Immediate effect of transcranial direct current stimulation combined with functional electrical stimulation on activity of the tibialis anterior muscle and balance of individuals with hemiparesis stemming from a stroke

ALINE MARINA ALVES FRUHAUF, MS, PT1*, FABIANO POLITTI, PhD, PT1, SIMONE DAL CORSO, PhD, PT1, GLÁUCIO CARNEIRO COSTA, MS, PT1, AMANDA DA CONCEIÇÃO TEODÓSIO, MS, PT1, SORAIA MICAELA SILVA, PhD, PT1, JOÃO CARLOS FERRARI CORRÊA, PhD, PT1, FERNANDA ISHIDA CORRÊA, PhD, PT1

1) Postgraduate Program in Rehabilitation Sciences, University Nove de Julho: Rua Adolpho Pinto 109, Barra Funda, São Paulo, Brazil

Abstract. [Purpose] The aim of the present study was to evaluate the immediate effects of transcranial direct current stimulation (tDCS) and functional electrical stimulation (FES) on activity of the tibialis anterior muscle (TA) and static balance of individuals with hemiparesis stemming from stroke. [Subjects and Methods] A randomized, double-blind, crossover, clinical trial conducted with 30 individuals with chronic post-stroke hemiparesis. Median frequency of electrical activity of the TA were determined using electromyography in five contractions concentrics and Static balance (body sway velocity and frequency), both before and immediately after the intervention. The participants were submitted to four 20-minute intervention protocols with 48-hour interval: anodal tDCS + sham FES; sham tDCS + active FES; anodal tDCS + active FES and sham tDCS + sham FES. Anodal tDCS was administered over C3 or C4, the cathode was positioned in the supraorbital region on the contralateral side and FES was administered to the affected TA. [Results] No significant differences among the protocols were found regarding electrical activity of the TA and static balance. [Conclusion] The results demonstrate that tDCS alone or in combination with FES had no immediate effect on electrical activity of the TA and static balance of the 30 individuals analyzed. Key words: Hemiparesis, Transcranial direct current stimulation, Functional electrical stimulation

INTRODUCTION

According to the World Health Organization, stroke is the third most common cause of chronic disability in developing countries1. Hemiparesis (muscle weakness on one side of the body) is one of the classic manifestations of a stroke event and commonly affects the upper limb flexors and lower limb extensors2.

In the lower limb, the characteristic “foot drop” that occurs with this condition results from a reduction in the strength of the tibialis anterior (TA) muscle as well as spasticity of the plantar flexor musculature (triceps surae)3, which diminishes contact between the heel and ground, thereby affecting balance and locomotion and exerting a negative impact on functional independence5.

Functional electrical stimulation (FES) has been used for the treatment of motor impairment in patients with hemiparesis...
This method consists of the depolarization of the intact motor neuron to initiate and facilitate the voluntary contraction of paretic or paralyzed muscles to produce functional movement. Moreover, transcranial direct current stimulation (tDCS) is a new therapeutic modality used for the modulation of the central nervous system, which consists of the administration of a monophasic electrical current through two electrodes (anode and cathode) positioned strategically on the skull based on the area of the brain one wishes to stimulate.

In animal experimental models with cerebral ischemia, anodal tDCS administered over the injured hemisphere is reported to have significant effects related to the recovery of motor function. Positive effects regarding motor recovery have also been reported in experimental studies in humans. Cross-sectional study of Sohn et al. found an immediate significant increase in quadriceps strength and static postural stability following tDCS over the primary motor cortex of 11 individuals with hemiparesis. In the same direction, Madhavan et al. found an improvement in voluntary control of the ankle in nine patients with hemiparesis during 15 minutes of anodal tDCS over the injured primary motor cortex when combined with ankle motor training. Thus, it is supposed tDCS can modulate spontaneous neuronal excitability, promoting either the hyperpolarization or hypopolarization of the resting potential of the neuronal membrane, thereby facilitating the arrival of peripheral information stemming from the therapeutic process.

The largest benefit of tDCS may come from its use in combination with different forms of physical therapy, as this method is a way to modulate the activity of the cerebral cortex, opening a path for the enhancement and prolongation of the functional gains provided by physical therapy. It can therefore be said that stimulation evokes a change in the dysfunctional excitability pattern so that physical therapy can model the functional pattern of cortex activity with the activation of specific neural networks.

The aim of the present study was to evaluate the immediate effect of a single session of anodal tDCS combined with FES on electrical activity of the TA muscle and static balance in patients with hemiparesis stemming from a stroke. The hypothesis is that tDCS can potentiate the activity of the TA muscle promoted by the administration of FES, especially in the chronic phase of the disease (when it has already been installed in the mechanisms of maladaptive plasticity).

**SUBJECTS AND METHODS**

A randomized, sham-controlled, double-blind (patients and examiner), clinical trial was conducted following approval from the Human Research Ethics Committee of University under process number 767.866/2014. This study is registered with the International Clinical Trials Registry (ClinicalTrials.gov –NCT02389608) and all participants signed a statement of informed consent. The study was conducted in January 2016 at the Integrated Movement Analysis Lab of University Nove de Julho.

The 30 subjects (twenty-three men and seven women) who participated in this study were recruited from the physiotherapy clinic of the University Nove de Julho. The inclusion criterion was a diagnosis of hemiparesis stemming from a stroke. The exclusion criteria were a score of less than 11 points on the Mini Mental State Examination, reduced ankle mobility due to a history of fracture or the use of an ankle fixator, non-reducible foot drop, TA muscle strength <Grade 1 on the Kendall scale, self-declared severe vision impairment, contraindication for use of tDCS (history of seizure or recurrent epilepsy, brain tumor at stimulation site and metallic implants in skull), skin infection at the administration site for tDCS or FES, anesthesia or hyperesthesia at FES administration site, a diagnosis of deep vein thrombosis, Alzheimer’s patients, diagnosis of degenerative disease or polyneuropathy.

The tDCS was performed using the Tct Research 1 CH tDSC Simulator model 101, which measures 14.0 × 11.5 × 3.5 cm, weighs 350 g and is fed by two alkaline 9-volt batteries. The device has a high-precision microprocessor and a controlled direct electrical current. Stimulation was achieved with two sponge (non-metallic) electrodes moistened in saline solution (cathode: 5 × 5 cm; anode: 5 × 7 cm). The anode was positioned over either C3 or C4 (depending on the injured hemisphere) and the cathode was positioned in the supraorbital region contralateral to the anode. A current of 2 mA was administered for 20 minutes during cycles of standardized active contraction of the TA (six seconds of contraction and 12 seconds of rest). Sham stimulation followed the same procedures as active stimulation, but the device was only switched on for the first 20 seconds. Thus, the individuals receiving the sham procedure had the initial sensation of stimulation, but received no electrical current during the remainder of the session. This is considered a valid control procedure in studies involving tDCS.

FES was performed using the QUARK® FES, VIF 995 DUAL. Two self-adhesive rubber electrodes measuring 5 cm² were positioned –one over the motor point of the TA muscle and one immediately below the belly of the muscle. Active FES was conducted for 20 minutes with a pulse width of 250 µs, modulated at a frequency of 50 Hz and stimulation cycles of 1:2 (TON for six seconds and TOFF for 12 seconds) associated with active contraction of the TA muscle during the six seconds of TON. Sham FES followed the same procedures, but the device was switched on only for the initial 20 seconds, with the current then diminished to zero. The patients were informed of the possibility of feeling a slight initial tingling that would either diminish, disappear or continue during the 20-minute session.

Electromyographic (EMG) activity of the TA muscle during dorsiflexion was the primary outcome and static balance was the secondary outcome, both before and immediately after the intervention protocols.

The activity of the TA was analyzed by the variable median frequency and RMS, collected by the an electromyograph
(FREEEMG® –BTS Engineering), with a four-channel conditioner module (BTS FREEEMG 100®), analog/digital converter with 16 bits of resolution, common rejection mode ratio>100 dB and 20–450 Hz band pass filter was used for the analysis of TA muscle activity. The EMG signals were amplified (gain: 2,000 fold), with wireless transmission using a sampling frequency of 1 kHz.

Each patient was instructed with regard to the execution of the movements for the evaluations and the EMG data were captured with the patient seated on a chair with knees flexed at 90° and the ankles in the neutral position29. After cleaning the sites with 70% alcohol, disposable self-adhesive Ag/AgCl electrodes measuring 1 cm in diameter (Medi-Trace 200 Kendall Healthcare/Tyco, Canada) positioned 2 cm center to center were used to capture the EMG signal of the TA muscle, following the SENIAM guidelines (Surface Electromyography for the Non-Invasive Assessment of Muscles)28; which was not altered even after the intervention protocol.

The patient performed three maximum voluntary contractions (MVCs) of the TA muscle for 10 seconds with a two-to-three-minute rest between contractions19. After one minute of rest, the patient was instructed to perform five consecutive dorsiflexion movements of the foot (isotonic contraction) three times with a two-to-three-minute rest between repetitions.

The amplitude of the signal captured during isotonic contraction was analyzed based on the root mean square (RMS) after being normalized by the largest RMS obtained during the three MVCs (µmV/µV × 100: % MVC). The median frequency was estimated using the Fourier fast transform considering windows with 1,024 points and 50% overlap (Hamming window). The median frequency was chosen because it is an indicator of recruitment of motor units. The higher the median frequency, the greater the input generated in each muscle fiber thus increasing the contraction factor of the muscle.

Static balance was evaluated using a force plate (Kistler model 9286BA) with a 100-Hz acquisition frequency and four piezoelectric sensors measuring 400 × 600 mm positioned at the extremities of the platform. The patient was instructed to remain in quiet standing on the force plate with feet positioned at the base of a triangle. Static balance was evaluated with eyes open (EO –gaze fixed on the horizon) and eyes closed (EC)29. Three 30-second readings were taken under each condition with a five-minute rest period between trials.

Movement of the center of pressure (COP) in the anteroposterior and mediolateral directions was used for the analysis of postural balance. The COP signals were filtered (Butterworth 10-Hz low-pass filter) for the subsequent calculation of the following indicators of postural control: i) mean sway velocity and ii) mean sway frequency10. Sway velocity in both directions was calculated based on the total distance of the movements divided by the data collection time31. Sway frequency was determined by the frequency band with 80% of spectral power32, 33.

The EMG and stabilometric data were processed using specific routines developed in MathLab, version 2010b (The MathWorks Inc., Natick, MA, USA).

The statistical analysis was based on the systematic review addressing the effects of tDCS and transcranial magnetic stimulation on motor function in stroke survivors, in which the mean per study was 30 participants16.

The order of the protocols was determined using a randomization table implemented in Excel by an independent researcher who did not participate in the recruitment of the patients. A crossover design was used, with a period of 48 hours respected between sessions to avoid the potential additive effect of the stimulations18, 34 (padronized protocols on Monday, Wednesday, Friday and Sunday). At each step, the individuals were submitted to pre-intervention and post-intervention evaluations (EMG and stabilometry). The following protocols were conducted each in a single 20-minute session:

1. Active anodal tDCS + sham FES;
2. Sham tDCS + active FES;
3. Active anodal tDCS + active FES;
4. Sham tDCS + sham FES.

The participants and researchers in charge of the evaluations were blinded to the arm of treatment (active or sham stimulation). Only the tDCS operator was aware of the treatment being administrated.

Descriptive statistics (measures of central tendency and dispersion) were used for the characterization of the sample and distribution of the inferential data: mean and standard deviation for parametric variables; median and interquartile range for nonparametric variables; and frequency and percentage for categorical variables.

The Shapiro-Wilk test was used to determine the distribution of the data. Data with asymmetric distribution were log-transformed prior to analysis to negate the effects of heteroscedasticity. The stabilometric data were not normally distributed even after log-transformation and were therefore expressed as median and inter-quartile range (25% and 75%) and analyzed using nonparametric tests. The Mann-Whitney test was used for the comparison of pre-intervention and post-intervention sway velocity and frequency scores. The EMG data exhibited normal distribution (log-transformed median frequency values) and two-way repeated-measures analysis of variance (ANOVA) considering the factors time (pre-intervention and post-intervention) and groups (1, 2, 3 and 4) was used for the intergroup and intragroup comparisons with the Bonferroni post hoc test. The SPSS 20.0 program (SPSS Inc., Chicago, IL, USA) was used for all analyses and the level of significance was set to 5% (p<0.05) for all interactions.
RESULTS

Table 1 displays the demographic and clinical characteristics of the participants (n=30). Thirty-three patients were initially recruited, three of whom did not meet the eligibility criteria (Fig. 1).

In the analysis of the primary outcome (EMG data), no significant time vs. group interactions were found for median frequency (F=0.85, p=0.44; η²=0.01) or the RMS (F=0.24, p=0.86; η²=0.004) (Table 2). Moreover, no significant differences were found between the pre-intervention and post-intervention evaluations of the stabilometric data (median, inter-quartile range and effect size) (Table 3).

DISCUSSION

In the present study, the combination of anodal tDCS and active FES had no significant effect on electrical activity of the TA muscle or static balance in stroke victims with hemiparesis. These findings suggest homeostatic defense mechanisms of the central nervous system. According to Bienenstock-Cooper-Munro35 a high level of synaptic activity may subsequently reduce any task that requires a further increase in neuronal activity35. Thus, the stimulus during the post-intervention EMG evaluation (which was also a motor task) may have required an increase in neuronal activity, which was already excited by the 20 minutes of stimulation, thereby causing an immediate reduction in activity36.

However, immediate effects (p<0.05) from tDCS over the primary motor cortex combined with other forms of physical therapy have been demonstrated: Madhavan et al.19 found an increase in evoked motor potential (EMP) during 15 minutes and immediately after the practice of ankle dorsiflexion combined with tDCS in nine patients with hemiparesis. Sriraman et al.22 evaluated EMP before, during and 24 hours after tDCS combined with ankle biofeedback. Rizzo et al.37 evaluated EMP after 10, 20, 30 and 60 minutes of tDCS combined with repetitive electrical stimulation of the median nerve in healthy individuals.

However, it is not possible to affirm whether the positive effects found in the nine stroke survivors in the study by Madhavan19 are representative of larger populations, such as the sample employed in the present study (30 volunteers). Moreover, the trials conducted by Sriraman et al.22, Rizzo et al.37 and Dutta et al.20 that involved tDCS in healthy individuals, the physiology and cortical excitability differs from individuals with a central nervous system injury. Maladaptive neuroplasticity is found in the chronic phase following a stroke. Thus, greater afferent information is required so that motor neurons surrounding the injured area can be molded to increase the number of connections and improve synaptic transmission pathways for effective motor recovery38. In contrast, such compositions are intact in healthy individuals39.

Based on these physiopathological concepts, a single session of tDCS and FES was likely insufficient to promote neuroplasticity, since this phenomenon requires constant, repetitive, low-frequency stimuli to enable the motor cortex to codify information and remodel itself through learning mechanisms40–42. Moreover, brain damage differs in terms of location and size as well as other characteristics among stroke survivors, which can interfere with the results43–45.

Another explanation for the present findings regards the electrode montage. The cathode in the supraorbital region may have diminished activity in the prefrontal cortex, which is responsible for motor planning45 thereby exerting a negative

| Variable                  | Participants (n=30) |
|---------------------------|--------------------|
| Gender (M/F)              | 30 (23/7)          |
| Age (years)               | 61.0 ± 9.7         |
| Weight (kg)               | 74.1 ± 15.2        |
| Body mass index (kg/m²)   | 26.3 ± 4.6         |
| Height (m)                | 1.67 ± 0.11        |
| Mini Mental State Examination (score) | 26 [21 to 29] |
| Fugl-Meyer scale (score)  | 65.5 ± 23.6        |
| Ashworth scale (grade)    | 1 [1 to 3]         |
| Muscle strength TA (grade)| 3 [2 to 4]         |
| Hemorrhagic stroke        | 8 (26.7%)          |
| Ischemic stroke           | 22 (73.3%)         |
| Left-side hemiparesis     | 15 (50.0%)         |
| Right-side hemiparesis    | 15 (50.0%)         |
| Time since stroke (months)| 37.0 [28.0 to 86.0]|

Data expressed as mean ± standard deviation, median [interquartile range] and frequency and percentage; M/F: male/female.
influence on the motor task solicited. Although the montage employed is well referenced in the literature\textsuperscript{46}, studies have tested new electrode placement protocols that can diminish the influence of the cathode and enhance the focus of the anode to achieve specific objectives in cortical regions\textsuperscript{47, 48}.

The issue of the ideal time for the evaluation of a motor task in protocols involving tDCS should also be considered. If the evaluation had been performed during treatment, the results may have been different. Studies have suggested that tDCS during the practice of a task promotes a better motor performance due to neuro-excitatory mechanisms attributed to the immediate change in the membrane potential\textsuperscript{49–52}.

The analysis of FES also revealed no immediate changes in activity of the TA muscle. According to the literature, the best therapeutic response occurs when FES is administered over a longer period of time. Newsam et al.\textsuperscript{53} found a significant improvement in the recruitment of motor units following a three-week FES protocol. Knutson et al.\textsuperscript{54} found a significant increase in active ankle dorsiflexion following a six-week FES protocol and Mesci et al.\textsuperscript{55} found an increase in ankle dorsiflexion as well as a reduction in spasticity following a four-week FES protocol.

The lack of an immediate effect on static balance in the present investigation is in disagreement with data described in previous studies. Kaski et al.\textsuperscript{55} found improvements in balance and gait in individuals with leukoaraiosis following a single session of tDCS combined with physical training. Duarte et al.\textsuperscript{56} report improvements in anteroposterior sway with EO and

\[ \text{Fig. 1. Flowchart of study.} \]
Table 2. Mean and standard deviation of RMS (root mean square) and median frequency (MDF)

| Intervention | Differences between interventions |
|--------------|----------------------------------|
|              | Pre Post | Adjusted Mean Difference (95% CI) |
| MDF (hz)     |          |                                 |
| ta+Fs        | 103.3 ± 24.9 (98.6 ± 23.0)       | 4.42 (1.72 to 7.11) |
| ts+Fa        | 101.0 ± 25.3 (95.9 ± 24.7)       | 5.09 (1.33 to 8.84) |
| ta+Fa        | 100.8 ± 21.2 (100.8 ± 22.5)      | 0.01 (-3.40 to 3.42) |
| ts+Fs        | 99.3 ± 24.8 (95.2 ± 24.4)        | 4.07 (0.13 to 8.01) |
| RMS (µV)     |          |                                 |
| ta+Fs        | 69.7 ± 10.2 (68.7 ± 13.7)        | 1.04 (-3.49 to -5.56) |
| ts+Fa        | 70.7 ± 12.1 (70.7 ± 14.3)        | -0.01 (-4.26 to 4.22) |
| ta+Fa        | 70.9 ± 16.2 (68.4 ± 19.0)        | 2.55 (-3.17 to 8.27) |
| ts+Fs        | 71.8 ± 12.0 (68.3 ± 12.1)        | 3.48 (-1.36 to 8.31) |

Table 3. Median, inter-quartile range (25% and 75%) and effect size of stabilometric data observed in antero-posterior (COPap) e medio-lateral (COPml) directions

| Velocity (mm/s) | Pre Intervention | Post intervention | p value | Effect size |
|-----------------|------------------|-------------------|---------|-------------|
| COPap ta+Fs     | 15.70 (10.98–26.27) | 15.97 (10.91–23.94) | 0.91 | 0.02 |
| COPml ts+Fa     | 13.97 (10.23–18.32) | 13.51 (10.74–18.28) | 0.37 | 0.17 |
| COPap ta+Fa     | 12.08 (9.90–19.00) | 12.17 (10.10–17.39) | 0.74 | 0.06 |
| COPml ts+Fs     | 13.67 (10.27–18.78) | 13.09 (10.20–19.09) | 0.67 | 0.08 |
| COPap ta+Fa     | 14.85 (10.67–23.25) | 14.11 (11.53–22.62) | 0.91 | 0.02 |
| COPml ts+Fa     | 12.70 (10.03–15.02) | 11.94 (9.62–18.28) | 0.77 | 0.05 |
| COPap ta+Fa     | 12.70 (10.62–18.60) | 12.19 (11.24–18.45) | 0.47 | 0.13 |
| COPml ts+Fs     | 13.67 (10.27–18.78) | 13.09 (10.20–19.09) | 0.67 | 0.08 |
| COPap ta+Fa     | 14.85 (10.67–23.25) | 14.11 (11.53–22.62) | 0.91 | 0.02 |
| COPml ts+Fa     | 12.70 (10.03–15.02) | 11.94 (9.62–18.28) | 0.77 | 0.05 |
| COPap ta+Fa     | 12.70 (10.62–18.60) | 12.19 (11.24–18.45) | 0.47 | 0.13 |
| COPml ts+Fs     | 13.67 (10.27–18.78) | 13.09 (10.20–19.09) | 0.67 | 0.08 |
| COPap ta+Fa     | 14.85 (10.67–23.25) | 14.11 (11.53–22.62) | 0.91 | 0.02 |
| COPml ts+Fa     | 12.70 (10.03–15.02) | 11.94 (9.62–18.28) | 0.77 | 0.05 |
| COPap ta+Fa     | 12.70 (10.62–18.60) | 12.19 (11.24–18.45) | 0.47 | 0.13 |
| COPml ts+Fs     | 13.67 (10.27–18.78) | 13.09 (10.20–19.09) | 0.67 | 0.08 |

The values in parentheses represent the range of the interquartile range (25% and 75%).
EC, mediolateral sway and the results of the Pediatric Balance Scale in children with cerebral palsy both one week and one month after the conclusion of an intervention involving tDCS and treadmill gait training. Dumont et al.\(^7\) found reductions in anteroposterior sway, sway area and sway velocity in a stroke survivor after a single session of tDCS over the primary motor cortex combined with treadmill training; however, it is not possible to affirm that the immediate effect on balance in this case report was due to tDCS or that tDCS had potentiated the effects of treadmill training, as the author suggests. Immediate effects of tDCS when not combined with other therapies have also been reported. Grecco et al.\(^8\) found significant increases in gait velocity, cadence and body sway in children with cerebral palsy. Sohn et al.\(^24\) found a significant improvement in general postural stability as well as an increase in muscle strength in patients with hemiparesis. Zhou et al.\(^9\) report an increase in gait velocity and a significant reduction COP area and velocity in healthy individuals. Regarding FES, Chung et al.\(^60\) and Hyun et al.\(^89\) report improvements in ankle movements in patients with hemiparesis, but only after training for five days and six weeks, respectively, suggesting the need for long-term repeated stimulation for the achievement of learning.

However, from the results presented in this present study, it can be inferred that the immediate stimulation of the tDCS and FES associated or isolated did not modify the electrical activity of the TA muscle and the static balance of hemiparetic patients due to stroke.

The authors of the present study believe that the lack of a significant change in TA muscle activity and static balance in individuals with hemiparesis after the tDCS and FES protocols may be related to factors such as the amount of stimulus (a single session of the combined methods may be insufficient to generate neuroplasticity), homeostatic defense mechanisms, the electrode montage employed and the chronic nature of the disease (duration of maladaptive plasticity). The reproduction of this study with treatment involving multiple sessions could lead to different results. Nonetheless, the lack of an effect of this technique (tDCS) can contribute to a greater perception in future studies regarding possible methodologies and target population, which are aspects that have not been previously addressed and are important in the context of trials involving noninvasive brain stimulation.

ACKNOWLEDGEMENTS

The authors are grateful to the Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP-2014/18128–6), Quark Medical Equipment and the Integrated Human Movement Analysis Lab (University Nove de Julho).

REFERENCES

1) Murray CJ, Vos T, Lozano R, et al.: Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet, 2012, 380: 2197–2223. [Medline] [CrossRef]

2) Mirbagheri MM, Albiglou L, Thajchayapong M, et al.: Muscle and reflex changes with varying joint angle in hemiparetic stroke. J Neuroeng Rehabil, 2008, 5: 6. [Medline] [CrossRef]

3) Brandalize D, Brandalize M: Efeitos da toxina botulínica no tratamento do pé eqüino em individuos com sequelas de acidente vascular encefálico. Revista Polidisciplinar Eletrônica da Faculdade Guairacá, 2010: 3–13.

4) Iki K, Kamikubo T, Takehara I, et al.: Dynamic postural control in patients with hemiparesis. Am J Phys Med Rehabil, 2003, 82: 463–469, quiz 470–472, 484. [Medline] [CrossRef]

5) Lavados PM, Hennis AJ, Fernandes JG, et al.: Stroke epidemiology, prevention, and management strategies at a regional level: Latin America and the Caribbean. Lancet Neurol, 2007, 6: 362–372. [Medline] [CrossRef]

6) Pomeroy VM, King L, Pollock A, et al.: Electrostimulation for promoting recovery of movement or functional ability after stroke. Cochrane Database Syst Rev, 2006, 19: CD003241. [Medline]

7) Rushton DN: Functional electrical stimulation and rehabilitation—an hypothesis. Med Eng Phys, 2003, 25: 75–78. [Medline] [CrossRef]

8) Kim JH, Lee JK, Lee JU, et al.: A pilot study on the effect of functional electrical stimulation of stroke patients in a sitting position on balance and activities of daily living. J Phys Ther Sci, 2013, 25: 1097–1101. [Medline] [CrossRef]

9) Mesci N, Ozdemir F, Kabayel DO, et al.: The effects of neuromuscular electrical stimulation on clinical improvement in hemiplegic lower extremity rehabilitation in chronic stroke: a single-blind, randomised, controlled trial. Disabil Rehabil, 2009, 31: 2047–2054. [Medline] [CrossRef]

10) Martins FL, Guimarães LH, Vitorino DF, et al.: Eficácia da eletrostimulação funcional na amplitude de movimento de dorsiflexão de hemiparéticos. Revista Neurociências, 2004: 103–109.

11) Robbins SM, Houghton PE, Woodbury MG, et al.: The therapeutic effect of functional and transcutaneous electric stimulation on improving gait speed in stroke patients: a meta-analysis. Arch Phys Med Rehabil, 2006, 87: 853–859. [Medline] [CrossRef]

12) Howlett OA, Lannin NA, Ada L, et al.: Functional electrical stimulation improves activity after stroke: a systematic review with meta-analysis. Arch Phys Med Rehabil, 2015, 96: 934–943. [Medline] [CrossRef]

13) Lindenberg R, Renga V, Zhu LL, et al.: Bihemispheric brain stimulation facilitates motor recovery in chronic stroke patients. Neurology, 2010, 75: 2176–2184. [Medline] [CrossRef]

14) Miranda PC, Lomarev M, Hallett M: Modeling the current distribution during transcranial direct current stimulation. Clin Neurophysiol, 2006, 117: 1623–1629. [Medline] [CrossRef]

15) Jiang T, Xu RX, Zhang AW, et al.: Effects of transcranial direct current stimulation on 52 hemichannel pannexin-1 and neural plasticity in rat model of cerebral
infarction. Neuroscience, 2012, 13: 221–226.

16) Adjeomu BO, Simis M, Macea DD, et al.: Systematic review of parameters of stimulation, clinical trial design characteristics, and motor outcomes in non-invasive brain stimulation in stroke. Front Psychiatry, 2012, 3: 88. [Medline] [CrossRef]

17) Kang N, Summers JJ, Cauraugh JH: Transcranial direct current stimulation facilitates motor learning post-stroke: a systematic review and meta-analysis. J Neurol Neurosurg Psychiatry, 2016, 87: 345–355. [Medline] [CrossRef]

18) Sohn MK, Jee SJ, Kim YW: Effect of transcranial direct current stimulation on postural stability and lower extremity strength in hemiplegic stroke patients. Ann Rehabil Med, 2013, 37: 759–765. [Medline] [CrossRef]

19) Madhavan S, Weber KA 2nd, Stinear JW: Non-invasive brain stimulation enhances fine motor control of the hemiparetic ankle: implications for rehabilitation. Exp Brain Res, 2011, 209: 9–17. [Medline] [CrossRef]

20) Dutta A, Paulus W, Nitsche MA: Facilitating myoelectric-control with transcranial direct current stimulation: a preliminary study in healthy humans. J Neurol Neurosurg Psychiatry, 2011, 82: 767–771. [Medline] [CrossRef]

21) Chang MC, Kim DY, Park DH: Enhancement of cortical excitability and lower limb motor function in patients with stroke by transcranial direct current stimulation. Brain Stimul, 2015, 8: 561–566. [Medline] [CrossRef]

22) Sriraman A, Oishi T, Madhavan S: Timing-dependent priming effects of tDCS on ankle motor skill learning. Brain Res, 2014, 1581: 23–29. [Medline] [CrossRef]

23) Kendall FP, Mccreary EK, Provance PG: Músculos: Prova e Funções com postura e dor. 4. ed. São Paulo: Manole, 1995.

24) DaSilva AF, Volz MS, Bikson M, et al.: Electrode positioning and montage in transcranial direct current stimulation. J Vis Exp, 2011, 1–11. [Medline] [CrossRef]

25) Mendonça ME, Fregni F: Neuromodulação com estimulação cerebral não invasiva: aplicação no acidente vascular encefálico, doença de Parkinson e dor crônica. Conclusões práticas e fisioterapia neurológica. São Paulo: Manole, 2012, pp 307–339.

26) You G, Liang H, Yan T: Functional electrical stimulation early after stroke improves lower limb motor function and ability in activities of daily living. NeuroRehabilitation, 2014, 35: 381–389. [Medline] [CrossRef]

27) Ambrosini E, Ferrante S, Pedrocchi A, et al.: Cycling induced by electrical stimulation improves motor recovery in postacute hemiparetic patients: a randomized controlled trial. Stroke, 2011, 42: 1068–1073. [Medline] [CrossRef]

28) Hermens HJ, Freriks B, Disselhorst-Klug C, et al.: Development of recommendations for SEMG sensors and sensor placement procedures. J Electromyogr Kinesiol, 2010, 10: 361–374. [Medline] [CrossRef]

29) Horak F: Mechanistic and physiological aspects. Postural orientation and equilibrium: what do we need to know about neural control of balance to prevent falls? Age Ageing, 2006, 7–11.

30) El Hage Y, Politis F, de Sousa DF, et al.: Effect of mandibular mobilization on electromyographic signals in muscles of mastication and static balance in individuals with temporomandibular disorder: study protocol for a randomized controlled trial. Trials, 2013, 14: 316. [Medline] [CrossRef]

31) Oliveira LF, Simpson DM, Nadal J: Calculation of area of stabilometric signals using principal component analysis. Physiol Measur, 1996: 305–312.

32) Doyle TL, Newton RU, Burnett AF: Reliability of traditional and fractal dimension measures of quiet stance center of pressure in young, healthy people. Arch Phys Med Rehabil, 2005, 86: 2034–2040. [Medline] [CrossRef]

33) Ogata M, Sato H, Aoki T, et al.: Effect of transcranial direct current stimulation on sensory thresholds in chronic stroke patients. Phys Ther, 2000, 80: 365–371. [Medline] [CrossRef]

34) Ehsani F, Bakhtiary AH, Jaberzadeh S, et al.: Differential effects of primary motor cortex and cerebellar transcranial direct current stimulation on motor learning in healthy individuals: a randomized double-blind sham-controlled study. Neurosci Res, 2016, 112: 10–19. [Medline] [CrossRef]

35) Bienenstock EL, Cooper LN, Munro PW: Theory for the development of neuron selectivity: orientation specificity and binocular interaction in visual cortex. J Neurosci, 1982, 2: 32–48. [Medline] [CrossRef]

36) Thirugnanasambandam N, Sparing R, Dufotakis M, et al.: Isometric contraction interferes with transcranial direct current stimulation (tDCS) induced plasticity: evidence of state-dependent neuromodulation in human motor cortex. Restor Neurol Neurosci, 2011, 29: 311–320. [Medline] [CrossRef]

37) Rizzo V, Terranova C, Crupi D, et al.: Increased transcranial direct current stimulation after effects during concurrent peripheral electrical nerve stimulation. Brain Stimul, 2014, 7: 113–121. [Medline] [CrossRef]

38) Madhavan S, Rogers LM, Stinear JW: A paradox: after stroke, the non-lesioned lower limb motor cortex may be maladaptive. Eur J Neurosci, 2010, 32: 1032–1038. [Medline] [CrossRef]

39) Rossini PM, Desiato MT, Caramia MD: Age-related changes of motor evoked potentials in healthy humans: non-invasive evaluation of central and peripheral motor tracts excitability and conductivity. Brain Res, 1992, 593: 14–19. [Medline] [CrossRef]

40) Lindberg P, Schmitz C, Forssberg H, et al.: Effects of passive-active movement training on upper limb motor function and cortical activation in chronic patients with stroke: a pilot study. J Rehabil Med, 2014, 36: 117–123. [Medline] [CrossRef]

41) Nudo RJ, Wise BM, SiFuentes F, et al.: Neural substrates for the effects of rehabilitative training on motor recovery after ischemic infarct. Science, 1996, 272: 1791–1794. [Medline] [CrossRef]

42) Madhavan S, Shah B: Enhancing motor skill learning with transcranial direct current stimulation—a concise review with applications to stroke. Front Psychiatry, 2012, 3: 66. [Medline] [CrossRef]

43) Jung P, Ziemann U: Homeostatic and nonhomeostatic modulation of learning in human motor cortex. J Neurosci, 2009, 29: 5597–5604. [Medline] [CrossRef]

44) Turrigiano GG, Nelson SB: Homeostatic plasticity in the developing nervous system. Nat Rev Neurosci, 2004, 5: 97–107. [Medline] [CrossRef]

45) Carlos AM, Luciene BR: Integração de Três Conceitos: Função Executiva, Memória de Trabalho e Aprendizado. Psicol Teor Pesqui 2011, 309–314.

46) Monte-Silva K, Kuo MF, Liebetanz D, et al.: Shaping the optimal repetition interval for cathodal transcranial direct current stimulation (tDCS). J Neurophysiol, 2010, 103: 1735–1740. [Medline] [CrossRef]

47) Penolazzi B, Pastore M, Mondini S: Electrode montage dependent effects of transcranial direct current stimulation on semantic fluency. Behav Brain Res, 2013, 248: 129–135. [Medline] [CrossRef]

48) Rossini PM, Burke D, Chen R, et al.: Non-invasive electrical and magnetic stimulation of the brain, spinal cord, roots and peripheral nerves: basic principles and procedures for routine clinical and research application. An updated report from an I.F.C.N. Committee. Clin Neurophysiol, 2015, 126: 1071–1107. [Medline] [CrossRef]
49) Ziemann U, Siebner HR: Modifying motor learning through gating and homeostatic metaplasticity. Brain Stimul, 2008, 1: 60–66. [Medline] [CrossRef]
50) Boggio PS, Castro LO, Savagim EA, et al.: Enhancement of non-dominant hand motor function by anodal transcranial direct current stimulation. Neurosci Lett, 2006, 404: 232–236. [Medline] [CrossRef]
51) Reis J, Schambra HM, Cohen LG, et al.: Noninvasive cortical stimulation enhances motor skill acquisition over multiple days through an effect on consolidation. Proc Natl Acad Sci USA, 2009, 106: 1590–1595. [Medline] [CrossRef]
52) Stagg CJ, Jayaram G, Pastor D, et al.: Polarity and timing-dependent effects of transcranial direct current stimulation in explicit motor learning. Neuropsychologia, 2011, 49: 800–804. [Medline] [CrossRef]
53) Newsam CJ, Baker LL: Effect of an electric stimulation facilitation program on quadriceps motor unit recruitment after stroke. Arch Phys Med Rehabil, 2004, 85: 2040–2045. [Medline] [CrossRef]
54) Knutson JS, Chae J: A novel neuromuscular electrical stimulation treatment for recovery of ankle dorsiflexion in chronic hemiplegia: a case series pilot study. Am J Phys Med Rehabil, 2010, 89: 672–682. [Medline] [CrossRef]
55) Kaski D, Domínguez RO, Allum JH, et al.: Improving gait and balance in patients with leukoaraiosis using transcranial direct current stimulation and physical training: an exploratory study. Neurorehabil Neural Repair, 2013, 27: 864–871. [Medline] [CrossRef]
56) Duarte NA, Grecco LA, Galli M, et al.: Effect of transcranial direct-current stimulation combined with treadmill training on balance and functional performance in children with cerebral palsy: a double-blind randomized controlled trial. PLoS One, 2014, 9: e105777. [Medline] [CrossRef]
57) Dumont AJ, Araujo MC, Lazzari RD, et al.: Effects of a single session of transcranial direct current stimulation on static balance in a patient with hemiparesis: a case study. J Phys Ther Sci, 2015, 27: 955–958. [Medline] [CrossRef]
58) Grecco LA, Duarte NA, Zanon N, et al.: Effect of a single session of transcranial direct-current stimulation on balance and spatiotemporal gait variables in children with cerebral palsy: a randomized sham-controlled study. Braz J Phys Ther, 2014. [CrossRef]
59) Zhou J, Hao Y, Wang Y, et al.: Transcranial direct current stimulation reduces the cost of performing a cognitive task on gait and postural control. Eur J Neurosci, 2014, 39: 1343–1348. [Medline] [CrossRef]
60) Chung E, Park SI, Jang YY, et al.: Effects of brain-computer interface-based functional electrical stimulation on balance and gait function in patients with stroke: preliminary results. J Phys Ther Sci, 2015, 27: 513–516. [Medline] [CrossRef]