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Original Articles

It's the Thought That Counts: Examining the Task-dependent Effects of Transcranial Direct Current Stimulation on Executive Function

Jay Gill [a,b], Priyanka P. Shah-Basak [a], Roy Hamilton [a,b,c,*]

[a] Laboratory for Cognition and Neural Stimulation, University of Pennsylvania, Philadelphia, PA, USA
[b] Center for Cognitive Neuroscience, University of Pennsylvania, Philadelphia, PA, USA
[c] Department of Neurology, University of Pennsylvania, Philadelphia, PA, USA

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ABSTRACT

Background: Prior investigations employing transcranial direct current stimulation (tDCS) have shown that stimulation can elicit subsequent improvement on tests of various cognitive abilities, including working memory. While stimulation parameters such as intensity and duration are known to determine the effects of tDCS, the degree to which stimulation effects are influenced by the nature of cognitive activities during stimulation remains unclear.
Objective/hypothesis: To determine whether manipulating the working memory load of a task performed during stimulation would modulate tDCS-induced enhancement of performance on a different, related measure after stimulation.
Methods: In two separate but closely related sham-controlled experiments, two groups of healthy subjects underwent anodal tDCS (2 mA) of the left dorsolateral prefrontal cortex (DLPFC) for 20 min. In Experiment 1, subjects ($n = 11$) trained on a letter 3Back task during stimulation. In Experiment 2 subjects ($n = 11$) trained on a letter 1Back task, which resembled the 3Back task but featured a lower working memory load. In both experiments, before and after stimulation, subjects completed an adjusting Paced Auditory Serial Addition Task (A-PASAT). Both the experimenter and subjects were blind to stimulation conditions in both experiments.
Results: Subjects were both faster and more accurate on the A-PASAT task after receiving real tDCS paired with 3Back training (Experiment1) compared to sham+3Back, real+1Back, and sham+1Back conditions.
Conclusions: The cognitive demands of a task performed during tDCS can influence the effects of tDCS on post-stimulation performance. This finding has direct relevance to the use of tDCS as an investigative tool in cognitive neuroscience and as a therapy.

Introduction

While a growing body of experiments have shown that transcranial direct current stimulation (tDCS) can be employed to modulate a variety of complex cognitive abilities [1–4], the methods employed in this large and growing body of work remain heterogenous. This variability reflects, in part, incomplete understanding of how different properties of tDCS such as current intensity [5], duration of stimulation, electrode placement, and direction of current flow impact changes in neural excitability [6] and cognitive function [3,7,8]. One potential determinant of stimulation effects that remains to be fully characterized is task-dependency, that is the degree to which the cognitive or behavioral activity that an individual is engaged in during tDCS influences the subsequent neurophysiologic and behavioral effects of stimulation [8–10].

Numerous studies have paired tDCS with specific cognitive or behavioral tasks [5,11,12], operating under the assumption that a complementary or additive relationship exists between stimulation and task rehearsal. On one level the logic of this approach is intuitive: if tDCS and rehearsal independently improve task performance, then it stands to reason that combining them may lead to further enhanced performance changes. However, a potentially

* Corresponding author. Goddard Laboratories, Room 518, University of Pennsylvania, 3710 Hamilton Walk, Philadelphia, PA 19104, USA. Tel.: +1 215 573 7090; fax: +1 215 898 1982.
E-mail address: Roy.Hamilton@uphs.upenn.edu (R. Hamilton).

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more nuanced argument in favor of this approach is that tDCS, by virtue of its relatively subtle modulatory effects on neural activity, may be more effective in brain networks that are already selectively engaged by a cognitive activity. By that account, cognitive and behavioral tasks used in conjunction with tDCS may play a determinative role in which brain regions, connections, and pathways are most affected by stimulation [13]. Extending this reasoning further, one could hypothesize that pairing stimulation with tasks that engage specific cognitive domains would result in selective changes in brain activity, the magnitude of which would be dependent on the degree to which the tasks paired with stimulation engaged the cognitive domains and brain networks in question. However, few studies to date have explored whether tDCS paired with behavioral tasks results in change in performance on cognitively related tasks [9,10], and no study has directly tested whether the effects of tDCS can be influenced by varying the level of domain-specific cognitive demand of a concurrent training task.

We sought to examine the role of training task-dependency in enhancing the effects of tDCS on executive function abilities in healthy adults. In a two-part experiment (Fig. 1), we explored whether varying the degree to which working memory was engaged during stimulation affected the ability of anodal tDCS to transiently enhance working memory performance after stimulation. Prior work in normal controls has indicated the crucial role of the left dorsolateral prefrontal cortex (DLPFC) in working memory functions [14–16] as well as other executive functions [17–19]. Therefore, in Experiment 1, subjects received anodal tDCS to the left DLPFC [1] while completing a letter 3Back working memory task. In Experiment 2, a different group of subjects underwent an identical stimulation paradigm but performed a 1Back task—a task that was identical in design to the prior task except less dependent on working memory function—during stimulation. Due to the higher working memory demand of the 3Back compared to the 1Back, we predicted that anodal tDCS combined with training with the 3Back task would be associated with transient improvement on a different task that required working memory. We tested this hypothesis by administering an adjusting version of the Paced Auditory Serial Addition Test (A-PASAT) before and after stimulation [20].

Materials and methods

Stimulation parameters

TDCS was delivered by a constant-current battery operated stimulator unit (Magstim Eldith 1 Channel DC Stimulator Plus, Magstim, Whitland, UK) via two 5 $\times$ 5 cm^2 electrodes soaked in a saline solution. All subjects received both anodal and sham stimulation for 20-min in 2 separate sessions (3.92 $\pm$ 3.7 days separated these sessions). The active electrode was placed over F3 using the 10-20 International EEG system, a region corresponding to the left DLPFC. The reference electrode was placed over the right supraorbital region. Anodal stimulation was delivered at 2 mA for 20-min (current density: 0.80 μA/mm^2). During sham stimulation, current was ramped up to 2 mA and then back down to 0 mA in the first 30 s, which remained at 0 mA for the rest of the 20 min period. The order in which subjects received real and sham stimulation was counterbalanced. Both subjects and the experimenter were blinded to the type of stimulation applied during each session.

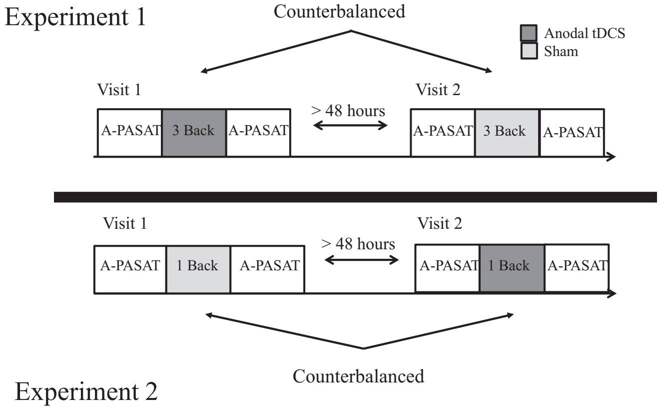

Figure 1. Overview of Experiments 1 and 2.

Adjusting Paced Auditory Serial Addition Task (A-PASAT)

We employed an adjusting version of the Paced Auditory Serial Addition Task (A-PASAT) [20] to assess changes in performance immediately after stimulation in both Experiments 1 and 2. Single digits ranging from 1 to 9 were presented aurally. Subjects were instructed to sum the two most recently presented numbers and respond verbally prior to the presentation of the next digit. Interstimulus intervals (ISIs) were altered depending on subjects' performance. When a subject answered correctly within the stimulus presentation window prior to the appearance of the next digit, the ISI was reduced by 20 ms; when a subject answered incorrectly, the ISI increased by 20 ms. The number stimuli were comprised of pre-recorded audio files (500 ms in duration) that were played using the E-Prime E Studio (v1.2 Psychology Software Tools, Inc.) on a laptop computer (Dell Latitude E6400). The task was composed of 4 blocks of 60 trials. The initial ISI was 2400 ms at the beginning of block 1, and was subsequently adjusted based on subject accuracy. Subject responses were captured using a digital audio recorder and scored offline. Performance was scored with respect to overall accuracy. Accuracy was also evaluated as a function of ISI, ranging from 2400 ms up to 220 ms. For the purposes of this analysis, ISIs were grouped into intervals of 200 ms. Lastly, we evaluated trial frequencies, which is the number of trials that subjects completed in each ISI grouping.

Experiment 1

Subjects

Eleven right-handed young adults (3 females) ages 18–25 years (21.8 $\pm$ 2.7 years) with no history of neurological or psychiatric disorders were enrolled in Experiment 1. Subjects completed an average of 15.6 years of education (SD = $\pm$1.5). None were taking prescribed anti-depressants or other psychoactive medications, and none had contraindications to receiving tDCS. This study was approved by the Institutional Review Board of the University of Pennsylvania. All subjects provided informed consent.

Training task – letter 3Back

Subjects completed the letter 3Back task during stimulation in Experiment 1 (Fig. 1). Stimuli were displayed on a laptop computer (Dell Latitude E6400) centered in front of the subject and were generated using E-prime E Studio (v1.2 Psychology Software Tools, Inc.). The task consisted of 10 lower-case letters [a, b, c, d, e, i, l, o, p, q] presented in a pseudorandom order over 764 trials (20-min). Letters that resembled each other (homolyphs) were intentionally incorporated and presented in sequence to increase the difficulty of the task. Each letter was displayed on the screen for 1300 ms and was followed by a 50 ms blank screen. Subjects were instructed to press "2" if the letter on the screen matched with the letter that