Spinal direct current stimulation with locomotor training in chronic spinal cord injury

Turki S. Abualait, PT, PhD, Alaa I. Ibrahim, PT, PhD.

ABSTRACT

Transcutaneous spinal direct current stimulation (tsDCS) is a non-invasive method of stimulating spinal circuits that can modulate and induce changes in corticospinal excitability (CE) in incomplete spinal cord injury (SCI). A double-blinded sham controlled study of 2 male patients (A and B) with SCI was carried out. Patient A received sham and cathodal tsDCS, while Patient B received sham and anodal tsDCS. Four baselines were recorded prior to each arm of stimulation. Outcomes were then measured post each arm of stimulation; 10-meter walk test, modified ashworth scale, berg balance scale, manual muscle testing, and spinal cord independence measure-III. Transcranial magnetic stimulation, assessed motor evoked potentials. Cathodal tsDCS increased the scores in few of the outcome measures and decreased others. Anodal stimulation increased scores in all measures. Motor evoked potentials increased in post-cathode and deteriorated in post-anode. In conclusion, tsDCS modulated gait parameters, spasticity, and CE in incomplete SCI.

Keywords: spinal cord injury, transcutaneous spinal direct current stimulation, transcranial magnetic stimulation, neuroplasticity, corticospinal excitability

Saudi Med J 2020; Vol. 41 (1): 88-93
doi: 10.15537/smj.2020.1.24818

Disclosure. Authors have no conflict of interests, and the work was not supported or funded by any drug company.
as on the ascending and descending neural pathways in humans. In this study, the differential effects of tsDCS were investigated in 2 patients with chronic incomplete SCI (American Spinal Injury Association-C or ASIA-C). Functional measures such as walking speed, muscle strength, balance, and spasticity and neurophysiological parameters were assessed pre- and post-tsDCS.

**Case Report.** Two male patients, A and B, aged 22 and 24 years, respectively, with incomplete SCI type ASIA-C at spinal levels T10-T11 with a chronicity of 2 years were studied. Informed consents were signed prior to data collection, and the experiment was approved by the Institutional Review Board (IRB) at Imam Abdulrahman Bin Faisal University. This double-blind, sham-controlled study consisted of 2 arms for each participant. The first arm for patient A included sham tsDCS and the second included cathodal tsDCS. The first arm for patient B included sham tsDCS, while the second included anodal tsDCS. Each arm consisted of 30 sessions, with 5 sessions per week for 6 weeks with a washout period of 2 weeks between each arm of the study. Four baselines were measured prior to each arm of stimulation (Figure 1). Transcutaneous spinal direct current stimulation was administered by an independent assessor to ensure blindness.

**Therapeutic interventions.** Transcutaneous spinal direct current stimulation was administered online using a Magstim current stimulator (The Magstim Co., Whitland, UK) with saline soaked electrodes 5 × 7 cm. The active electrode was placed over the spinous process T10-T11 and the reference electrode was placed horizontally over the left deltoid muscle. Each session included 20 minutes of stimulation with a set intensity of 2.5 mA, resulting in a current density and total charge density of 0.07 mA/cm² and 85.6 C/cm². Sham tsDCS was ramped up only during the first 30 seconds of the session to ensure the procedure remained blind. Electrode placement was similar in all 3 arms of the experiment.

**Intervention-Robot-assisted gait training.** Both patients participated in a robot-assisted gait training program, while tsDCS was administered simultaneously. Gait training was performed on a Lokomat (Hocoma AG, Voletswil, Switzerland), which partially supports body weight using straps tied around the patient’s trunk. This system includes a treadmill, a body support harness, 2 light-weighted robotic arms connected to the legs, and a monitoring system for gait parameters. Functional gait training was facilitated using reciprocal walking movements of the lower extremities at the fastest speed that the patients could tolerate. The speed was then gradually increased by 0.1 km/hour every 10 min and lowered by 0.1 km/hour in case of poor foot contact or increased spasticity. To ensure good stance phase kinematics, the level of body weight support was adjusted to the minimum tolerated by the patient.

**Outcome measures.** Outcomes were measured at baseline twice: prior to sham tsDCS (tA0) and prior to cathode tsDCS (tA1) for patient A. Similarly, outcomes for patient B were also measured twice: prior to sham tsDCS (tB0) and prior to anode tsDCS (tB1). Outcomes were also measured immediately following each arm of tsDCS: post-sham (t1) and post-cathode (t2) for patient A. (tB0): prior to sham tsDCS; (tB1): prior to anode tsDCS; (t3): post-sham and (t4): post-anode for patient B). TMS: transcranial magnetic stimulation; TMS (t0): baseline stimulation; TMS (t1): post-sham; TMS (t2): post-cathode and TMS (t3): post-anode.
Stimulation of chronic spinal cord injury ... Abualait & Ibrahim

was represented by a single score. All post-training No formal statistical tests were used, as each outcome the SCIM-III determines patient functional ability. plantar flexion with a cumulative score of 50. Finally, strength of hip flexion, hip extension, hip abduction, hip adduction, hip internal rotation, hip external rotation, knee flexion, knee extension, dorsiflexion, and plantar flexion with a cumulative score of 50. Finally, the SCIM-III determines patient functional ability. No formal statistical tests were used, as each outcome was represented by a single score. All post-training scores were compared to baseline scores for all outcome measures. For patient A, comparisons were made between baseline and sham tsDCS (t1-tA0 comparison) and between a second baseline and cathode tsDCS (t2-tA1 comparison). For patient B, comparisons were made between baseline and sham tsDCS (t3-tB0 comparison) and a second baseline and anode tsDCS (t4-tB1 comparison).

Neurophysiological parameters. To evaluate the integrity of the corticospinal tract excitability (CE), transcranial magnetic stimulation (TMS) was used to elicit bilateral triceps surae motor evoked potentials (MEPs). Motor evoked potentials amplitudes were measured at baseline (t0) for both patients A and B, post-sham (t1) for patient A and patient B, post-cathode (t2) for patient A, and post-anode (t3) for patient B. Motor evoked potentials recruitment was recorded at rest using a pair of Ag-AgCl surface electrodes (diameter =10 mm) placed bilaterally over the belly of the soleus muscles. A total of 5 MEPs were collected at ~10-s intervals with each TMS intensity ranging from 80% to 130% of the resting motor threshold (RMT). Resting motor threshold was measured at baseline (pre-training). Motor evoked potentials measurements were then averaged for each time point, and the MEP size was measured based on peak-to-peak amplitude for each stimulus intensity. Transcranial magnetic stimulation was delivered using a high-powered Magstim 2002 stimulator (Magstim Co., UK) fitted with a figure-of-8 coil with an external diameter of 70 mm placed over the motor cortex. Stimulation intensity (%RMT) was determined at rest based on the lowest stimulator intensity that is capable of evoking MEPs higher than 50 μV at peak-to-peak amplitude in at least 50% of 10 trials. Both patients completed all arms of the experiment without any reported complications.

Patient A. Speed on the 10MWT increased by 0.07 m/s following sham stimulation (t1-tA0 comparison) and showed a further increase of 0.06 m/s following cathodal stimulation (t2-tA1 comparison). The scores on the BBS increased by 4 points following sham stimulation (t1-tA0 comparison) and further increased by 4 points following cathodal stimulation (t2-tA1 comparison). Manual muscle testing of the right lower extremity muscle groups increased by 12 points following sham tsDCS (t1-tA0 comparison), but decreased by 7 points following cathodal tsDCS (t2-tA1 comparison). The left lower extremity showed an increase in 9 points on MMT scores (t1-tA0 comparison) and then decreased by 3 points following the second arm (t2-tA1 comparison). SCIM-III showed an increase of 2 points following each of the two arms of stimulation t1-tA0 and t2-tA1 comparisons. Finally, sham tsDCS showed no changes in MAS (t1-tA0 comparison), while cathodal tsDCS showed a decrease of one point (t2-tB1 comparison) for both lower extremities (Figure 2).

Patient B. Walking speed, represented by the 10MWT result, increased by 0.06 m/s following sham stimulation (t3-tB0 comparison) and showed a further increase of 0.06 m/s following anodal stimulation (t4-tB1 comparison). BBS showed a continuous increase of 3 and 4 points following sham (t3-tB0 comparison) and anodal stimulations (t4-tB1 comparison), respectively. MAS showed no changes after sham tsDCS (t3-tB0 comparison), but the scores of spasticity were increased by 1 point for both the left and right lower extremities following the second arm of stimulation (t4-tB1 comparison). MMT of the right lower extremity muscle groups increased by 8 points following sham tsDCS (t3-tB0 comparison) and further increased by 7 points following anodal tsDCS (t4-tB1 comparison). The left lower extremity muscle groups showed a 5-point increase following sham (t3-tB2 comparison), and increased by 6 points following anode stimulation (t4-tB1 comparison). Spinal cord independence measure-III showed a 3-point increase following sham stimulation (t3-tB0 comparison), and scores increased by 1 more point following anodal stimulation (t4-tB1 comparison) (Figure 3).

Transcranial magnetic stimulation and MEP amplitudes. Patient A with an incremental increase of 10% of stimulus intensity (%RMT), the MEP amplitudes showed a gradual increase of 5 points on average (t0). Similarly, the increase in %RMT consistently increased MEP amplitudes post sham
Figure 2 - Graphical representation of outcome measures of patient A. A) 10 minute walk test (10MWT), B) spinal cord independence measure-III C) Berg balance scale points, D) manual muscle test, and E) modified ashworth scale. tA0: first baseline prior to sham stimulation, t1: post-sham stimulation, tA1: second baseline prior to cathodal stimulation, t2: post-cathodal stimulation

Figure 3 - Graphical representation of outcome measures of patient B. A) 10 minute walk test (10MWT), B) spinal cord independence measure-III, C) berg balance scale, D) manual muscle test, and E) modified ashworth scale. tB0: first baseline prior to sham stimulation, t3: post-sham stimulation, tB1: second baseline prior to anodal stimulation, t4: post-anodal stimulation
Stimulation of chronic spinal cord injury ... Abualait & Ibrahim

stimulation and also highlights that anodal stimulation modulated the supraspinal inhibitory mechanisms of muscle tone. Moreover, cathodal stimulation also modulated the supraspinal inhibition of tone in an opposite way. Surprisingly, following multiple sessions of cathodal stimulation (t2), functional ability, represented by SCIM-III scores, did not deteriorate despite a decrease in spasticity on the MAS. This might be attributed to the repetitive execution of gait training, which led to an increase in functional ability. It is possible that the decrease in spasticity did not reach the threshold for deterioration of functional activities.

Discussion. In this study, sham tsDCS induced a slight improvement in walking speed, muscle strength, balance, and functional ability of both patients (A) and (B). A possible explanation might be that repetitive motor learning, via locomotor training, improves these functional mobility measures. However, sham stimulation showed no effect on spasticity which indicates that sham has no effect on the supraspinal inhibitory mechanisms of muscle tone. Spasticity has been used as a means to support and help with functional activities such as standing and walking. This explains how an increase in spasticity on the MAS led to an increase in functional ability following anodal stimulation and also highlights that anodal stimulation modulated the supraspinal inhibitory mechanisms of muscle tone.

Patient B, the increase in %RMT led to a parallel increase in MEP amplitudes at baseline (t0) and post sham (t1). Post anodal stimulation (t3), MEP amplitudes increased initially and then plateaued at 0.55 mV (at 130% RMT) with the increase in %RMT to the right brain. Alternatively, an increase in stimulus intensity to the left brain initially increased MEPs and then led to their decrease at 130% RMT (Figure 4).

**Figure 4** - Relationship between stimulus intensity (%RMT) and MEP amplitude (mV) following stimulation of the right and left brain in A& B) patient A and C & D) patient B.
level. The increase in MEPs post-sham might be due to repetitive practice of the functional walking task which eventually increased corticospinal output through neuroplastic changes. It is noteworthy that while sham stimulation increased corticospinal excitability with the increase in %RMT, anodal stimulation increased MEPs only to a point after which MEPs deteriorated. However, this observation is not surprising as previous studies have observed similar results. Previous evidence has highlighted the effect of anodal tsDCS in prompting a hyperpolarization block to the impulses of descending cortical pathways. Therefore, in line with previous studies, it can also be concluded that tsDCS modulates ascending and descending spinal pathways and affects lower extremity functional measures in patients with SCI.

In conclusion, transcutaneous spinal direct current stimulation can be used, as a therapeutic technique, in combination with other interventions to induce neuroplastic after-effects changes and promote functional outcome measures such as reducing muscle tone, improving balance, and gait characteristics in patients with incomplete SCI. Combining tsDCS with gait training appears to enhance lower extremity motor function. Anodal tsDCS improves lower extremity muscle strength and increases muscle tone, which may subsequently contribute in enhancing overall locomotor ability and independence level. On the other hand, cathodal tsDCS can be used to decrease spasticity in patients with incomplete SCI. Future work should be done with a bigger sample size to investigate changes in the functional abilities of patients with SCI. Moreover, the effect of the application of tsDCS on different chronicity of SCI should be assessed.

Acknowledgment. The authors are thankful to Mr. Abdullah Alghazwani, Department of Physical Therapy, College of Applied Medical Sciences, Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia, for his great help in this work. Authors would like to thank Scribendi, the Editing and Proofreading Services for English Documents (http://www.scribendi.com) for the English language editing services.

References

1. Khan F, Amatya B, Galea MP, Gonzenbach R, Kesselring J. Neurorehabilitation: applied neuroplasticity. J Neurol 2017; 264: 603-615.
2. Labruyère R, van Hedel HJ. Strength training versus robot-assisted gait training after incomplete spinal cord injury: a randomized pilot study in patients depending on walking assistance. J Neuroeng Rehabil 2014; 11: 4.
3. Boes AD, Kelly MS, Trapp NT, Stern AP, Press DZ, Pascual-Leone A. Noninvasive brain stimulation: challenges and opportunities for a new clinical specialty. J Neuropsychiatry Clin Neurosci 2018; 30: 173-179.
4. Stagg CJ, Antal A, Nitsche MA. Physiology of transcranial direct current stimulation. J ECT 2018; 34: 144-152.
5. Bocci T, Marceglia S, Vergari M, Cognetto V, Cogiamanian F, Sartucci F, et al. Transcutaneous spinal direct current stimulation modulates human corticospinal system excitability. J Neurophysiol 2015; 114: 440-446.
6. Powell ES, Carrico C, Raithatha R, Salyers E, Ward A, Sawaki L. Transvertebral direct current stimulation paired with locomotor training in chronic spinal cord injury: A case study. Neurorehabilitation 2016; 38: 27-35.
7. Sadeghi M, McEvor J, Finlayson H, Sawatzky B. Static standing, dynamic standing and spasticity in individuals with spinal cord injury. Spinal Cord 2016; 54: 376.
8. Ahmed Z. Trans-spinal direct current stimulation modifies spinal cord excitability through synaptic and axonal mechanisms. Physiol Rep 2014; 2: 12157.
9. Vrabec T, Bhadra N, Van Acker G, Bhadra N, Kilgore K. Continuous direct current nerve block using multi contact high capacitance electrodes. IEEE Trans Neural Syst Rehabil Eng 2016; 25: 517-529.
10. Albuquerque PL, Campêlo M, Mendonça T, Fontes LA, de Mattos Brito R, Monte-Silva K. Effects of repetitive transcranial magnetic stimulation and trans-spinal direct current stimulation associated with treadmill exercise in spinal cord and cortical excitability of healthy subjects: A triple-blind, randomized and sham-controlled study. PLoS One 2018; 13: 0195276.