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*RESEARCH ARTICLE*

# Bihemispheric Anodal Corticomotor Stimulation Using Transcranial Direct Current Stimulation Improves Bimanual Typing Task Performance

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**ABSTRACT.** Transcranial direct current stimulation (tDCS) is associated with improved unimanual skilled hand use. The authors assessed effects of bihemispheric anodal corticomotor tDCS (BAC-tDCS) on bimanual skilled hand use. Twenty-eight nondisabled subjects were randomized to either BAC-tDCS or sham-tDCS, 20 min daily for 5 consecutive days. Performance on a bimanual typing (BT) task and a short-term memory (STM) task was assessed daily and at 1-week follow-up. Mean change between Day 1 and Day 5 in BT score with BAC-tDCS (19.4 points; 95% CI [12.82, 25.99]) was significantly greater ($p = .04$) than change with sham-tDCS (12.5 points; 95% CI [7.6, 17.3]). Neither group retained improvements in BT score at follow-up. BAC-tDCS had no effect on STM. These results may have implications for interventions to improve hand function in persons with bilateral hand dysfunction.

*Keywords*: bimanual, motor performance

Transcranial direct current stimulation (tDCS), the application of low-intensity, monophasic electrical current through the scalp via surface electrodes, has neuromodulatory effects, changing the membrane potential (and therefore the activation threshold) of underlying neural structures. Thresholds are reduced in the vicinity of the anodal electrode, facilitating the occurrence of action potentials, thereby promoting excitation. Conversely, thresholds are increased in the vicinity of the cathodal electrode, impeding the occurrence of action potentials, thereby promoting inhibition (Nitsche & Paulus, 2001). tDCS is clinically accessible as it is a simple, noninvasive, and painless modality that seems to have value as a means to modulate cortical excitability (Fregni & Pascual-Leone, 2007; Heinrichs, 2012).

Studies of bihemispheric anodal-cathodal tDCS for neuromodulation have been prompted by the evidence for decreased excitability of the lesioned cortex and an imbalance in interhemispheric excitability that develops after stroke (Butefisch, Netz, Wessling, Seitz, & Homberg, 2003). In these studies, the anode is placed over the motor cortex of the lesioned hemisphere to promote excitation, while the cathode is placed over the motor cortex of the nonlesioned hemisphere to promote inhibition (Fregni & Pascual-Leone, 2007). This approach is associated with increased hand motor performance in tests of unimanual motor function (Lindenberg, Renga, Zhu, Nair, & Schlaug, 2010; Vines, Cerruti, & Schlaug, 2008). The bihemispheric anodal-cathodal stimulation approach is logical as a therapy for persons with stroke given that the goal is to increase excitability of the lesioned cortex.

While unimanual tasks are associated with unilateral cortical excitation, there is bilateral excitation during bimanual movements that require simultaneous use of both hands (referred to synchronous tasks; McCombe Waller, Forrester, Villagra, & Whitall, 2008) and also during activities requiring alternating finger movements between hands (referred to as asynchronous tasks) such as keyboard typing and playing the piano. The bilateral cortical activity observed with performance of asynchronous tasks has been found to be greater than that observed during performance of synchronous tasks (Haslinger et al., 2004). In the study of Haslinger et al., the task required one finger from each hand to be moving continuously. We used a different task, wherein only one finger from each hand was moving while the fingers from the other hand were maintained in pose of readiness in anticipation of ensuing action, such as when one is typing on a computer.

While the outcomes of studies investigating the use of tDCS in persons with stroke are promising, there are neurologic conditions such as spinal cord injury that result in bilateral impairment of hand function. Consequently it seems useful to design interventions targeting the broad spectrum of hand activities that comprise daily life activities that include bimanual hand use (Trapp, Lepsien, Sehm, Villringer, & Ragert, 2012). Given the evidence for improvements in unimanual typing tasks with anodal tDCS, the next logical step is to assess the influence of bihemispheric anodal corticomotor tDCS (BAC-tDCS) on a bimanual typing task. To our knowledge no prior studies of this type had been completed; therefore, it was necessary to first assess the effects and the safety of this approach in persons without disability.

To assess the effects of BAC-tDCS on bimanual typing performance and the possible retention of these effects, we adapted a previously published protocol that had shown performance changes in unimanual typing performance after multiday application of unihemispheric corticomotor anodal tDCS (Vines et al., 2008). As our testing required subjects to perform a bimanual typing (BT) task for 30 s before and after application of BAC-tDCS, we anticipated that simply performing the BT task as part of testing would result in practice-related improvements; therefore we compared BAC-tDCS to a sham-tDCS condition to account for these practice

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effects. Another consideration is that tDCS has relatively low focality (Nitsche, 2011) and may have the potential to influence cortical areas contiguous to the motor cortex that was the target of our studies. Therefore, we included a secondary outcome measure to assess possible influences of BAC-tDCS on short-term memory (STM), a function subserved by the temporal lobe.

Performance of novel bimanual sequences engages a number of different cortical areas, including primary motor, premotor, and supplementary motor areas (Sadato, Yonekura, Waki, Yamada, & Ishii, 1997). While this provides many possible cortical areas to target with tDCS, we based our hypotheses and study design on previously published studies that demonstrated unimanual performance improvements in sequence tasks in healthy individuals who participated in multiday tDCS interventions with tDCS applied to the primary motor area (M1; Reis et al., 2009; Vines et al., 2008). Because BAC-tDCS is a novel electrode montage, we purposefully designed the present study to parallel those prior studies, such that the only novel elements were the use of bilateral anodal stimulation and the use of a bimanual task. We hypothesized that following participation in the five-day study both the BAC-tDCS and sham-tDCS groups would exhibit improved bimanual typing performance but that change with BAC-tDCS would be greater. We also hypothesized that bihemispheric anodal corticomotor stimulation would have no effect (either beneficial or adverse) on STM.

## Method

### Participants

Healthy volunteers gave written and verbal informed consent to participate in the study, which had been approved by the Human Subjects Research Office of the University of Miami Miller School of Medicine, Miami, Florida. Recruitment was performed through email to the university community and through verbal recruitment performed by the investigators. The inclusion criterion was that the participant be a healthy adult (age = 19–65 years old). Exclusion criteria were neurological, orthopedic, or cognitive conditions that would affect performance of the BT task or STM task. Subjects were enrolled sequentially following initial screening and randomized into the BAC-tDCS experimental group or bihemispheric sham-tDCS control group utilizing a random number list, and no attempt was made to stratify subjects with respect to their pre-existing bimanual skills. The randomized assignment order was placed in sequentially numbered envelopes and remained concealed until the time of group assignment.

### Procedures

The optimal stimulation sites to activate the right and left corticomotor hand areas (i.e., the hot spots) were identified using transcranial magnetic stimulation (Magstim200, Dyfed, Wales); detailed methods are described elsewhere (Hoffman & Field-Fote, 2007). The location of each hot spot was documented using a coordinate system (Jasper, 1958) to define the anterolateral and mediolateral distance from the vertex; the site was located each day for placement of the tDCS anodal electrode. Subjects underwent five consecutive days of either BAC-tDCS or sham-tDCS. TDCS was delivered by two constant current stimulators (Phoresor, Iomed Inc., Salt Lake City, UT) for which the output of the device was concealed from the subjects. Intensity was set at 1 mA, according to safety guidelines (Bikson, Datta, & Elwassif, 2009). Four saline-soaked, disposable iontophoresis electrodes (Optima, Iomed Inc, Salt Lake City, UT) were used for the stimulation: two active (anodal) electrodes with an area of 28 $cm^2$ each were placed on the scalp over the hot spot (resulting in a total current density of 35 $\mu A/cm^2$), and two reference electrodes were placed on the supraorbital area bilaterally. The area of the inactive electrodes was approximately 37 $cm^2$.

The sham-tDCS protocol used a previously published method (Gandiga, Hummel, & Cohen, 2006) that was identical to the BAC-tDCS condition with the exception that, without the knowledge of the subject, the current was reduced to zero after 30 seconds, and was maintained at zero for the remainder of the stimulation period. Published reports substantiate that the stimulation parameters used in this protocol elicit mild tingling/itching only during the initial seconds of stimulation, fading soon after onset (Gandiga et al., 2006). Our approach allowed the groups to be blinded to the stimulation condition. The duration of the BAC-tDCS and the sham-tDCS period was 20 min each day; subjects were asked to report any adverse effects experienced during or after stimulation.

### Experimental Tasks

*BT task.* Performance on a keyboard sequence task was the primary outcome measure. Using this same task, Vines et al. (2008) observed improvement in unimanual performance in a study of bihemispheric anodal-cathodal tDCS in persons without disability. We modified the published protocol to a bimanual asymmetrical sequential task with bihemispheric (anodal-anodal) stimulation to measure the effects of BAC-tDCS on bimanual task performance. As in the study of Vines et al. we used a different sequence on each day in order to foster novelty of the task.

At the start of the BT task, subjects were asked to rest digits 2–5 of each hand on the respective *a*, *s*, *d*, *f* and *h*, *j*, *k*, *l* keys of a standard keyboard, and an eight-letter sequence (generated utilizing custom software; Matlab, The MathWorks, Natick, MA, version 7.5.0, R2007b) was displayed on a computer screen. All sequences consisted of two keystrokes performed with one hand, followed by two keystrokes performed with the opposite hand. This pattern was chosen to best mimic the typical use of a computer keyboard, wherein it is necessary to alternate use of the hands. The subjects were instructed to perform this bimanual pattern of eight sequential keystrokes

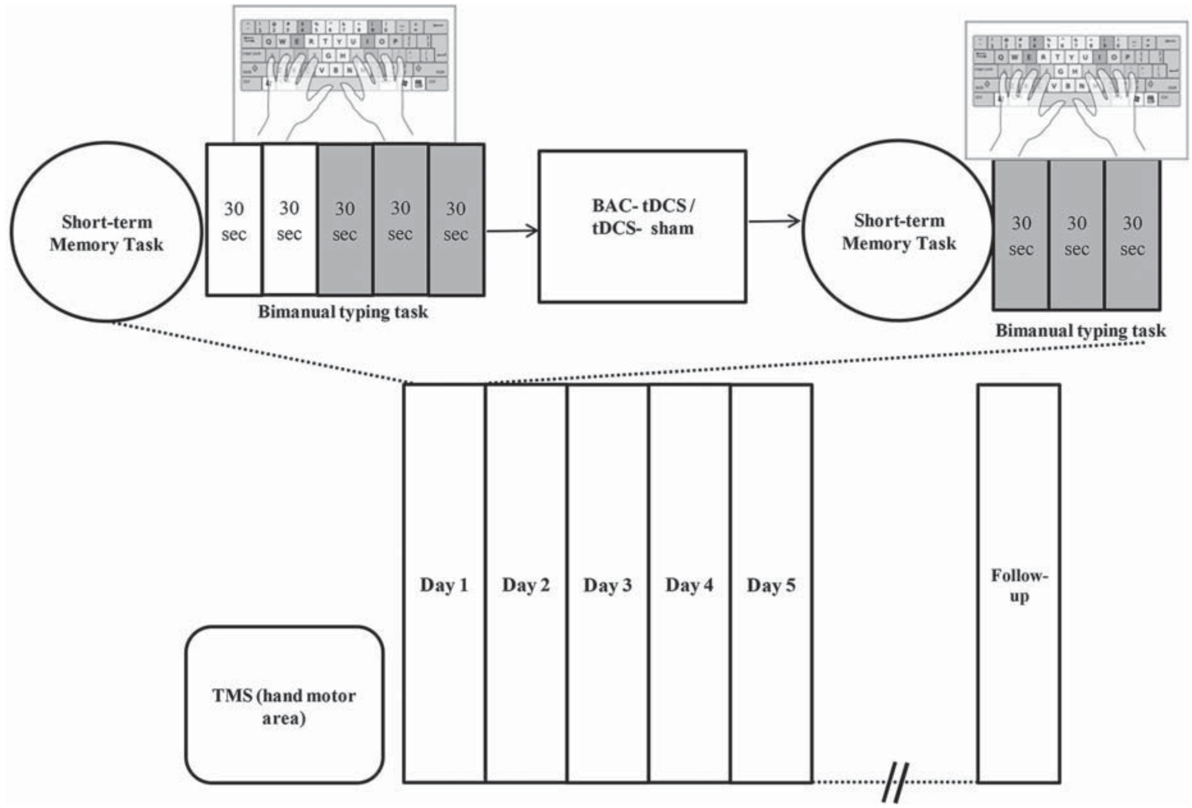


**FIGURE 1.** Experimental design. Subjects participated in a total six of sessions. Measurements of bimanual typing and short-term memory tasks were obtained daily prior to and following stimulation (bihemispheric anodal corticomotor transcranial direct current stimulation [BAC-tDCS] or sham-tDCS, 20 min) for five days, and at follow-up. TMS = transcranial magnetic stimulation.



as accurately and quickly as possible for 30 s. Five trials of the same sequence were captured daily prior to stimulation and after stimulation, and at the follow-up assessment one week after the final stimulation session (Figure 1). The first two (warm-up) trials of each capture were discarded; the subsequent three trials were analyzed.

Performance on the bimanual typing task was scored as described by Vines et al (Vines et al., 2008), wherein points were awarded for correct sequences, and points were deducted for errors. A correctly typed 8-letter sequence (e.g., *as-df-hj-kl*) was awarded four points; correctly typing the sequence four times during the 30-s capture epoch earned 16 points. An incorrect letter pair or missing space was scored as an error; the total number of errors was deducted from points earned. This method of scoring addresses the speed-accuracy tradeoff (Fitts, 1954; Reis et al., 2009), because if an individual increased the typing speed with a proportional increase in the number of errors, this would not result in an increased score. The difference in the number of correct keystrokes between the Day 1 prestimulation test (pre-Day1) to the Day 5 poststimulation test (post-Day5) was our primary measure of cumulative change in motor performance. Retention of effects was assessed through comparisons between pre-Day1 and follow-up scores, as in other studies performed by our group (Field-Fote & Roach, 2011).

### STM Task

Our secondary outcome measure was STM to assess possible effects of BAC-tDCS on temporal lobe function. We used a modified version of a published protocol that reported changes in STM following unilateral excitatory tDCS applied over the temporal lobe (Boggio et al., 2009). Two series of 27 words were presented on a computer screen. Words in the first series all belonged to the same theme (e.g., fruits: apple, pear, strawberry). Each word remained onscreen for 3 s. Subsequently, subjects viewed a second series of 27 words comprising nine words from the first series, nine words from the same theme as the first series but not included in that series, and nine unrelated words. While viewing the second series, subjects were asked to indicate (by checking “yes” or “no”) whether the displayed word had appeared in the first series. The percentage of correctly identified words was calculated. As with the test of bimanual motor function, this test was performed before and immediately after each of the five consecutive daily BAC-tDCS stimulation sessions, and at the follow-up assessment one week later.

### Statistical Analysis

Data were inspected for homogeneity of variance and normality of distribution. Outliers, trials in which the number of errors was greater than two standard deviations from the mean of total errors for all trials for that subject (Vines et al., 2008), were removed along with the associated pre- or posttest. Baseline equivalence of the two groups was assessed based on pre-Day1 BT scores. The cumulative effects of BAC-tDCS and sham-tDCS on the BT and STM tasks and the possible retention of these effects were examined by comparing the differences in the magnitude of change between the two groups from pre-Day1 to post-Day5.

Data were analyzed using SAS (SAS Institute Inc., Cary, North Carolina) with significance set at $\alpha < .05$. The primary purpose of the hypothesis testing in this study was to identify between-group differences in mean performance improvement. A recent systematic review and meta-analysis of the literature reported that anodal tDCS (wherein the anode is applied over the motor cortex) is associated with large effect sizes supporting increased hand motor performance in nondisabled individuals (Bastani & Jaberzadeh, 2011). Based on prior evidence related to the cumulative effects of anodal tDCS (Reis et al., 2009; Vines et al., 2008) and based on the known effects of practice, we hypothesized that there would be an improvement in performance of in the BT task after the five-day stimulation/sham period in both groups, but that the BAC-tDCS group would exhibit larger magnitude of change.

Given our intention to directly address the question of the size of difference between treatments, and because we had declared a hypothesized direction of expected change, the one-tailed, two-sample $t$ test was deemed the most appropriate statistical approach. Following testing of the primary hypothesis, post hoc, within-group analyses were carried out using one-tailed, paired-sample $t$ tests. Confidence intervals (CI) related to 95% upper and lower limits were calculated. The effect size (Cohen's $d$) for each of these comparisons was calculated by subtracting the postscores from the prescores and dividing this mean change score by the baseline standard deviation.

## Results

Twenty-eight subjects (11 men, 18 women) with a mean age of $27 \pm 7$ years completed the study. Other than itching (reported by both groups in the initial seconds of stimulation) no adverse effects were reported. Data from one subject were excluded from the analysis, as his BT scores met our rigorous criteria to be considered an outlier (see Method section). The groups were equivalent at baseline with respect to their BT and STM scores, as there were no between-groups differences in baseline performance on either task ($p = .7$ for BT, and $p = .1$ for STM scores). The mean pre-Day1 scores for the BT task (BAC-tDCS = $28.6 \pm 10.13$, sham-tDCS = $23.7 \pm 8.0$) and for the STM task (BAC-tDCS = 90%, sham-tDCS = 92%) were not significantly different between groups. Based on the results of prior studies (Reis et al., 2009; Vines et al., 2008) we anticipated no within-session change in performance, however for completeness we also assessed the within-session change in scores and identified no between-groups difference ($p > .05$) in these comparisons.

Change in BT score was observed in both groups; posttest scores were $48.07 \pm 17.5$ for BAC-tDCS and $36.21 \pm 11.51$ for sham-tDCS (Figure 2). The within-group change for each group was associated with a large effect size ($d = 1.9$ and 1.5 for BAC-tDCS and sham-tDCS, respectively). However, there was a significant between-group difference in BT task performance, as the magnitude of change in BT performance from pre-Day1 to post-Day5 was larger for BAC-tDCS (19.4 points; 95% CI [12.82, 25.99]) compared with sham-tDCS (12.5 points; 95% CI [7.6, 17.3]).

For the STM task, mean pre-Day1 scores for the BAC-tDCS and sham-tDCS groups were $0.9 \pm 0.3$ and $0.92 \pm 0.11$, respectively. Post-Day5 scores for the BAC-tDCS and sham-tDCS groups were $0.93 \pm 0.35$ and $0.93 \pm 0.08$, respectively (Figure 3). There was no significant between-groups difference ($p > .05$) or within-group differences in STM ($p = .38$ for each).

There were no differences in retention of BT change in either group. Although the absolute follow-up scores ($M$s = 28.66 and 23.71 for BAC-tDCS and sham-tDCS, respecively) were higher than the pre-Day1 scores in both groups, this difference was not significant ($p = .9$).

## Discussion

In the present study we found that a multiday application of BAC-tDCS in persons without disability was associated with improved performance of a BT task beyond that achieved by practice alone. The improvements in bimanual performance are consistent with findings of improvements in unimanual performance observed in prior multiday studies of unihemispheric anodal corticomotor tDCS (Reis et al., 2009) and bihemispheric anodal-cathodal tDCS (Vines et al., 2008), wherein cumulative effects were observed in the absence of within-session differences. These findings are supported by results of neurophysiologic changes in a multiday study of anodal corticomotor tDCS (Alonzo, Brassil, Taylor, Martin, & Loo, 2012). Alonzo et al., in a study of 12 healthy subjects, found that multiday consecutive application of tDCS was associated with greater increases in amplitude of motor evoke potentials compared to tDCS application on alternate days. Taken together these studies support the conclusion that multiday application of tDCS is associated with cumulative or offline effects that are responsible for the maintenance of an increased state of corticomotor excitability between sessions (Alonzo et al., 2012; Reis et al., 2009). Further, our results are in agreement with the conclusions of a recently published meta-analysis of corticomotor anodal tDCS

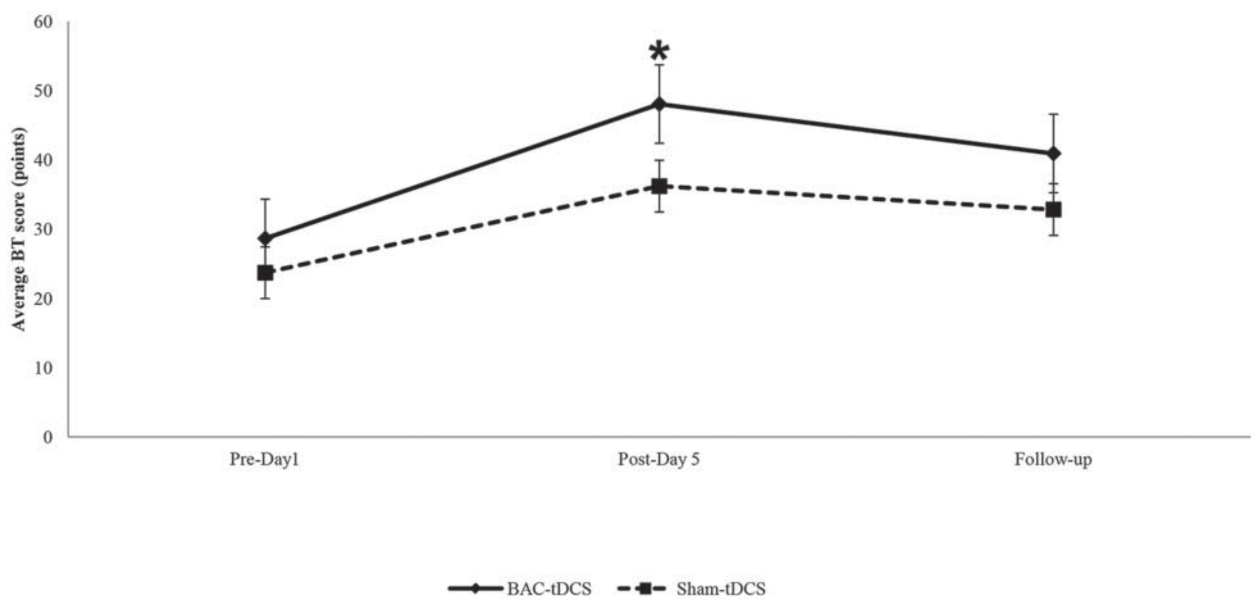


**FIGURE 2.** Change in scores for the assessment of acquisition and retention for the bimanual typing (BT) task by group (solid line = bihemispheric anodal corticomotor transcranial direct current stimulation [BAC-tDCS], dashed line = sham-tDCS). Magnitude of change in scores between pre-Day 1 and post-Day 5 was significantly different between the 2 groups (*$p = .04$, for comparison between pre-Day 1 and post-Day 5). This was not retained at follow-up (one week after cessation of stimulation and practice).



(Bastani & Jaberzadeh, 2011), which identified a large effect size associated with unimanual motor function improvement in nondisabled persons ($d = 0.92$, 95% CI [–1.02, 2.87], $p = .35$). No effects (positive or negative) were observed on STM function, and no adverse effects beyond itching were observed.

This is the first study to report the use of a bihemispheric anodal-anodal tDCS electrode montage over the motor cortex to improve bimanual hand performance. In this study we used a bimanual typing task that required alternating movements between hands. Bimanual movements are associated with bilateral increased cortical excitability (McCombe Waller et al.,

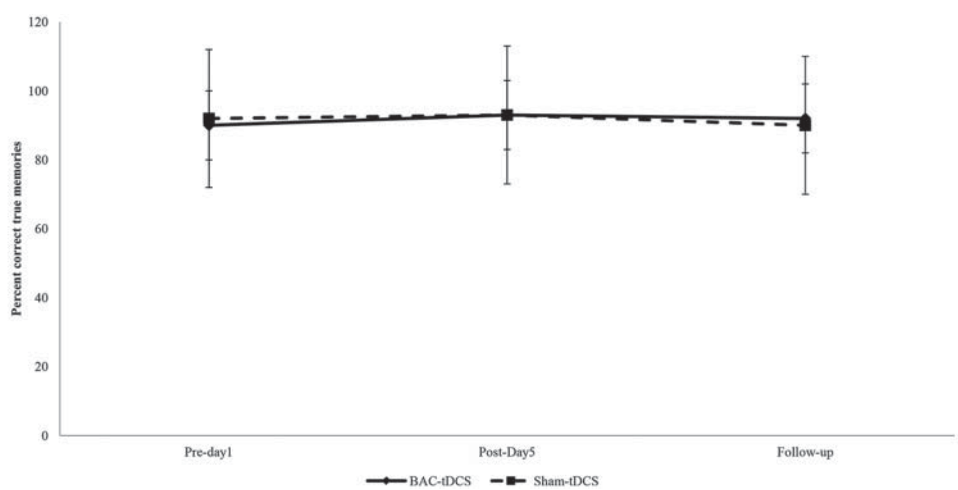


**FIGURE 3.** Change in short-term memory scores by group (solid line = bihemispheric anodal corticomotor transcranial direct current stimulation [BAC-tDCS], dashed line = sham-tDCS). There was no significant between-groups difference.

2008). While asynchronous bimanual tasks have been studied less extensively than synchronous tasks, there is evidence that cortical activity during performance of asynchronous and synchronous tasks is similar. Haslinger et al. (2004) compared the blood-oxygen-level-dependent (BOLD) signals during bimanual tasks using functional magnetic resonance imaging and observed greater cortical activation during the asynchronous task when compared to a synchronous bimanual task. Although the task performed in the present study required finger movement from one hand while the other hand was actively held in position (i.e., elbow flexion, wrist extension, finger extension in anticipation of its next movement), future researchers could assess similarities in cortical activity between our task and other bilateral tasks that require simultaneous movement between both hands. In addition, future researchers could assess if both tasks could be enhanced to a similar degree with BAC-tDCS.

Theoretically, augmenting practice-related excitability with BAC-tDCS enhances excitatory effects beyond those of bimanual practice alone. This is consistent with previous evidence from our lab regarding the relationship between peripheral electrical stimulation and unimanual motor practice. We showed that in persons with tetraplegia, unimanual motor training combined with peripheral electrical stimulation (which, similar to BAC-tDCS, is intended to increase corticomotor excitability) is associated with greater improvements in skilled hand function than when either modality is administered in isolation (Beekhuizen & Field-Fote, 2008). We believe this is the reason for the larger magnitude of change in scores from pre-Day1 to post-Day5 in the BAC-tDCS group.

The mean change for the sham-tDCS group (12.5 points) lies in the lower end of the confidence interval for the BAC-tDCS group, and the latter showed a greater magnitude of mean change (19.4 points). Further, some subjects in the BAC-tDCS group demonstrated change values nearly 2 times larger than the mean change in the sham group. In terms of clinical interpretation, these results suggest that the magnitude of improvement achieved with physical practice alone was on the lower end of the range improvements achieved when practice was augmented by BAC-tDCS. While effects were not retained at one-week follow-up, we believe this may be because subjects were nondisabled persons whose hand function was close to optimal and therefore had small margin for change. In theory, retention could be greater in persons with bilateral hand impairment engaging in motor training concurrently with stimulation.

No significant effects of BAC-tDCS on STM were observed. Boggio et al. (2009) found significant improvements in STM in nondisabled subjects with unihemispheric anodal tDCS applied over the temporal lobe. tDCS exerts local effects at the stimulated site, but it is not a focal brain stimulation modality (Nitsche et al., 2007). Our primary intent for testing STM was to identify possible nonmotor effects arising from activation of cortical areas contiguous to the motor cortex as part of our assessment of safety associated with BAC-tDCS, as this approach has not previously been studied. There was no detrimental (or beneficial) effect of BAC-tDCS on STM function and no other adverse effects were reported by any subject. These results indicate BAC-tDCS was associated with improvements in performance of a bimanual task, and was safe as applied in this investigation.

First, a limitation of the present study was that we used only performance-based measures. Therefore, we can only infer that there were changes in neural excitability based on related published evidence (Nitsche & Paulus, 2001). However, the primary intent of this study was to determine whether further study of BAC-tDCS in persons with disability was warranted based on evidence of effects and safety in nondisabled subjects. Second, the BT task we used required asynchronous rather than synchronous use of the both hands, and it is possible that results may not generalize to bimanual tasks requiring simultaneous use of both hands. Last, we did not stratify the group randomization on the basis of preexisting bimanual skills, and pre-existing skill may affect task performance and learning. However, the results of testing for baseline equivalence indicated that there were no differences between the two groups at baseline; therefore we believe it is unlikely that differences in preexisting bimanual skill levels influenced the results of this study.

The results of this study showed that a five-day course of bihemispheric anodal corticomotor tDCS applied over the corticomotor hand area had a positive influence on bimanual skilled hand performance in persons without disability. STM was not affected and no adverse effects were reported. Further work is needed to assess this approach in persons with neurological conditions who have bilateral hand impairment.

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