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ORIGINAL RESEARCH

Intensity Dependent Effects of Transcranial Direct Current Stimulation on Corticospinal Excitability in Chronic Spinal Cord Injury

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Abstract

Objective: To investigate the effects of anodal transcranial direct current stimulation (a-tDCS) intensity on corticospinal excitability and affected muscle activation in individuals with chronic spinal cord injury (SCI).

Design: Single-blind, randomized, sham-controlled, crossover study.

Setting: Medical research institute and rehabilitation hospital.

Participants: Volunteers (N=9) with chronic SCI and motor dysfunction in wrist extensor muscles.

Interventions: Three single session exposures to 20 minutes of a-tDCS (anode over the extensor carpi radialis [ECR] muscle representation on the left primary motor cortex, cathode over the right supraorbital area) using 1mA, 2mA, or sham stimulation, delivered at rest, with at least 1 week between sessions.

Main Outcome Measures: Corticospinal excitability was assessed with motor-evoked potentials (MEPs) from the ECR muscle using surface electromyography after transcranial magnetic stimulation. Changes in spinal excitability, sensory threshold, and muscle strength were also investigated.

Results: Mean MEP amplitude significantly increased by approximately 40% immediately after 2mA a-tDCS (pre: 0.36±0.1mV; post: 0.47±0.11mV; $P=.001$), but not with 1mA or sham. Maximal voluntary contraction measures remained unaltered across all conditions. Sensory threshold significantly decreased over time after 1mA ($P=.002$) and 2mA ($P=.039$) a-tDCS and did not change with sham. F-wave persistence showed a nonsignificant trend for increase (pre: 32%±12%; post: 41%±10%; follow-up: 46%±12%) after 2mA stimulation. No adverse effects were reported with any of the experimental conditions.

Conclusions: The a-tDCS can transiently raise corticospinal excitability to affected muscles in patients with chronic SCI after 2mA stimulation. Sensory perception can improve with both 1 and 2mA stimulation. This study gives support to the safe and effective use of a-tDCS using small electrodes in patients with SCI and highlights the importance of stimulation intensity.

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In 2013, an estimated 273,000 individuals (range, 238,000–332,000) in the United States were reported to be suffering from impairment as a result of spinal cord injury (SCI).[1] The estimated incidence rate of new cases was 12,000 per annum, with approximately half of the reported cases resulting in tetraplegia

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(injury to the cervical spine),[1] leading to loss of arm and/or hand function. This loss of upper-limb function is perceived by many to be the greatest debilitating loss after SCI.[2,3] Varying degrees of impairment can severely limit the level of independence[4-6] and increase the risk of developing secondary health problems (eg, cardiovascular disease) because of physical inactivity.[7] Consequently, recovery of motor activity and residual muscle strength is a major area of interest in rehabilitation, aiming to improve the quality of life of individuals with SCI.[8]

Rehabilitation strategies for individuals with tetraplegia are extensive, involving surgical, pharmacologic, and/or physical exercise interventions.[9] Existing SCI therapies involving exercise training,[7] neuromuscular stimulation,[10] massed practice,[11] and robotic-assisted training[12] have all shown some degree of improved motor strength and/or function. Despite these exciting results, more effective interventions for improving upper-limb function and understanding the mechanisms of motor recovery are still needed.

A previous study by the authors showed that clinically weak muscles caused by chronic SCI may still have intact motor-evoked responses when tested by transcranial magnetic stimulation (TMS),[13] uncovering an anatomic substrate for recovery. Therefore, paralyzed muscles that respond to TMS may have the ability to regain some functionality by exploiting therapeutic approaches targeting the brain, such as transcranial direct current stimulation (tDCS). The most encouraging evidence for the use of anodal transcranial direct current stimulation (a-tDCS) in patient populations is derived largely from studies conducted in the area of stroke. Studies show that an increase in cortical excitability targeting areas of the brain-controlling muscles with reduced output is correlated with better motor performance.[14] Although recovery of motor function after SCI largely depends on the amount of intact anatomic connections, recovery may also depend on plasticity of the motor cortex and the corticospinal tract (CST),[6] as seen in the stroke population.

Neural plasticity occurs spontaneously after SCI, supported by evidence that the sensory motor cortex can undergo reorganization after SCI.[15,16] Other recovery mechanisms may include nerve root recovery, axonal sprouting, and changes in gray matter at or neighboring the level of the spinal cord lesion.[17-19] Rearrangement or creation of new circuitry within the CST may also be crucial for functional recovery, as shown in rodent studies.[20] Despite these findings, more work is needed to understand how plasticity in the human primary motor cortex (M1) and CST is associated with recovery of motor function.

The main aim of this feasibility and proof-of-principle study was to investigate the effectiveness of single-session a-tDCS interventions at different intensities (1mA, 2mA, sham) when targeting upper-limb muscles, caudal to the spinal lesion, with diminished motor output in individuals with chronic SCI. Smaller electrodes have been shown to increase focality and local intensity in the produced electric fields compared with standard larger electrodes ($35cm^2$)[21,22]; therefore, smaller Pi electrodes ($3.14cm^2$) have been used to deliver the direct current stimulation in the present study. A secondary aim was to test the safety of 1 and 2mA a-tDCS using $3.14cm^2$ (Pi) electrodes on individuals with chronic SCI. We hypothesized that a-tDCS would be a safe and effective method for enhancing corticospinal excitability, and the magnitude of change would be dependent on stimulation strength.

List of abbreviations:

AIS	**American Spinal Injury Association Impairment Scale**
ANOVA	**analysis of variance**
a-tDCS	**anodal transcranial direct current stimulation**
CST	**corticospinal tract**
ECR	**extensor carpi radialis**
ES	**electrical stimulation**
MEP	**motor-evoked potential**
MSO	**maximal stimulator output**
MVC	**maximum voluntary contraction**
M1	**primary motor cortex**
RMS	**root-mean-square**
rMT	**resting motor threshold**
SCI	**spinal cord injury**
tDCS	**transcranial direct current stimulation**
TMS	**transcranial magnetic stimulation**
UEMS	**upper extremity motor score**
VAS	**visual analog scale**

Methods

Participants and study design

Nine volunteers with SCI (5 men, 4 women; age range, 20–56y) participated in the study. Individuals were recruited if they fulfilled the following criteria: traumatic SCI at the cervical level (C4-7); some degree of motor function in wrist extension scoring 1 to 4 out of 5 on the Medical Research Council Scale for motor strength in the right extensor carpi radialis (ECR) muscle; a chronic injury (>8mo after injury); and tolerance to sitting upright for at least 1 hour. Individuals were excluded if they were medically unstable or had a change in medication during the study, a progressive neurodegenerative disorder, concomitant traumatic brain injury or stroke, clinically significant cognitive impairment, or presented contraindications to brain stimulation (history of seizures/epilepsy, presence of metallic implants in the brain, pacemaker, pregnancy).

Participants randomly received either 1 or 2mA a-tDCS or sham stimulation. Clinical and functional evaluations were performed prior to the brain stimulation intervention and included the upper extremity motor score (UEMS), American Spinal Injury Association Impairment Scale (AIS), Spinal Cord Independence Measure version III, and visual analog scale (VAS) pain questionnaires. Outcome measures included changes in corticospinal excitability, spinal excitability, sensory threshold, and muscle maximum voluntary contraction (MVC). These measures were recorded before (pre), immediately after (post), and 20 minutes after (follow-up) the end of each intervention (fig 1).

The study was approved by the Burke Medical Rehabilitation Institutional Review Board and conformed to the standards set out by the 1964 Declaration of Helsinki.

tDCS intervention

Participants remained seated in their own wheelchair or were provided with a comfortable chair. The Starstim noninvasive wireless tDCS neurostimulator[a] was used to deliver the direct current. The Starstim neurostimulator included a wireless neoprene cap based on the international 10-20 system, which was placed on each participant's head by aligning the central CZ electrode position with the vertex.

Small silver/silver chloride gelled electrodes, with a surface contact area of $3.14cm^2$, specific to the Starstim device (Pi electrodes[a]), were placed over the left M1 at the optimal site for the right ECR muscle (C3; anode) and the contralateral supraorbital

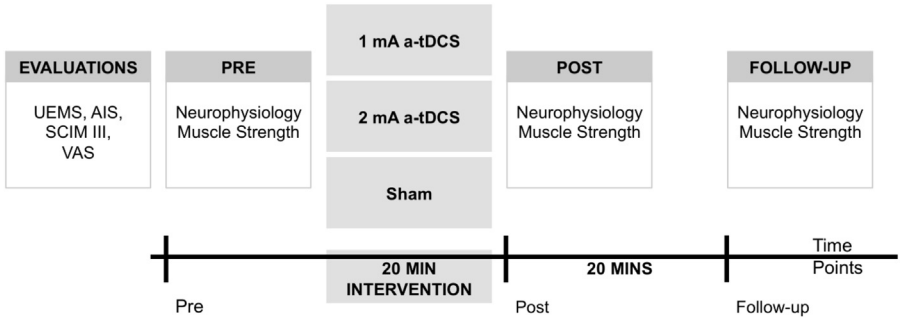

Fig 1 Study design schematic. During the first visit, initial evaluations (UEMS, AIS) and questionnaires (SCIM III, VAS) were completed. During the 20-minute intervention period, participants received either 1 or 2mA of a-tDCS or sham. Neurophysiology and muscle strength measures were recorded at 3 time points (pre, post, follow-up). Abbreviation: SCIM III, Spinal Cord Independence Measure version III.

area (AF8; cathode) (fig 2). The electrodes were connected to a control device, which was wirelessly connected to a computer with NIC software (version 1.2).[a]

During anodal stimulation, direct current was delivered from a current-control circuit in a battery-driven stimulator inside the control device. The current was set at either 1 or 2mA intensity and was applied for 20 minutes. For the sham stimulation, the electrodes were placed in the same position, and participants received a short ramp up/down event at the beginning and end of the stimulation period without any current between the 2 events.[23]

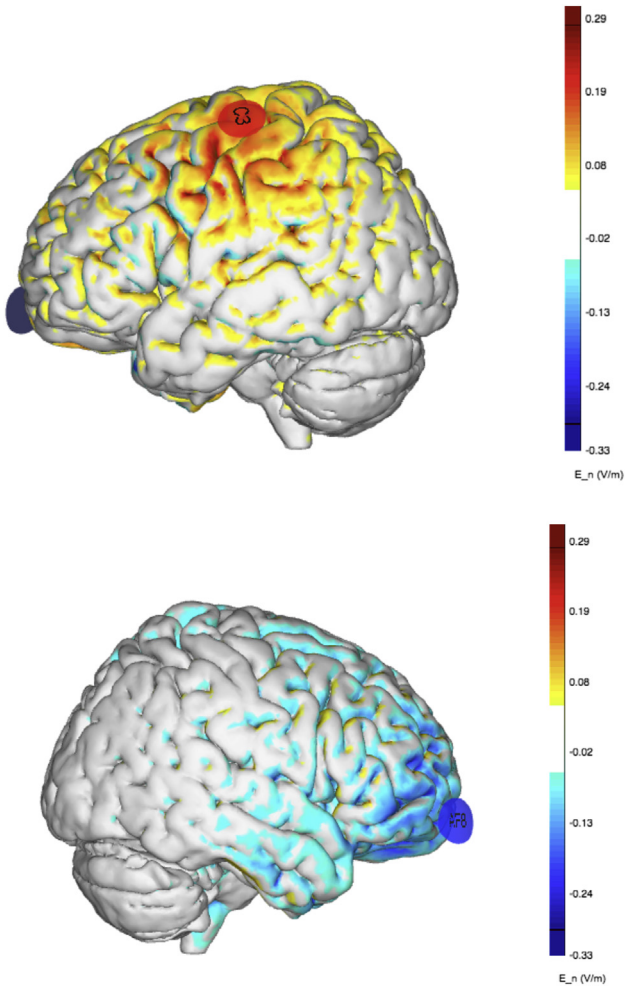

Fig 2 Electric field (normative component) generated by the montage (+C3, -AF8) using Pi electrodes (3.14cm^2 silver/silver chloride electrodes). Positive/negative values indicate anodal/cathodal stimulation (normative component of the electric field pointing inward/outward at the cortical surface).

Electromyography and TMS

A bipolar surface electromyography electrode (1cm diameter, 2cm interpole distance)[b] was placed over the right ECR muscle, with the forearm relaxed in a pronated position and supported by a cushion. The electromyographic activity was amplified and filtered on site (×1000 gain, band-pass filter 20–400Hz), digitized at 2kHz (CED 1401[c]), and stored for offline analysis using Spike 2.6 software.[c] Measurements were performed at rest and during a maximal muscle contraction. During the experiment, free-running electromyography was continuously monitored with visual feedback of electromyography silence to ensure complete muscle relaxation during resting trials.

The ECR muscle was selected for recording because restoration of motor function in this muscle can help increase independence with activities of daily living (eg, self-feeding, bathing, dressing, toileting) and mobility needs (eg, surface transfers, transitional movements, crutch walking, wheeled mobility).[3]

A figure-of-8 coil (Model DB-80),[d] connected to a MagPro X100 Series magnetic stimulator,[d] was placed congruent to the head with the handle rotated 45° lateral from midsagittal to induce currents in the brain perpendicular to the central sulcus. The optimal site for eliciting the greatest motor-evoked potential (MEP) amplitude from the right ECR muscle was identified by moving the coil in 1-cm steps around the initial stimulation site while delivering single TMS pulses at a constant suprathreshold intensity. The resting motor threshold (rMT) was defined as the minimum TMS intensity required to elicit a reliable MEP amplitude of >50μV in at least 50% of consecutive trials.

Care was taken to control the stimulus parameters, time of day, equipment, and procedure between sessions and the participant's arousal level.

Peripheral nerve stimulation

Electrical stimulation (ES) to the right radial nerve was delivered using a Digitimer DS7AH constant current stimulator[e] (200μs duration; square pulses), with surface bipolar electrodes secured in place 8 to 10cm above the elbow on the lateral upper arm. The same intensity was used throughout the session, and the supramaximal M-wave amplitude was monitored to ensure it remained constant across each time point.

Outcome measures

Neurophysiological outcomes

The neurophysiology evaluation consisted of corticospinal excitability (resting MEP amplitude), sensory threshold, and spinal excitability (F-wave persistence).

The resting MEP amplitude was measured during 12 single-pulse TMS stimuli set at 130% of the rMT and applied to the left M1 optimal site for the right ECR muscle.

The sensory perceptual threshold was measured using ES to the right radial nerve. The sensory threshold was determined by decreasing the stimulation intensity in large decrements every 5 seconds, with smaller steps of 0.5mA when approaching the threshold. At every step, the participant was asked if they could still feel the ES. The lowest stimulation perceived by the participant was recorded.

To investigate the effects of a-tDCS on spinal excitability, F-wave persistence was calculated by applying supramaximal ES over the right radial nerve during 20 consecutive stimuli, separated by a 5-second rest period.

Maximal voluntary contraction

To determine the effects of a-tDCS on voluntary motor activity, root-mean-square (RMS) measured surface electromyographic activity during 3 attempted MVCs of the right ECR muscle.

Safety

Safety using 1 and 2mA a-tDCS was assessed through a standard adverse event report questionnaire recording responses to the following question: Did you experience any headaches, neck and scalp pain, scalp redness or burns, tingling sensations, sleepiness, trouble concentrating, or acute mood changes as a direct result of the tDCS?[24]

Data analysis

Average peak-to-peak amplitude was determined for MEPs during rest and maximal contraction. The first 2 resting responses were excluded to allow responses to settle, resulting in 10 MEPs being used for analysis. During each attempted MVC, voluntary motor activity measured by RMS was assessed (rectified, average electromyography over a 0.5-s window).

The sensory threshold was recorded as a single value at each time point. The supramaximal M-wave amplitude was measured and averaged from 20 stimuli. F-wave persistence was calculated by dividing the number of present F waves by the number of peripheral stimuli (20 stimuli) and representing the value as a percentage.

Raw and normalized values were used for analysis. Results are presented as mean ± SD unless otherwise stated.

Statistical analysis

A 2-way repeated-measures analysis of variance (ANOVA) was used to compare changes in outcome measures induced by the 3 interventions (1mA/2mA/sham; N=9) at the 3 different time points (pre, post, follow-up). Multiple 2-way repeated-measures ANOVAs were also performed to compare changes between pairs of interventions (1mA/sham, 2mA/sham, 1mA/2mA) at 3 different time points. One-way repeated-measures ANOVAs of individual interventions were performed when a significant effect was found in the pairs. Two-tailed paired *t* tests of individual time points, between different interventions or within the same intervention, were also performed. The stimulus intensities of both the cortical and peripheral stimuli were analyzed by a 2-tailed paired *t* test between sessions.

When a significant interaction effect was found, post hoc comparisons were performed using a Bonferroni correction for multiple comparisons. If the Mauchly test for sphericity was violated, the Huynh-Feldt correction was used. Statistical analysis was carried out with predictive analytics software (SPSS version 21.0[f]). Significance was set at $P<.05$.

Results

Participant clinical characteristics: baseline data

Nine participants with SCI (5 men, 4 women; 40.8±14.2y; range, 20−56y) with motor complete or incomplete (5 AIS grade B, 4 AIS grade C) chronic traumatic lesions at the cervical level (C4-6) completed the study (Table 1). All but 1 participant was right-handed prior to injury, and the average time since injury was 5.9±2.9 years (range, 0.75−10.5y).

All participants had severe upper-limb impairment, with lack of motor control in the forearm muscles. The UEMS graded 5 muscles from 0 (total paralysis) to 5 (full range active movement against gravity and normative resistance).[25] The total UEMS for the right arm was 13.7±3.9 (median, 12; range, 10−21) and for the left arm was 13.4±4.8 (median, 13; range, 6−24). More specifically, motor power for the 5 muscles on the right were as follows: elbow flexors was 4.9±0.3 (median, 5; range, 4−5); wrist extensors was 3.6±0.7 (median, 4; range, 2−4); elbow extensors was 3.2±1.1 (median, 3; range, 2−5); finger flexors was 0.9±1.4 (median, 0; range, 0−4); and finger abductors was 1.1±1.5 (median, 1; range, 0−4).

The Spinal Cord Independence Measure version III questionnaire was completed to assess 3 areas of function (self-care, respiration and sphincter management, mobility), with an overall score ranging from 0 (total dependence) to 100 (complete independence). The total and 3 subdomain scores were 49.4±24.9 (Spinal Cord Independence Measure version III total), 9.9±6.9 (self-care), 27.1±8.7 (respiratory and sphincter management), and 12.4±10.3 (mobility: in and out). Based on the VAS, 3 participants were classified as pain free, 2 participants were classified as having low-intensity pain, and 4 participants were classified as having high-intensity pain.

Corticospinal excitability results

Baseline values for resting MEP amplitude were similar between interventions (mean ± SE, 0.37±0.05mV). A significant interaction effect ($F_{4,32}=4.955$; $P=.003$) was found for the changes in MEP amplitude among the interventions. Further analysis showed a significant mean increase of 21% post 2mA a-tDCS when compared with baseline ($F_{2,16}=7.377$; $P=.005$) (fig 3), with a significant increase of approximately 40% seen from pre to post (mean ± SE, 0.36±0.1 to 0.47±0.11mV; $P=.001$). No changes were observed for 1mA a-tDCS or sham.

The stimulation intensities used to obtain the rMT were not significantly different between 1mA (64%±17% maximal stimulator output [MSO]), 2mA (59%±9% MSO), or sham (66%±16% MSO). All participants presented MEP responses.

Sensory threshold

The baseline sensory threshold was similar between interventions. A repeated-measures ANOVA showed a significant difference between interventions ($F_{2,16}=13.63$; $P=.000$).

Table 1 Patient characteristics

Identification No.	Age (y)	Sex	Handedness	Time Since Injury	Level of Injury	AIS Grade	Right ECR Motor Power	UEMS Score	SCIM III Score	VAS Score
1	34	M	R	10y 6mo	C4	B	2	21	31	PF
2	32	F	R	5y 8mo	C6	B	3	22	29	HI
3	55	F	R	5y	C6	B	3	24	31	HI
4	55	M	R	4y 11mo	C5	B	4	28	20	PF
5	45	M	R	8y 10mo	C5	C	4	27	52	HI
6	22	M	L	6y 10mo	C5	C	4	25	43	PF
7	20	M	R	9mo	C5	B	4	27	68	LI
8	48	F	R	5y 6mo	C4	C	4	25	88	LI
9	56	F	R	5y 6mo	C5	C	4	45	83	HI

Abbreviations: AIS grade B, motor complete injury; AIS grade C, sensory and motor incomplete injury; ECR, right motor power; 0—5; F, female; HI, high-intensity pain; L, left; LI, low-intensity pain; M, male; PF, pain free; R, right; SCIM III, Spinal Cord Independence Measure version III questionnaire (0—100); UEMS, UEMS from the AIS (right and left; 0—50).

Further analysis showed significant changes for both 1mA ($F_{2,16}=9.673$; $P=.002$) and 2mA ($F_{2,16}=4.0$; $P=.039$) a-tDCS. An additional t test analysis revealed a significant difference between pre and post (mean ± SE, 4.7±1.2 to 4.2±1.2; $P=.009$) and pre and follow-up (mean ± SE, 4.7±1.2 to 4.0±1.2; $P=.012$) for 1mA a-tDCS and pre and follow-up (mean ± SE, 5.2±1.9 to 4.4±1.2; $P=.05$) for 2mA a-tDCS. No changes were observed after sham.

Spinal excitability results

F waves were present in approximately 33% of stimuli and remained constant throughout the study. Despite the lack of significant changes, 2mA a-tDCS displayed a tendency for increased spinal excitability in F-wave persistence (mean ± SE, pre: 32%±12%; post: 41%±10%; follow-up: 46%±12%). Supramaximal M-wave amplitude was not significantly different across interventions and remained consistent throughout the study.

Muscle strength results: MVC

No changes in RMS were found among the 3 interventions.

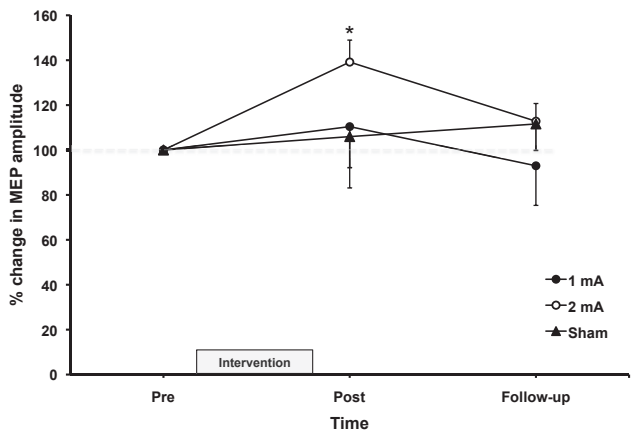

Fig 3 Normalized MEP amplitude changes over time (N=9). Values are presented as mean ± SE. *Significant difference ($P=.001$).

Safety assessment

Overall, participants tolerated the intervention well. One participant reported a dull headache around the right supraorbital region after 2mA a-tDCS. Another reported sensitivity to light after 1mA a-tDCS. The same individual reported a mild transient headache after sham. Four participants reported itching under the electrodes during 1mA a-tDCS, and 5 reported itching under the electrodes during 2mA a-tDCS. All symptoms dissipated soon after the cessation of the intervention and ranged from mild to moderate in intensity. Importantly, active a-tDCS did not worsen pain in any of the participants, with 2 participants (high-intensity pain: n=1, low-intensity pain: n=1) reporting a decrease in pain symptoms the next day after 1mA a-tDCS. Only 1 of these participants (with the high-intensity pain) reported a further decrease in pain symptoms after 2mA a-tDCS.

Discussion

The observed transient improvements in the human motor and sensory systems after a-tDCS for 20 minutes supports the application of a-tDCS in individuals after chronic SCI. The magnitude of change in corticospinal excitability appeared to be intensity dependent, and improvements in sensory perception were more sensitive. These findings lend support to the theory that muscles with reduced motor output can demonstrate an a-tDCS—related improvement in corticospinal activation, regardless of the preexisting deficit in motor performance/strength.

Corticospinal excitability after a-tDCS

Several studies have investigated corticospinal excitability after 1mA[26-28] and 2mA[29-33] a-tDCS, usually with large sponge electrodes (25 or 35cm^2).[22] However, there are some studies investigating stimulation strength as low as 0.2mA[14,28] and as high as 5mA.[26] Stimulation duration is commonly reported between 10 and 20 minutes; however, shorter durations of ≤5 minutes also have been used.[28,34] The results of these studies suggest that longer-lasting robust effects are usually found with higher intensities (2mA)[28] and/or longer (≥10min) durations[28,34]; however, higher intensities and longer durations have not been extensively tested. Nitsche and Paulus[28] attribute the enhanced effects to more robust neurophysiological changes. However, the relation of physiological changes to stimulation is less understood

in neurologic populations, and no study to date has systematically investigated corticospinal excitability after 20 minutes of 1 and 2mA a-tDCS in a single-session, randomized, sham-controlled study in chronic SCI.

In the present study, increased MEP amplitude was observed after 20 minutes of 2mA a-tDCS, in line with the assumption that motor excitability is dependent on stimulation intensity, because 1mA failed to significantly increase responses. Based on healthy studies, increased corticospinal excitability after brain stimulation can be associated with increased spontaneous firing rates, prolonged membrane potential shifts,[28,35] long-term potentiation-like mechanisms,[35,36] and/or decreased inhibitory interneuronal activity.[37,38] After SCI, some axons of the CST at the site of the injury will be damaged. It is possible that spontaneous creation of alternate circuits may restore some function by rerouting the signals from above to below the injury.[17] However, because the study involved a single session of a-tDCS, sprouting of corticospinal axons is unlikely to have occurred because of the effects of stimulation. More research is needed to further elucidate the part that each mechanism plays.

Despite the postintervention MEP amplitude increase after 2mA, changes in corticospinal excitability were relatively short-lived. A possible explanation for the lack of prolonged effects is that the responses after a-tDCS ceased prematurely. In the present study, excitability was measured immediately and 20 minutes after the application of a-tDCS. These time points may not have been long enough to uncover tDCS-related effects. Based on the findings of Batsikadze et al[33] with healthy subjects, 2mA a-tDCS over the first dorsal interosseous motor area of the left M1 for 20 minutes led to significant increases in MEP amplitudes at 60 and 90 minutes, and not before. This may also be true for lower intensities. Alternatively, extending the intervention for another 10 minutes may have produced a more robust effect. However, Nitsche and Paulus[28] previously showed that 3 minutes of 1mA, or 5 minutes of 0.6mA, was enough to induce after effects in healthy subjects. It is possible that 1mA was ineffective at reducing intracortical inhibition compared with 2mA, which may have been more prominent at increasing activity in the excitatory circuits. An additional explanation may be that insufficient current was delivered to the targeted motor area (because of shunting); however, the use of small electrodes should decrease this effect with respect to traditional large sponges (depending on factors, eg, interelectrode distance). However, more studies are needed to test these theories in patient populations.

The stimulation parameters used in the present study failed to produce changes in voluntary muscle activation measured by RMS. Despite the increase of MEP amplitude in the wrist extensor muscle after a-tDCS stimulation, there was no parallel increase in the generation of muscle voluntary activation.

Peripheral nerve stimulation after a-tDCS

To see if changes in the MEP responses are attributed to changes at the spinal level, peripheral stimulation of the radial nerve was used to measure sensory threshold and spinal excitability.

In the present study, sensory threshold significantly decreased irrespective of stimulation intensity when compared with sham, supporting heightened somatosensory ability after a-tDCS. Increases in spinal excitability lacked significance but showed a tendency for increased F-wave persistence (+33%) after 2mA a-tDCS. Continued poststimulation may have significantly changed spinal excitability because of a possible delay in responses, as previously seen with TMS-elicited MEP amplitudes.[33] The results of the present study suggest that a-tDCS at higher intensities (2mA) may stimulate spinal pathways, whereas stimulation at lower intensities (1mA) is insufficient at producing spinal effects.

The theory that noninvasive brain stimulation techniques (eg, repetitive TMS) can modify both cortical and spinal network excitability is further strengthened by results of several studies where transcranial stimulation, either above or below the rMT, changed excitability of nonmonosynaptic and monosynaptic spinal reflex pathways.[39,40] Although the study design did not allow us to draw these conclusions, if the 2 networks overlap after a-tDCS, changes in both cortical and spinal motor circuits should be considered when interpreting results and when designing future studies. Overall, the results of the present study reveal that spinal and cortical networks may benefit from a-tDCS interventions at higher intensities.

Safety aspects of a-tDCS

To date, all tDCS studies have been performed free of serious adverse events (eg, psychotic episodes, seizures).[41] Commonly reported side effects include transient skin reactions below the stimulating electrodes (eg, local erythema)[42] and focal tingling (70.6%), fatigue (35.3%), itching (30.4%), slight burning (21.6%) or mild pain sensations (15.7%) under the electrodes, and headaches (4.9%) after tDCS.[41,43] However, these effects are also reported after sham, consisting of the ramp up/down events without sustained current.

Skin lesion after tDCS is rare, but it has been reported.[44,45] Previous studies have shown no evidence of neuronal damage[46] or magnetic resonance imaging−measured cerebral edema[47] after the application of 1mA a-tDCS. Increasing anodal stimulation to 2mA for 20 minutes has also shown no evidence of heating under the electrodes[37] or pathologic waveforms during electroencephalography recordings.[48] Other side effects (eg, nausea, sleepiness, difficulties with concentration) are rare.[43] In addition, single and repeated sessions (5d) of 1 and 2mA are reported as safe.[33,49,50]

Despite the known safety aspects of a-tDCS, stimulation paradigms tend to differ between both healthy and patient population studies. Therefore, it is important to include the safety aspects of the present study. All participants tolerated 20 minutes of active a-tDCS with ease, confirming the safe use of a-tDCS in chronic SCI populations while using small gelled electrodes.

Before the application of 2mA a-tDCS, great care and consideration was given to safety. Because several studies using smaller silver/silver chloride Pi gelled electrodes[51-53] have been performed without relevant side effects, we considered it safe to apply a single session of 1 and 2mA a-tDCS using 3.14cm^2 silver/silver chloride Pi electrodes for 20 minutes. Furthermore, current density (current intensity to the electrode contact area) is not a good parameter to linearly extrapolate the magnitude of the generated electric fields[54] in the brain or the levels of discomfort.[55]

Study limitations

There are several limitations of this study that need to be considered when interpreting the results. Small numbers and the highly heterogeneous clinical presentation, even for participants with the same level of injury, may have contributed to the lack of significant differences seen in some measures. The findings are also limited by the study design, with only 2 postmeasures

performed; conclusions regarding the long-term effects cannot be made. Stimulation parameters used in the current study (20min; 1mA, 2mA, sham tDCS; left M1; anode C3 and cathode AF8 placement in the 10/20 system; 3.14cm^2 gelled electrodes) have not been performed before; therefore, the results cannot be directly compared with other studies. Given the placement of the anode electrode over the left M1 (C3), the precise targeting of the ECR muscle may have been different for each participant because of a possible cortical reorganization after injury. Moreover, the investigator was not blinded to the intervention, and it was not verified whether the participants were effectively blinded. Despite these limitations, the randomized sham-controlled nature of the study supports the significance of the findings.

Conclusions

The findings of the present study demonstrate for the first time, to our knowledge, that a 20-minute single session of a-tDCS leads to increases in corticospinal excitability for individuals with chronic SCI. Not only does a-tDCS modulate activity in the motor system, but changes in the sensory systems also occur. The magnitude of these changes may be intensity dependent; however, future studies should not rule out the potential of stimulation strength, duration, or frequency of sessions when investigating other experimental conditions. Overall, the study demonstrates the safety and efficacy of using a-tDCS to modulate changes in both motor and sensory systems after chronic SCI. It remains to be tested if the study findings translate into a long-term rehabilitative therapy, where multiple sessions of a-tDCS yield stronger and longer-lasting changes in sensorimotor physiology and function. More studies are warranted to confirm the therapeutic effect of a-tDCS at enhancing motor function in chronic SCI.

Suppliers

a. Neuroelectrics.
b. Biometrics Ltd.
c. Cambridge Electronic Design Ltd.
d. MagVenture Tonika Elektronik.
e. Digitimer Ltd.
f. IBM Corp.

Keywords

Anodal stimulation transcranial direct current stimulation; Rehabilitation; Spinal cord injuries; Upper extremity

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