. However, follow-up of such studies has been limited, and testing in other populations, such as children, is lacking. The effects of tDCS may be related to an improvement in the magnitude or retention of the effects⁷. Most studies have explored the use of NIBS for the rehabilitation of the upper limbs alone, whereas few studies have tested the method on the lower limbs. A study by Kaski et al.¹⁴ involving the use of tDCS found that anodal stimulation over the primary motor cortex (M1) induced changes in motor cortex excitability relating to the lower limbs, thereby improving gait. These results encourage the use of tDCS on motor and premotor areas to improve musculoskeletal control in patients with neurological injuries for gains in gait performance¹⁴. While few studies have tested the use of tDCS on children, good tolerance and minimal adverse effects have been reported^{11, 15}.

The aim of the present study was to explore the feasibility and preliminary results of anodal stimulation of M1 combined with gait training in a young child with delayed neuro-psychomotor development and impairment in the acquisition of gait without support. The hypothesis was that the use of the two techniques would have a synergistic effect, improving gains in motor function. We also hypothesized that this intervention was feasible and associated with only minor adverse effects.

SUBJECT AND METHODS

Description of case

The present case involved a female child aged three years and eight months (height, 105 cm; weight, 15 kg) with a diagnosis of delayed neuro-psychomotor development. The child had been born through cesarean section at a gestational age of 38.5 weeks with a body mass, stature and head circumference within the standards of normality and Apgar scores of 8 (1st minute) and 9 (9th minute). During the first months of life, she exhibited hypotonia and global hypoactivity, with a consequent delay in neuro-psychomotor development. Resonance imaging of the brain and spine at one year and five months of age led to the diagnosis of Arnold-Chiari I malformation, with cervical (C5–C7) and thoracolumbar (T10–L1) hydrosyringomyelia. The child was subjected to decompression surgery of the posterior fossa. The neurosurgical procedures was performed with another neurosurgical team.

One month following the procedure, the patient exhibited excessive sleepiness and was hospitalized, unconscious, with spinal fluid accumulation and compression of the posterior fossa treated with a cystoperitoneal shunt. Cranial and spinal resonance imaging revealed the maintenance of preoperative neurological abnormalities and a significant reduction in the thickness of the parieto-occipital white matter (Figs. 1A and 1B).

A physical exam revealed hypotonia of the trunk and a global lack of motor coordination. The child acquired cervical control at six months of age, sat up without support at

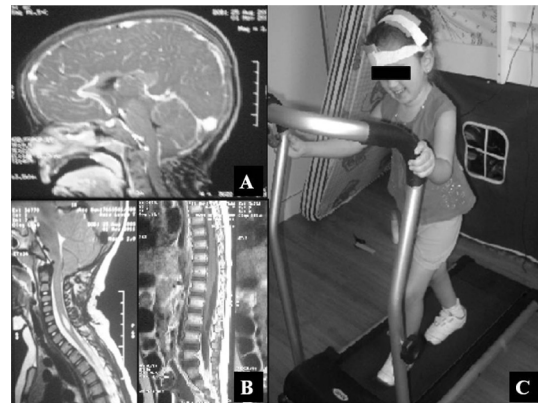


Fig. 1. Postoperative brain (1A) and cervical spine (1B) magnetic resonance imaging. Photograph of applying tDCS during treadmill training (1C).

eight months, rolled over at 12 months and could stand with support at 14 months of age. Gait with support (triangular walker) was achieved at 28 months (2 years and 4 months of age). The child has impairment of the upper limbs, with slow, uncoordinated reaching and gripping movements. She also does not pronounce words.

While the patient exhibited a gradual improvement in neuro-psychomotor development as determined using the Bayley Scales of Infant and Toddler Development¹⁶ (applied every four months since six months of age), neuro-psychomotor stabilization occurred at the age of two years and six months, with few motor gains despite intensive motor training. The only gain observed with motor training was an increase in gait speed with support (0.2 m/s) following the implementation of treadmill training without body weight support. Treadmill training was initiated when the child was three years of age and has been performed in five weekly sessions of physical therapy, with the velocity determined by the child's tolerance (2.5 km/h).

To ensure the observation of any side effects from the noninvasive brain stimulation protocol, the child underwent magnetic resonance imaging (MRI) of the cranium, electroencephalography (EEG) and a neuropsychological evaluation before and two months after the intervention. The second MRI and EEG evaluation revealed no changes, with the maintenance of the neurological patterns seen prior to the protocol. The neuropsychological evaluation was performed blindly using the Griffiths Mental Development Scale¹⁷ for ages two to eight years. Prior to the intervention, the child's development score suggested a mental age of 15.8 months, with the maintenance of this result two months following the protocol. These results suggest no worsening in the child's neurological status following the proposed protocol.

The present study was complied with the principles of the Declaration of Helsinki and the Regulating Norms and Guidelines for Research Involving Human Subjects formulated by the Brazilian National Health Council, Ministry of Health, established in October 1996. The present study received approval from the Human Research Ethics Commit-

tee of the Universidade de Nove de Julho, São Paulo, Brazil, under protocol number 69803/2012. The guardians agreed to participation in the study and the use of the images presented herein by signing a statement of informed consent.

Description of the intervention

After a discerning evaluation of neurological status, noninvasive cerebral stimulation was initiated when the child was three years and eight months of age. Stimulation was performed with a tDCS device (Soterix Medical Inc.) using two sponge surface electrodes (5–5 cm) moistened with saline solution. tDCS was applied with an intensity of 1 mA over the primary motor cortex. The electrodes were placed with the anode positioned over C3 (international 10–20 electroencephalography system)¹⁸⁾ corresponding to the primary motor cortex, and the cathode positioned in the supraorbital region contralateral to the anode⁷⁾. Ten consecutive tDCS sessions (Monday to Friday) were performed with stimulation of the right and left hemispheres. tDCS was applied during treadmill training for 20 minutes per session. The electrodes were placed with the child seated. The child was then positioned on the treadmill and stimulation was initiated together with the onset of treadmill training.

The primary motor cortex was stimulated during repetitive gait training to reinforce motor learning during the phases of the gait cycle. It should be stressed that the child had already performed treadmill training in 20-minute sessions five times a week and was completely adapted to the procedure. The child habitually trained at a velocity of 2.5 km/h (velocity increased and reduced in the initial and final two minutes, respectively), which was a speed at which the child was comfortable, with no signs of muscle or cardiopulmonary overload. This velocity had been increased over the previous eight months of treadmill training and was maintained throughout the tDCS protocol. The child held onto the support bars of the treadmill, and the physiotherapist remained alongside the child. Treadmill training was performed without body weight support or inclination of the treadmill.

Outcome measures

The child was evaluated by a physiotherapist who was blinded to the objectives and procedures of the study. Four evaluations were carried out: 1) one month prior to the intervention, 2) one week prior to the evaluation, 3) one week after the intervention, and 4) two months after the intervention. The Bayley Scales of Infant and Toddler Development (Third Edition) were used to determine changes in neuro-psychomotor development and to evaluate global alterations in the child. Although the Bayley Scales were not developed for short-term applications, they were selected due to their known validity in the assessment of developmental delays. Furthermore, these scales had been employed throughout the child's rehabilitation process from the first year of life. The scales were applied one month and one week before the implementation of the protocol, with no changes observed in this period. These evaluations were performed to determine that the possible changes stemmed from the protocol

employed and were not the result of natural learning or previous treatments.

Spatiotemporal gait variables were evaluated in a movement analysis laboratory using a SMART-D 140[®] system (BTS Engineering) with eight cameras sensitive to infrared light and a SMART-D INTEGRATED WORKSTATION[®] with 32 analog channels. This analysis was performed with the child wearing a swimsuit. Reflective markers were placed on the skin at anatomic points based on the simple Davis biomechanical model¹⁹⁾. Using her habitual walker, the child was positioned at one end of the laboratory and was called by her mother to walk on a demarcated track measuring three meters in width by five meters in length.

A force plate (Kistler 9286BA) was used for the assessment of static balance, allowing stabilometric analysis with the record of oscillations of the center of pressure in the anteroposterior and mediolateral directions. The reading was performed for 30 seconds. The child was placed on the platform using her walker for support, which was positioned off the platform. A drawing was positioned at the height of the glabellum at a distance of one meter. The child was instructed to look at the figure, but did not remain with her gaze fixed due to difficulties in concentration stemming from her age.

The gait and stabilometric analyses were performed twice. For each gait analysis, the child walked along the track three times, with only the second reading used for analysis. In Evaluation 4, the child was able to walk without support. Thus, the gait and stabilometric analyses during this evaluation were performed as described above, but without the support of the walker.

Description of outcomes

The treatment was well tolerated, with no signs of discomfort during the sessions. Table 1 displays the results of the four evaluations. Although this is the report of a single case and statistical analysis of motor performance was not possible, we measured and report changes with regard to gross motor development, spatiotemporal gait variables (increased gait velocity and cadence) and static balance (decreased anteroposterior oscillation). The child began to walk without support in the eighth session and was capable of walking two meters without support (10 consecutive steps) in Evaluation 3. In Evaluation 4 (two months after the end of the protocol), the child was walking independently and without support. Her gait velocity remained below the expected velocity for her age, but the gains were considered significant by the rehabilitation team and her family. The child exhibited frequent falls, which were attributed to gait immaturity and postural instability still present in Evaluation 4. Figure 2 shows the evolution of the child with regard to motor development, walking speed and oscillation of the center of pressure.

Specifically with regard to gross motor scale after the protocol (Evaluation 3), the child was able to perform activities involving the support of her own weight for a few seconds without assistance, crawl at least five meters, stand up with coordinated movements using support, walk in a coordinated pattern and alternating steps, walk sideways

Table 1. Results before and after transcranial direct current stimulation in combination with treadmill training

	Evaluation 1	Evaluation 2	Evaluation 3	Evaluation 4
Bayley Scales of Infant and Toddler Development				
Cognitive subscale	20	21 (5.0%)	28 (40.0%)	31 (55.0%)
Receptive communication subscale	15	15 (0%)	15 (0%)	16 (6.6%)
Expressive communication subscale	8	8 (0%)	8 (0%)	8 (0%)
Fine motor subscale	22	23 (4.5%)	25 (13.6%)	28 (27.2%)
Gross motor subscale	32	32 (0%)	41 (28.1%)	48 (50.0%)
Oscillation from center of pressure				
Anteroposterior (mm)*	256.7	239.2 (-6.8%)	177.4 (-30.8%)	153.2 (-40.3%)
Mediolateral (mm)*	217.3	146.5 (-32.5%)	149.2 (-31.3%)	139.9 (-36.0%)
Spatiotemporal gait parameters				
Cadence (steps/minute)	112	106 (-5.3%)	123 (9.8%)	142 (26.7%)
Step length (m)	0.14	0.16 (14.2%)	0.23 (64.2%)	0.33 (135.7%)
Step width (m)	0.10	0.09 (-10%)	0.14 (40.0%)	0.17 (70.0%)
Mean velocity (m/s)	0.3	0.3 (0%)	0.7 (133%)	1.1 (266%)

mm: millimeters; m, meters; s, seconds. * Values expressed as mean. (%) The values in parentheses express the percentage improvement compared with evaluation 1.

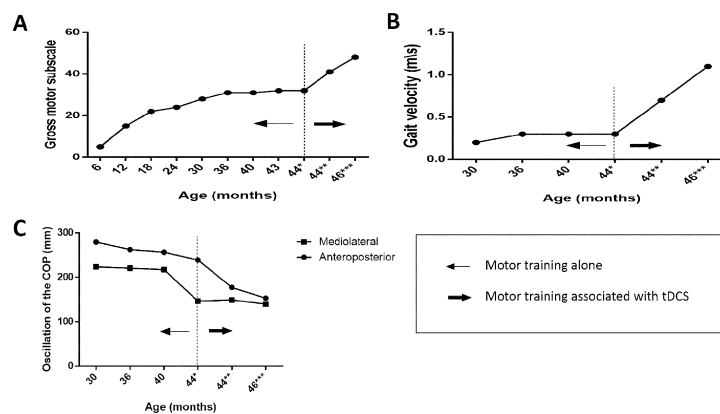


Fig. 2. Evolution curves of the child; A) motor development curve (6–46 months), B) gait speed curve (36–46 months), C) curve for the oscillation of the center of pressure (36–46 months).

*Evaluation 2 (before intervention); **Evaluation 3 (one week after intervention); ***Evaluation 4 (two months after intervention)

with coordination, stand alone for a few seconds, and walk at least three steps without support, but with little coordination (items 33, 34, 35, 37, 38, 39, 40, 41, and 42). In the fourth evaluation, the child was able to perform activities such as throwing a ball without support, crouching with balance, going up and down three steps with support, and walking sideways and forward for at least five meters without support (items 43, 44, 46, 47, 48, 53, and 56). On the fine motor subscale, changes were observed in activities such as moving objects in the midline, raising a cup by the handle, grasping a pencil, making spontaneous scribbles and stacking at least two blocks (items 23, 25, 28, 30, and 31).

The child also showed changes on the cognitive scale regarding the following activities: eyes tracking an object, manipulation of objects, banging in play, searching for fallen objects, manipulating a bell and looking at it with

interest, pulling a cloth to get an object, and picking up objects (items 23, 24, 25, 26, 27, 28, 29, 30, 33, 34). Many of the cognitive changes after the protocol involved motor actions. The authors believe that these changes were related to changes in motor skills. However, it is not possible to make this connection in a report of a specific case.

DISCUSSION

The present case report demonstrates that tDCS combined with motor training led to an improvement in motor gains in a child in a prolonged rehabilitation program during which reduced gains occurred with motor therapy alone. Moreover, tDCS combined with motor training proved feasible for this child and was associated with only mild adverse effects.

The first important point to discuss is the rationale for combining tDCS with motor training. It has been shown that, when tDCS is used properly, a significant amount of current reaches the cortex²⁰, inducing changes in neural excitability that affect local plasticity²¹. The effects of tDCS depend on the location and polarity of the electrodes. Anodal stimulation applied over the primary motor cortex increases the excitability of this region of the brain⁸. Our rationale was to induce changes in motor cortex excitability that would result in the optimization of motor training. Indeed, the effects of tDCS on motor consolidation are evidenced by both the magnitude of motor learning and long-term retention⁷.

Most studies evaluating the effects of tDCS for the enhancement of motor learning have involved upper limb training. Only one previous study was found that analyzed the effect of tDCS on gait performance. Kaski et al.¹⁴ evaluated the use of tDCS applied to the primary motor cortex (bi-hemispheric; 2 mA for 15 minutes at rest) followed by gait training on a moving platform in 30 healthy adults. The group that received active tDCS exhibited an increase in gait speed, suggesting better adaptation of the locomotion apparatus. While the intervention protocol was different in the case reported herein and the child needed a gait-assistance device (walker), the results are also encouraging. The child exhibited a clinical improvement in gait speed (from 0.3 m/s before intervention to 0.7 m/s one week after intervention and 1.1 m/s two months after the protocol) even with the use of a walker (the evaluations before and one week after the intervention were performed with a walker). It should be addressed that the child had already walked independently using a walker for 16 months, with reduced motor improvement. After the intervention, she was able to walk short distances without support. The learning curve of this child before and after the intervention was plotted to show the changes in the slope (Fig. 2).

Another important point to emphasize is that, when tDCS was combined with a therapy that had reached a plateau, further improvement was observed. This finding suggests that the lack of improvement after extensive training may be due to the exhaustion of the mechanisms induced by motor training alone and that further improvement is possible when combined with a therapy that can increase excitability in neural networks, such as tDCS. The improvement observed after the introduction of tDCS was similar to initial gains that are observed in children undergoing therapy. Randomized, controlled studies involving children with cerebral palsy report an improvement in gait speed of between 0.05 and 0.12 m/s with training protocols ranging from two to 12 weeks^{22, 23}. In the present case, the child exhibited an improvement of 0.4 m/s after two weeks of intervention and further improvement of 0.9 m/s two months after the end of the protocol.

An interesting finding was the reduction in the oscillation of the center of pressure, especially in the anteroposterior direction. Stabilometric analysis is one of the most reliable ways to assess static balance and provides valid information on the oscillation of the center of pressure³. This assessment was included in the present case due to the

fact that postural stability is a well-defined prerequisite for motor development in children. This parameter is related to the complex task of maintaining the center of gravity within the support base of the body²⁴ and is dependent on the integration of sensory and proprioceptive information, the commands of which are triggered in the central nervous system and stem from neuromuscular responses^{3, 24}. Thus, the authors set out to determine whether an increase in cortical excitability in M1 would exert a positive influence on motor processing at the cortical level and neuromuscular responses, leading to improved postural stability. While no conclusion can be drawn based on this slight reduction in the oscillation of the center of pressure due to the fact that the present study is merely a case report, this is an interesting aspect for investigation in further studies involving tDCS on children.

Another important result of this case report was the tolerance to treatment. Although a number of studies conducted with adults report minimal adverse effects⁶, only few studies have addressed the use of tDCS on children^{11, 15} and none have analyzed a tDCS protocol in combination with the training of motor tasks in young children. It is important to consider the safety of tDCS in children, as there are differences between children and adults with regard to important factors that affect the flow of the current through the brain, such as skull thickness and volume of cerebrospinal fluid. Mattai et al.¹⁵ analyzed tolerance to tDCS in children with schizophrenia in early childhood and found good tolerance when the technique was performed with 2 mA for 20 minutes, with no severe adverse side effects. A computational modeling study showed that the intensity of the current with conventional tDCS is twofold greater in 12 year-olds with typical development in comparison with adults, and the authors suggest that parameters considered acceptable for adults need to be adjusted for children²⁵. Thus, the decision was made in the present study to perform tDCS with an intensity of 1 mA, which is half of that conventionally used on adults for similar rehabilitation protocols.

EEG evaluations were performed prior to the intervention as well as one week after the end of the 10-session protocol. The exams were analyzed by a neurologist who was blinded to the procedures, and no changes were found. To investigate adverse effects with regard to neuropsychological and cognitive aspects, specific evaluations were carried out by a neuropsychologist with ample experience in the field. While there are clear difficulties in the assessment of a child under four years of age who does not talk, no negative changes were observed. It should also be stressed that, although such data are not particularly reliable, the reports of family members were very encouraging.

There are some limitations that need to be addressed in this case report. Conclusions regarding the efficacy of combined treatment are limited due to the case report design. However, in this specific case, the tDCS protocol combined with treadmill training demonstrated additional beneficial effects in a child for whom gains had been reduced in the months prior to tDCS. While spontaneous improvement in the present case report is possible, the magnitude of the

changes in motor development and postural control and the acquisition of independent gait for short distances (along with the lack of improvement with gait training alone) suggest that the combination of tDCS and treadmill training made an important contribution to the positive motor acquisitions observed. This case report provides useful initial data for designing randomized, controlled trials.

A potential mechanism that can explain the large effect observed in this study is that tDCS could have unmasked motor-related neural circuits that may have been partially blocked because of the child's neurological condition, thereby making it possible to activate these circuits with treadmill training. Further controlled studies assessing neurophysiological changes associated with behavioral effects are necessary to provide further insight and develop this potential novel approach for children with delayed motor development.

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