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Original article

Transcranial direct current stimulation over multiple days enhances motor performance of a grip task

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ABSTRACT

Background: Recovery of handgrip is critical after stroke since it is positively related to upper limb function. To boost motor recovery, transcranial direct current stimulation (tDCS) is a promising, non-invasive brain stimulation technique for the rehabilitation of persons with stroke. When applied over the primary motor cortex (M1), tDCS has been shown to modulate neural processes involved in motor learning. However, no studies have looked at the impact of tDCS on the learning of a grip task in both stroke and healthy individuals.
Objective: To assess the use of tDCS over multiple days to promote motor learning of a grip task using a learning paradigm involving a speed-accuracy tradeoff in healthy individuals.
Methods: In a double-blinded experiment, 30 right-handed subjects (mean age: 22.1 ± 3.3 years) participated in the study and were randomly assigned to an anodal ($n = 15$) or sham ($n = 15$) stimulation group. First, subjects performed the grip task with their dominant hand while following the pace of a metronome. Afterwards, subjects trained on the task, at their own pace, over 5 consecutive days while receiving sham or anodal tDCS over M1. After training, subjects performed de novo the metronome-assisted task. The change in performance between the pre and post metronome-assisted task was used to assess the impact of the grip task and tDCS on learning.
Results: Anodal tDCS over M1 had a significant effect on the speed-accuracy tradeoff function. The anodal tDCS group showed significantly greater improvement in performance (39.28 ± 15.92%) than the sham tDCS group (24.06 ± 16.35%) on the metronome-assisted task, $t(28) = 2.583$, $P = 0.015$ (effect size $d = 0.94$).
Conclusions: Anodal tDCS is effective in promoting grip motor learning in healthy individuals. Further studies are warranted to test its potential use for the rehabilitation of fine motor skills in stroke patients.

1. Introduction

In recent years, transcranial direct current stimulation (tDCS) has emerged as a promising technique for the recovery of functional skills in persons with stroke. When applied over the primary motor cortex (M1), tDCS has been shown to modulate neural processes involved in motor learning [1–3]. Motor learning is defined as practice-induced acquisition of motor skills leading to improvements in performance that persist over time [4,5]. It is also characterized by a shift in the speed-accuracy tradeoff (SAT) resulting from increased accuracy and reduced performance variability [4–6]. The neuromodulatory effects of tDCS are of particular importance in the rehabilitation of stroke survivors, for whom motor recovery is hypothesized to be driven by plasticity

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mechanisms similar to those that govern motor learning in the intact brain [7–10].

Previous studies have shown that anodal tDCS can induce significant motor learning in a number of fine motor tasks in healthy subjects [6,11–14]. Notably, Reis et al. [6] reported that 5 consecutive days of repeated training on a sequential visual isometric pinch force task while undergoing tDCS resulted in greater skill acquisition for the anodal tDCS group than for the sham group. The beneficial effect of anodal tDCS remained significant 3 months after training, suggesting that tDCS-induced plasticity has long-term robustness. In contrast, one study using a visually-guided fine motor task found the rate of motor learning to be similar for both sham and anodal tDCS groups throughout a 2-session training period [15]. These divergent findings allude to the importance of methodological considerations regarding tDCS use, as its effects on motor learning are suggested to be dependent on individual motor task and training demands [16–18]. It is therefore of interest to investigate whether anodal tDCS can produce a beneficial effect on the learning of a motor task that involves grip force control, a reliable indicator of neurological and functional recovery in individuals with stroke [19–22] but one that is understudied in research on tDCS-induced motor skill learning. Validating the design of a motor learning protocol combining tDCS and grip training could provide valuable information on the optimal methodological approaches for maximizing the effects of tDCS-induced learning.

In this study, we investigated the effectiveness of a sequential visual isometric grip motor task in inducing learning in healthy young subjects, as well as evaluated whether anodal tDCS can boost learning of this motor task. As found in the study by Reis et al. [6], we hypothesized that healthy subjects receiving anodal tDCS when learning a grip task would exhibit significantly higher improvements in motor performance compared to subjects receiving sham stimulation.

2. Material and methods

2.1. Ethics

This study was approved by the Research Ethics Board at McGill University. Informed consent was obtained in written form from all subjects prior to their enrollment in the study and the collection of personal information. Subjects were compensated for their participation.

2.2. Subjects

Thirty-two subjects (10 males, mean age = 22.1 ± 3.3 years, range 18–35) participated in the study. Subjects were right-handed based on the Edinburgh Handedness Inventory [23] and screened for any contraindications to tDCS (e.g. epilepsy, pregnancy, etc.), as well as any neurological, psychiatric disorders, or cognitive impairment as measured by the NIH Toolbox Cognition Battery [24].

2.3. Study design

The study design was modified from the double-blinded experiment by Reis et al. [6]. Subjects were randomly assigned to an anodal or sham tDCS group (n = 16/group). Sixteen pairs of 5-digit codes pre-programmed into the stimulation machine (NeuroConn, Germany) were used, each pair containing an active and a sham stimulation code. On the first day, subjects performed a pre-training test on a metronome-assisted sequential visual isometric pinch task (SVIPT) targeting grip, which consisted of 9 blocks of predetermined movement time imposed by a metronome set at 24, 30, 38, 45, 60, 80, 100, 110 or 120 bpm. Each block contained 10 trials and the order in which the blocks were performed was randomized and balanced across groups. These blocks were used to calculate the speed-accuracy tradeoff function (SAF) described below. Following this baseline SAF assessment, subjects began a 5-day training period during which they trained on the SVIPT at their preferred speed without assistance from the metronome. Subjects practiced 2–3 warm-up trials to familiarize themselves with the motor task before each session. Then subjects performed approximately 45 minutes of repeated training (200 trials) per day, subdivided into 6 blocks (40 trials in blocks 1 and 6; 30 trials in blocks 2–5). Data from these blocks were used to calculate the total skill learning achieved by each subject. The tDCS was administered over M1 for a period of 20 minutes during the performance of blocks 2 to 5. Stimulation was not administered during blocks 1 and 6 to ensure that subjects' performances were free from any acute effects of tDCS. After completion of the training period on day 5, subjects performed a post-training SAF test on the SVIPT while assisted by the metronome.

2.4. Sequential visual isometric pinch task (SVIPT)

Subjects sat in front of a 20-inch screen monitor placed 42.5 cm from the edge of a table. Subjects used a grip force transducer (A-KAST Measurements and Control Ltd) to navigate a cursor on a screen, exerting greater grip force to move it horizontally to the right and slackening the grip force to bring it back to a rest (HOME) position. The transduction of each subject's maximum voluntary isometric (MVI) grip force into cursor movement followed a logarithmic path, with a maximum movement requiring 35%–45% of each subject's MVI. Subjects had to move the cursor smoothly and accurately between the HOME position and 5 gates from left to right, respectively, following the order Gate 1–Gate 2–Gate 3–Gate 4–Gate 5 (Fig. 1). Subjects were shown a START signal at the beginning of a trial and given a set amount of time to reach all 5 gates. If the cursor came short of the inner limit of the targeted gate or moved past the outer limit of the targeted gate, the movement was counted as an under- and over-shoot, respectively.

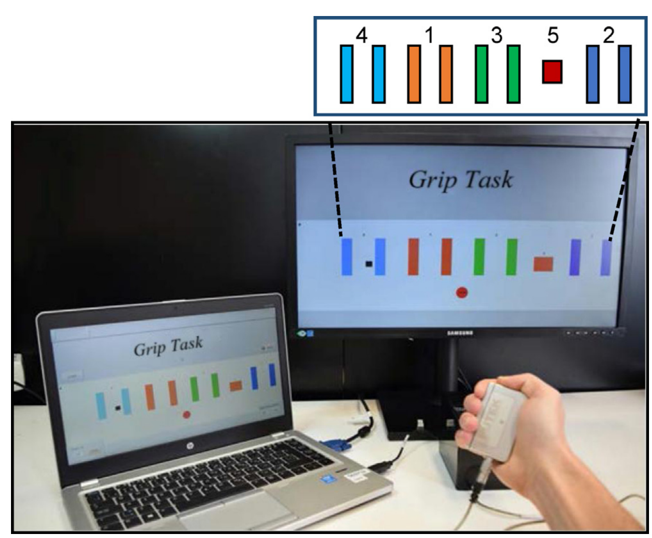

Fig. 1. Subjects pinched a force transducer with their dominant hand to control an on-screen cursor movement. The aim was to navigate the cursor quickly and accurately between a HOME position and 5 gates by alternating the grip force exerted onto the transducer. The practiced sequence was Gate orange (1) – Gate purple (2) – Gate green (3) – Gate blue (4) – Gate red (5).

2.5. Transcranial direct current stimulation

An electrical current was delivered via two 35 cm^2 sponge-covered electrodes soaked in saline solution. The anode was placed over the left M1 while the cathode covered the right supraorbital region. The location of M1 was determined using the EEG 10/20 system [25]. Anodal stimulation was given at 2 mA for 20 minutes during training; sham current was delivered in a ramp-like fashion over 8 s at the beginning and end of stimulation.

2.6. Outcome measures

The primary outcome measures were total skill learning and performance improvement. The former derives from error rate and speed while the latter derives from changes in the SAF, as detailed below.

2.6.1. Error rate and speed

The error rate was calculated as (1 – accuracy rate), accuracy being defined as the proportion of trials per block with hits to all 5 targets in the correct sequence order (e.g. without under- or over-shooting). Speed was captured by the mean sequence movement time per training block (time elapsed from movement onset to reaching Gate 5).

2.6.2. Skill measure and total skill learning

The skill measure, which was used to estimate subjects' skill during training, was defined as:

$$\ln\left(\frac{1-error\ \ rate}{error\ \ rate\left(\ln(movement\ \ time)^{b}\right)}\right), \text{with } b = 0.5424$$

where the movement time, paced at the subjects' preferred speed, and error rate are the mean values from each block. Reis et al. [6] originally set the b-value to 5.424; however, to allow for positive skill measure values, it was modified to 0.5424 in this study. Total skill learning, the amount of skill acquired over the training sessions, was then defined as the subtraction of the skill measure of Day 1 block 1 (average across 40 trials) from the skill measure of Day 5 block 6 (average across 40 trials).

2.6.3. Speed-accuracy tradeoff function (SAF)

The SAF is a logarithmic function which expresses changes in mean error rate (y) as a function of mean movement time (x) per metronome-assisted block (10 trials each) set at 24, 30, 38, 45, 60, 80, 100, 110 or 120 bpm. The best fit was found using the least squares method.

2.6.4. Performance scores and performance improvement

The performance scores were defined as:

$$1-\frac{\text{AUC}}{x_u - x_l}$$

where AUC is the area under the SAF, x_u is the upper bound and x_l is the lower bound of the SAF domain. As the pre-training AUC tends to be greater than the post-training one, this equation allows the performance score to be smaller before training compared to after, ensuring a positive value of improvement. The performance improvement was then defined as the change in percentage in performance scores before and after 5 days of training on the metronome-assisted task.

2.7. Statistical analysis

From the 5-day training sessions, as well as pre-post metronome-assisted performance assessments, trials were removed on the basis of the following criteria: premature start, offbeat movements, poorly defined curves, gradually or steeply ascending and descending curves, and curves that did not return to the HOME position. Distributions were visually inspected for skewedness and kurtosis, and tested for normality using the Kolmogorov-Smirnov test. Homogeneity of variances was assessed with Levene's test.

To compare the total skill learning between the anodal and sham tDCS groups, a non-parametric test (Mann-Whitney U test) was used as data for the sham group were not normally distributed ($P = 0.016$). Performance score improvements and pre-training performance scores were analyzed between groups by independent samples t-tests. Statistical significance for skill measure differences between baseline (Day 1 block 1) and the end of Day 5 in each group was determined using paired samples t-tests. The alpha level was set to 0.05 and Bonferroni correction was used when multiple comparisons were performed. Effect size was used to measure the magnitude of the stimulation effect on total skill learning and performance improvement. According to Cohen [26], d values of 0.2 are indicative of a small effect; 0.5, a moderate effect; and > 0.8, a large effect.

3. Results

3.1. Subjects' characteristics and side effects of tDCS

Thirty of the thirty-two subjects completed the study ($n = 15$/group) and were included in the statistical analysis. Subjects were not significantly different in sex, age and handedness score or cognitive ability between groups ($P > 0.05$). Both groups also started from comparable pre-training performance scores ($P = 0.439$). No adverse effects related to tDCS application were reported in either group (see supplementary material for details).

3.2. Effects of tDCS on skill measure and total skill learning

After five days of training, there was no significant difference in total skill learning between the sham (0.616 ± 0.320) and anodal tDCS (0.868 ± 0.406) groups ($U = 70$, $P = 0.078$). However, as predicted, both groups demonstrated significant positive total skill learning (sham: $t(14) = -7.463$, $P < 0.001$; anodal: $t(14) = -8.277$,

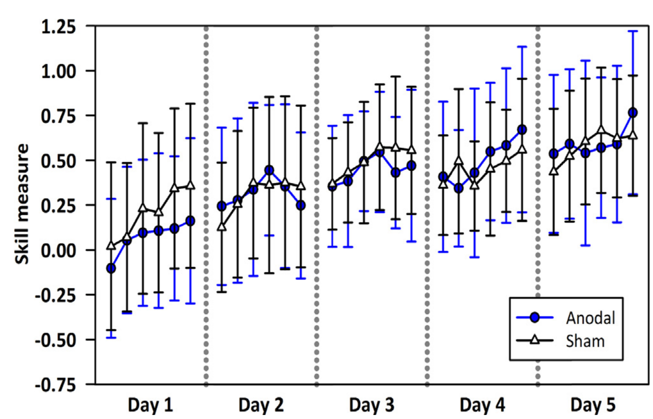

Fig. 2. Skill measure for the sham and anodal tDCS groups over the 5-day training period. Each marker represents the average skill measure per block of 40 trials (blocks 1 and 6) or 30 trials (blocks 2–5). Vertical lines separate each day of training. Both tDCS groups had similar baseline skills at the beginning of Day 1 ($P = 0.439$), as well as similar skill acquisition curves throughout training.

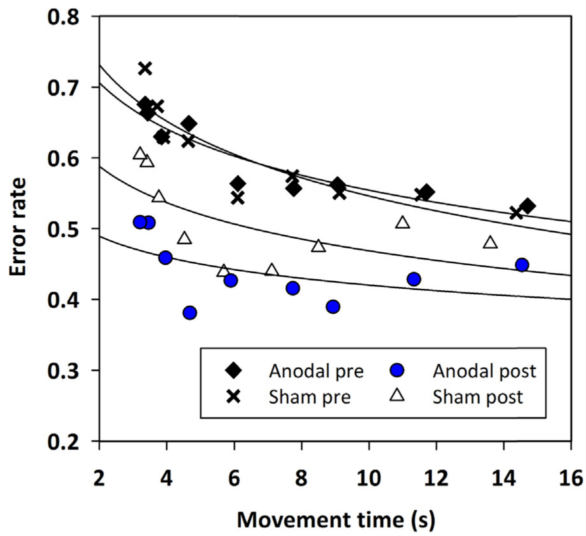

Fig. 3. Speed-accuracy tradeoff functions (SAF) for the sham and anodal tDCS groups, pre- and post-training. The SAF depicts the error rate (y) as a function of the movement time (x) at 9 different blocks, with each representing an imposed metronome speed (24, 30, 38, 45, 60, 80, 100, 110 and 120 bpm).

$P < 0.001$), i.e. an increase in skill measure from Day 1 to Day 5 of training (Fig. 2).

3.3. Effects of tDCS on performance scores and performance improvement

Anodal tDCS applied over the M1 had a significant effect on the SAFs underlying performance scores and performance improvement, as illustrated in Fig. 3. Indeed, after 5 days of training, the anodal tDCS group showed significantly greater improvement in performance (39.28 $\pm$ 15.92%) than the sham tDCS group (24.06 $\pm$ 16.35%) on the modified metronome-assisted SVIPT, ($t(28) = 2.583$, $P = 0.015$ (effect size $d = 0.94$)).

4. Discussion

In the present study, anodal tDCS stimulation applied over M1 during 5 consecutive sessions of training enhanced performance of a metronome-assisted grip task; supporting our hypothesis that anodal tDCS is beneficial in boosting the performance of a newly learned sequential grip task. While there were no differences in total skill learning between groups by the end of training, all subjects showed positive total skill learning irrespective of the type of stimulation received.

4.1. Anodal tDCS effect on learning and performance of a grip task

Previous studies using the SVIPT, namely those of Reis et al. [6] and Schambra et al. [11], reported the ability of anodal tDCS to induce greater total skill learning than sham, a result we did not reproduce. Instead, we found that anodal tDCS generated a significant positive effect only on grip performance in the metronome-assisted SVIPT. While these results are seemingly contradictory, they might be explained by the presence of a ceiling effect where subjects' freedom to train at their preferred speed, likely saturating an area of the brain that is already optimally activated, acted as a buffer against any additional learning effects that may have occurred over the 5-day period from increases in cortical excitability [6,14]. It could be hypothesized that for higher skilled subjects, the task might not have been challenging enough to translate into significant improvement in performance [27]. Indeed, subjects with higher baseline skill measures did not exhibit as much total skill learning as those who started with lower measures, regardless of the intervention received (data not shown). The metronome-assisted SVIPT, on the other hand, with its imposed movement times, represents a standardized measure of motor learning, and thus could be more robust in detecting change in performance on a grip task. Changes in the SAF do depend substantially on the error rates of higher speeds; therefore, a faster training speed may have had a positive impact on subjects' post-training performance on the metronome-assisted SVIPT. These results support our decision to use performance on the SAF rather than total skill learning as our main outcome measure of a grip motor learning task as the SAF provides a standardized measure of performance before and after training. Future studies will have to consider tailoring the training demands to each individual's needs and capabilities. For instance, a training protocol that requires subjects to train constantly at a set standardized speed might preferably be implanted in a future study that involved patients. It is also important to note that the plasticity-enhancing effects of tDCS reported by Reis et al. [6] might differ across different motor tasks, depending on the specific brain structures involved in their learning [16,17,28]. Therefore, the demands of the grip-targeting SVIPT might be recruiting and activating different cortical and subcortical areas than the pinch task devised by Reis et al. [6].

The divergence demonstrated between our results and those of previous studies may therefore depend on the choice of the outcome measure used in evaluating the impact of tDCS-induced motor learning (total skill learning vs. SAF). To improve the comparability of future tDCS studies, a consensus on the best outcome measure to choose would be important to allow a direct between-studies comparison of the effectiveness of tDCS in boosting motor performance. Nevertheless, our results support previous findings demonstrating the beneficial effect of anodal tDCS-induced modulation on motor learning [29–31].

4.2. Difficulties and limitations of the study

A challenge associated with the study design was the duration of training sessions. Subjects reported experiencing fatigue and lower levels of concentration towards the beginning of block 5 (after approximately 30 minutes of continuous, repetitive training). As it can be seen in both groups' skill acquisition curves on Days 2 and 3 (Fig. 2), learning on the SVIPT was mostly restricted to the first 4 blocks, with skill measure values plateauing or declining afterwards. This suggests that the training session length for optimal motor learning, while requiring repetition, is dependent on subjects' psychophysical characteristics at the time of training. Our study did not also investigate the long-term effects of tDCS on motor skill learning and performance or the effects of fatigue on learning itself, which limits its direct comparison with other studies past the training period.

5. Conclusions

Our finding that anodal tDCS produced a beneficial effect on the performance of a grip force task provides a starting point for understanding the effectiveness of grip force training and anodal tDCS in promoting motor learning in healthy individuals. Our results will inform future studies on their potential use as therapeutic tools for the rehabilitation of upper extremity motor skills after stroke. Larger, long-term RCTs are warranted to determine the effects of tDCS on the retention of motor performance and to explore the optimal methodology for enhancing tDCS-induced plasticity.

Disclosure of interest

The authors declare that they have no competing interest.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.rehab.2017.07.001.

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