

# Transcranial Direct Current Stimulation to Enhance Motor Function in Spinal Cord Injury: Pilot Data

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**Abstract**—Several lines of evidence indicate that a non-invasive form of brain stimulation called transcranial direct current stimulation (tDCS) can facilitate motor recovery after stroke. However, there is no available data about how tDCS may enhance outcomes of intensive, task-oriented upper extremity (UE) motor training in people with spinal cord injury (SCI). Moreover, there is a lack of effective interventions to enhance recovery of UE motor function after SCI, especially in chronic cases. Thus, we are conducting a double-blind, randomized, controlled study of how tDCS paired with intensive task-oriented training affects UE motor function in subjects with motor incomplete cervical SCI. Our central hypothesis is that subjects who receive *anodal* tDCS paired with intensive task-oriented training 3 days a week for 8 weeks will have significantly more improved UE motor performance than controls receiving *sham* tDCS paired with identical training. Furthermore, motor improvement will correlate with corticospinal reorganization (motor maps) measured by transcranial magnetic stimulation (TMS). Outcome measures for motor performance include Spinal Cord Independence Measure-III, Canadian Occupational Performance Measure, and Medical Research Council scale administered at baseline, at midpoint, and immediately post-intervention. Here, we present our preliminary results (n=2) of this ongoing study.

**Keywords**— neuroplasticity; neuromodulation; incomplete; occupational therapy; transcallosal modulation

## I. INTRODUCTION

According to the National Spinal Cord Injury Statistical Center, as many as 300,000 people in the United States are living with spinal cord injury (SCI) [1], with approximately 12,000 new cases each year [1]. Efforts to minimize neurologic damage in acute SCI have met with only limited success [2, 3]; and less than 1% of survivors completely recover [1]. Because the initial injury often occurs during early adulthood [1], SCI can translate to disproportionate health care costs associated with lifelong needs. Furthermore, almost two-thirds of SCI cases are cervical [1, 4], which constitutes etiology for

tetraplegia. The cost of clinical care for tetraplegia generally exceeds that of paraplegia because the presence or absence of upper extremity (UE) motor function can determine the difference between independence and need for assistance in many activities of daily living. In general, the loss of UE function that accompanies cervical SCI can dramatically affect meaningful, independent engagement in multiple life domains, including mobility, family relations/caregiver burden, societal integration, and general quality of life. Thus, it is important to establish effective interventions to maximize functional independence and prevent disability in chronic cervical SCI.

Extensive research validates the association between corticospinal neuroplastic change and motor recovery in neurological populations, including SCI [5-9]. Neuroplastic change can be upregulated by transcranial direct current stimulation (tDCS), a non-invasive form of neuromodulation [10-13]. Thus, tDCS is a promising therapeutic intervention to promote motor recovery in neurological populations [13-18]. Research in stroke shows that pairing tDCS with intensive task-oriented training can notably enhance neuroplasticity and UE motor function [10, 16, 19, 20]. This paired intervention may have similar effects in motor incomplete SCI, a condition in which a partially intact connection between the spinal cord and the brain allows persistent corticospinal responsiveness to sensory and motor input [21-24]. To establish first-ever evidence in subjects with motor incomplete SCI, we performed a feasibility study of whether anodal tDCS paired with intensive task-oriented training 3 days each week for 8 weeks leads to significantly more improved UE motor function than sham tDCS paired with identical training. We hypothesized that in both experimental conditions, motor improvement would correlate with corticospinal reorganization as measured by transcranial magnetic stimulation (TMS).

## II. METHODS

This feasibility study used a double-blind, sham-controlled, randomized, crossover design. Following baseline evaluation, we used an experimental design generator and randomizer program to determine the order of tDCS

conditions. We set the following inclusion criteria: **a)** traumatic, motor incomplete SCI sustained at neurological level C4-C8 and classified as C or D by the American Spinal Injury Association Impairment Scale (AIS; formerly known as ASIA; see also Table 1)[25]; **b)** SCI sustained at least 1 year prior to enrollment (ie, chronic); and **c)** at least 18 years old (no upper age range limit). By targeting the chronic phase of recovery, we minimized the potential confound of spontaneous recovery and focused on a population in great need of novel interventions. Exclusion criteria were targeted to minimize potential confounding variables and to ensure safety in TMS and tDCS. We excluded potential subjects who had **a)** history of head injury with loss of consciousness; **b)** history of seizures; **c)** history of severe alcohol or drug abuse, or psychiatric illness; **d)** cognitive deficits severe enough to preclude informed consent; **e)** positive pregnancy test or being of childbearing age and not using appropriate contraception; **f)** presence of ferromagnetic material in the cranium except in the mouth, including metal fragments from occupational exposure and surgical clips in or near the brain; **g)** pressure ulcers that might interfere with intervention; **h)** cardiac or neural pacemakers; **i)** fixed UE contractures; **j)** untreated depression; **k)** concurrent participation in occupational therapy; or **l)** within 3 months of recruitment, addition or change in the dosage of drugs known to affect neuroplasticity or exert detrimental effects on motor recovery.

We performed routine clinical and neurological evaluation during the screening of potential subjects, which included evaluation of sensory function (ie, light touch, temperature, pain (pin prick), vibratory sensation, proprioception, stereognosis, graphesthesia, and confirmation of AIS level). Past data, including radiographic studies and medical history, were obtained to confirm diagnosis, site, and type of lesion. Following Institutional Review Board approval of the study protocol, we consented and enrolled 2 male subjects with motor incomplete SCI. Subjects provided written consent after receiving a verbal and written explanation of the purposes, procedures, and potential hazards of the study. Table 1 shows subject demographics.

Table 1. Subject demographics.

Subject	Age	Time since injury	Etiology	ASIA; level	UE key muscles score (maximum 25)
1	30	12	MVA	C; C6-C6	R 13; L 17
2	62	1	MVA	C; C5-C6	R 13; L 13

Time since injury in years; MVA: motor vehicle accident; ASIA: Standard Neurological Classification of Spinal Cord Injury; UE: upper extremity; R: right; L: left

#### A. Evaluation

We conducted all evaluations at 3 time points (baseline; midpoint; immediately post-intervention). Outcome measures for motor performance included Spinal Cord Independence Measure-III (SCIM-III; primary outcome measure), Medical Research Council scale (MRC), and Canadian Occupational Performance Measure (COPM). The outcome measure for neuroplasticity was the change in UE motor map volume as determined with TMS (ie, normalized map volume (nMV)). nMV is a simple measure of the spread of the motor representation over multiple scalp sites. It is calculated as the sum of the normalized MEP (nMEP – the mean MEP at each scalp location, divided by the largest mean MEP) over all locations. The nMV ranges from 1 (for a map with only 1 active location) to a value that is equal to the number of active locations, if all locations gave equal responses. TMS procedures are considered very safe and well-tolerated [26]. There have been no adverse events reported, such as seizures, when TMS is applied following standard safety guidelines [26]. There is no evidence of long-term adverse effects, although short-term imaging changes may occur [27]. For TMS procedures, we applied silver/silver chloride ECG monitoring electrodes (P7, Lead-Lok, Sandpoint, ID) over the extensor digitorum communis muscles (EDC) bilaterally. We selected the EDC because it is the primary effector of a variety of functional motor tasks. The electromyographic signal (EMG) was amplified and filtered (band-pass 10Hz to 1kHz) using an isolated bioelectric amplifier (World Precision Instruments, Sarasota, FL) and was digitized for off-line analysis. We delivered TMS using a Magstim 200<sup>2</sup> stimulator fitted with a figure-eight shaped coil [28, 29] (Magstim, Whitland, Dyfed, UK). We located stimulus sites using a latitude/longitude-based coordinate system [30] co-registered with a template MRI using theBrainsight™ neuronavigation system (Rogue Research Inc, Montreal, Canada). The area of the motor cortex that, when stimulated, resulted in the largest response in the contralateral EDC, was designated the “hot-spot.” We defined the resting motor threshold at the hot-spot as the minimum TMS intensity (measured to the nearest 1% of maximum stimulator output) required to elicit motor evoked potentials (MEPs) of  $\geq 50\mu\text{V}$  in at least 5 out of 10 consecutive trials [31]. The motor cortex was mapped at a stimulation intensity at 110% of resting motor threshold, and 10 stimuli were delivered to each scalp site at a rate of 1 stimulus every 5 seconds. Stimuli were given in a semi-random order across the scalp until all active sites were mapped.

#### B. Intervention

Intervention comprised 24 sessions of tDCS paired with intensive, task-oriented UE motor training (3 sessions per week for 8 weeks). tDCS was the only independent variable. We randomized subjects to receive the following tDCS conditions, in a crossover design: a) 12 sessions of sham tDCS;

and b) 12 sessions of anodal tDCS. For anodal tDCS, as well as for sham tDCS, we placed the anode over the hot-spot and the cathode over the contralateral supraorbital region. This method, which uses the supraorbital region as the reference location, provided the greatest distance from skin surface to cortex of any acceptable location on the scalp (for safety reasons, both electrodes must be placed anterior to the brainstem)[32, 33]. Anodal tDCS was delivered at an intensity of 2.0mA for 20 minutes, which resulted in a current density of 0.08mA/cm<sup>2</sup> and a charge density of 960 Coulombs/M<sup>2</sup>. This intensity falls within the range of safe stimulation parameters [34]. We used an identical setup for sham tDCS except that we ramped up intensity over 30 seconds, held at 2.0mA for 30 seconds, then ramped down to 0mA over 30 seconds. Subjects received 0mA of current for the remainder of the 20 minutes. This sham protocol preserved the blinded fashion of the study by producing the same sensation as anodal tDCS [35]. Randomization resulted in each subject receiving sham tDCS for the initial 12 sessions and anodal tDCS for the subsequent 12 sessions. We visually monitored each subject during tDCS. Subjects, evaluators, and occupational therapists who administered training were all blinded to tDCS condition.

Immediately following each tDCS session, subjects participated in 2 hours of intensive, task-oriented UE training incorporating an evidence-based protocol [36, 37]. This protocol required baseline identification of subjects' occupational performance goals. Training used principles of training physiology, motor learning, neuroplasticity, and occupational therapy. In order to elucidate the effects of possible transcallosal transfer, training in each 12-session portion of intervention targeted the UE contralateral to the hemisphere receiving tDCS. In keeping with the occupational therapy domain and process, training was designed to comprise preparatory techniques (such as stretching), purposeful activities (such as simulated or partial task performance), or occupation-based intervention when possible (such as drinking from a cup, using mobile phone, or other occupations that subjects identified as meaningful and relevant to daily life). Our approach aligned closely and comprehensively with basic principles of neuroplasticity (ie, intensive, repetitive practice; task-specificity; gradual increase in demand; motivation; attention to task; active engagement; feedback) [38]. Training was in a 1:1 therapist-to-subject ratio.

### III. RESULTS

As shown in Figure 1a, initial 12 sessions of intervention (sham tDCS paired with motor training) did not yield clinically significant change in SCIM-III compared with baseline (mean±SE: -0.5±0.5 (left bar)). Increased by 4 points, which is considered clinically significant (mean±SE: 4.2±3.0 (right bar)).

Figure 1a

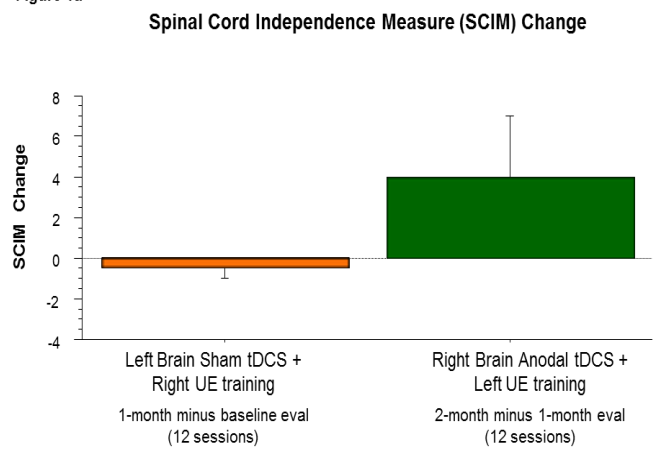


Figure 1a. Increase in SCIM-III scores (right bar) indicates greater improvement after anodal tDCS than sham tDCS.

Figure 1b

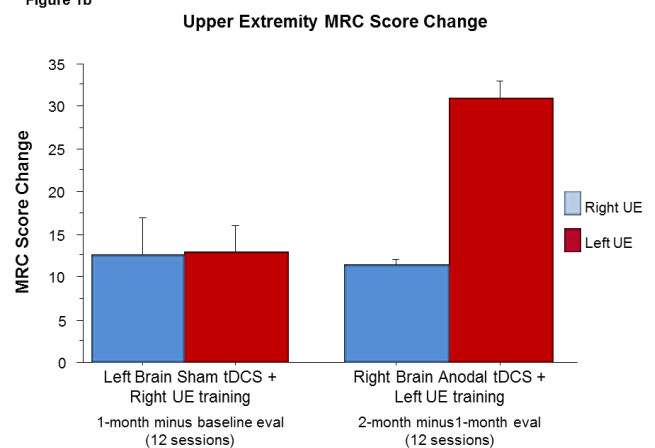


Figure 1b. Improvements in UE strength (increased MRC scores) after anodal tDCS paired with motor training. Unilateral training was associated with bilateral improvement. Thus, it appears that transcallosal transfer may play a significant role in UE motor recovery for people with incomplete SCI.

Figure 1c

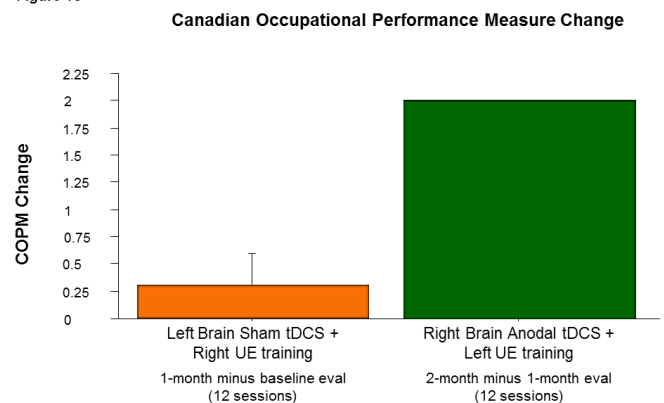
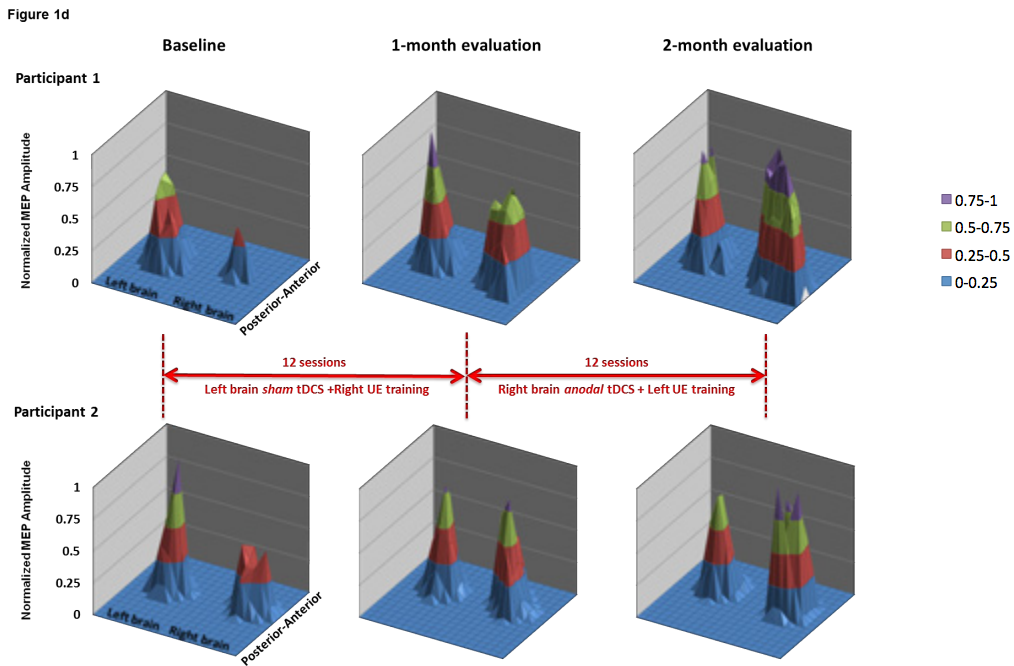


Figure 1c. Qualitative improvement measured by COPM is more pronounced after anodal tDCS paired with motor training (right bar).



**Figure 1d. Cortical reorganization may be optimized by pairing anodal tDCS and motor training.** Motor responses at each scalp position are shade-coded by normalized MEP amplitude (measured over extensor digitorum communis (EDC) muscles). Notable increases in cortical map volume were measured in the right brain (which received anodal tDCS only). Training paired with anodal tDCS (delivered to right brain only) led to a larger map volume change (between 1.9-2.2 in the right brain) than training paired with sham tDCS (delivered to left brain only; led to change between 0.9-1.2 in the left brain). The increase of the motor map ipsilateral to the trained UE suggests that transcallosal transfer may play a significant role in motor recovery and corticomotor reorganization after SCI.

Figure 1b shows that sham tDCS (left brain) plus UE training led to increased strength for the trained UE (right UE); mean $\pm$ SE: 12.6 $\pm$ 4.5, first blue bar). However, anodal tDCS (right brain) led to comparatively greater increase in strength for the trained UE (left UE) (mean $\pm$ SE: 31.0 $\pm$ 2.0, second red bar)—an approximately 19-point difference between conditions. Figure 1c shows that while the sham tDCS condition led to a COPM score increase indicating improvement (mean $\pm$ SE: 0.3 $\pm$ 0.3 (left bar), anodal tDCS yielded a greater COPM increase (mean $\pm$ SE: 2.0 $\pm$ 0; right bar). Figure 1d shows that anodal tDCS paired with UE motor training substantially increased corticospinal motor representation.

#### IV. DISCUSSION

This study is the first to evaluate adjuvant effects between tDCS and intensive task-oriented UE training in incomplete SCI. We have found evidence supporting tDCS as a relevant intervention to enhance the effects of motor training for people with incomplete SCI. Our supporting TMS evidence associates anodal tDCS with more neuroplastic change than sham tDCS. Furthermore, it appears that transcallosal transfer may play a crucial role in UE motor recovery in incomplete SCI, based on our evidence showing that the was associated with improvement of the non-trained UE.

Our related TMS results showed bilateral neuroplastic change after intervention, despite the unilateral nature of UE motor training. However, it is conceivable that anodal tDCS to the hemisphere contralateral to the trained UE increases excitability and reorganization in the ipsilateral corticospinal tract (i.e., the corticospinal tract connecting the stimulated hemisphere with the non-trained UE).

Our results highlight how UE motor recovery in SCI may differ from UE motor recovery associated with conditions involving unilateral brain lesions (such as stroke). In stroke, pathologically altered patterns of transcallosal inhibition occur and can affect outcomes of UE motor training [39]. Our discovery that this dynamic may not apply to incomplete SCI could have great clinical utility in terms of tailoring therapy to SCI survivors with tetraplegia. Furthermore, our finding that tDCS and training can have benefit even in the chronic stages of SCI recovery is particularly impactful.

Building on this study, we recommend future research in keeping with current trends in stroke literature to investigate different electrode configurations of tDCS (eg, anodal tDCS and cathodal tDCS delivered concurrently to bihemispheric motor areas). Additionally, studies are needed to determine the optimal dosing for tDCS plus training according to clinical features of SCI. Finally, we recommend larger trials to substantiate the preliminary findings of the feasibility study presented here.

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