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Research article

Differential effects of high-definition transcranial direct current stimulation on verbal working memory performance according to sensory modality

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ABSTRACT

Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique that modulates cortical excitability in a polarity-dependent manner. The diffuse nature of tDCS makes it difficult to investigate the optimal stimulation parameters for more effective and specific cognitive enhancement; to address this deficit, a more focalized stimulation technique, high-definition tDCS (HD-tDCS), has been developed. To date, only a few studies have examined the effects of HD-tDCS on cognitive functions; and none has investigated the effects of HD-tDCS on different sensory modalities of verbal working memory. Therefore, the present study compared the effects of prefrontal HD-tDCS on visual and auditory working memory tasks. Twenty healthy participants completed three sessions of each modality task, and additionally a sustained attention task. Anodal or sham HD-tDCS was administered to the dorsolateral prefrontal cortex (DLPFC) during the second session of the task in a parallel, single-blind design. Anodal stimulation to the DLPFC significantly enhanced the visual verbal working memory accuracy during and 20 min after the stimulation. In contrast, auditory verbal working memory performance was not modulated by anodal stimulation. Anodal stimulation to the DLPFC showed no effect on any other cognitive functions. The present study revealed the differential effects of HD-tDCS on two different modalities (visual vs. auditory) of working memory performance: important preliminary findings for the establishment of a more effective and specific use of tDCS.

1. Introduction

Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique characterized by portable size, relatively low cost and safety. In conventional tDCS, a weak direct current (1–2 mA) is delivered between two large pad electrodes (25 – 35 cm^2) attached to the scalp (positively charged anode and negatively charged cathode). A single session of tDCS has been reported to modulate cortical excitability for over an hour in a polarity-dependent manner [1–3]. Two mechanisms of the effects of tDCS have been proposed. The first involves depolarization and hyperpolarization of the resting membrane potential during anodal and cathodal stimulation. The second involves long-term potentiation (LTP) -like and long-term depression (LTD) -like neuroplastic changes after anodal and cathodal stimulation [4]. These neuromodulatory effects are also thought to underlie enhancement in learning and memory by tDCS. Extensive research has demonstrated that tDCS can enhance multiple cognitive functions such as executive function, learning and memory in both neuropsychiatric and healthy individuals [5,6,7]. However, the conventional large-pad electrode montage produces diffuse current flow through the brain [8,9], making it difficult to investigate the causal relationship between brain activity in the targeted region and behavior.

Recently, high-definition tDCS (HD-tDCS) has been developed to achieve more focalized stimulation using a 4 × 1 ring electrode configuration with an active center electrode on the targeted area surrounded by 4 reference electrodes [8,10]. HD-tDCS has also been shown to modulate cortical excitability in a polarity-dependent manner, and the excitability change lasted longer than conventional tDCS [3,11].

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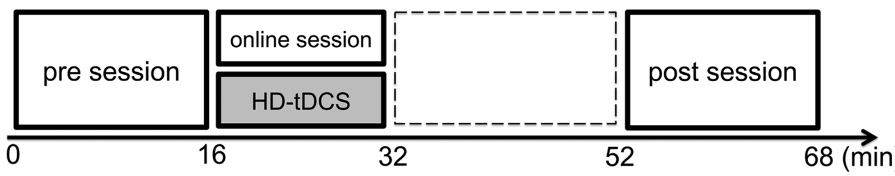

Fig. 1. Experimental procedure.
Participants performed three experimental sessions including pre, online and post sessions. They received 16 min of active or sham HD-tDCS during the online session. A 20 min rest period was set between the online and post sessions.

Although these findings in the motor cortical excitation have been established, only a few studies have examined the effects of HD-tDCS on cognitive functions, reporting that HD-tDCS to the dorsolateral prefrontal cortex (DLPFC) facilitated the rate of verbal learning, working memory speed [12], memory monitoring [13] and adaptive cognitive control [14] in comparison to the sham stimulation condition. More studies are needed to acquire detailed evidence about the effects of HD-tDCS on different cognitive functions and the optimal stimulation protocols for more effective and specific cognitive enhancement.

In the present study, we targeted the DLPFC because of its critical role for executive functions, especially working memory. The DLPFC is responsible for the maintenance, manipulation and integration of information in working memory [15,16]. Although working memory is an especially critical cognitive function [17,18] and the effects of tDCS on working memory have been explored in a number of studies [7,16,19], no published study has explored the potential differences in modality effects, e.g., visual versus auditory. The present study investigated the effects of prefrontal HD-tDCS on two different types (visual vs. auditory) of verbal working memory (VWM) as well as sustained attention. To this end, participants were randomly selected to receive active (excitatory anodal) or sham (placebo) stimulation; in addition, they performed visual and auditory VWM tasks before, during and 20 min after the stimulation to reveal the modality specificity in the effects of prefrontal HD-tDCS. Participants also performed a sustained attention task, as prefrontal tDCS enhanced sustained attention performance in several studies, and sustained attention may affect working memory task performance [20,21]. The results obtained in the present experiments will be useful for the establishment of more effective and tolerable use of tDCS required for basic studies to understand the cognitive processing in specific brain areas as well as clinical applications in neuropsychiatric patients such as attention-deficit hyperactivity disorder and schizophrenia. Moreover, the present study provided, to our knowledge, the first direct comparison of modality specificity in the effects of tDCS on working memory by assessing prefrontal HD-tDCS effects on both visual and auditory VWM performance using the same experimental paradigm.

2. Materials and methods

2.1. Participants

Twenty healthy right-handed participants (age 22.7 years ± 4.2, 10 females) were recruited for the experiment. The participants were randomly assigned to either sham ($n = 10$) or active ($n = 10$) conditions. Exclusion criteria were as follows: history of adverse reactions to transcranial magnetic stimulation (TMS) or tDCS, history or family history of seizure or stroke, history of severe head injury or brain surgery, any current psychiatric or neurological disorders, concurrent medication that could affect cognitive performance, and pregnancy. The study was approved by the local ethics committee of Chiba University Graduate School of Medicine, and the research was conducted in accordance with the 1964 Declaration of Helsinki. Written informed consent was obtained from each participant. To monitor adverse events, participants completed the tDCS Adverse Effects Questionnaire [22] during and after stimulation. Sleepiness was assessed using a visual analog scale (VAS; 10 cm) before the pre session and after the online and post sessions. The VAS score ranged from 0 (no sleepiness) to 100 (worst sleepiness).

2.2. Experimental procedure

The study used a single blind, sham-controlled, randomized, parallel design. The experiment consisted of three sessions (pre, online and post session) including a visual 3-back task, an auditory 3-back task and a modified version of the rapid visual information processing (RVIP) task. The pre, online and post session were carried out before, during and 20 min after the active or sham stimulation, respectively. Each session lasted approximately 16 min; participants received active or sham HD-tDCS during the online session. A 20-min rest period was set between the online and post session. Participants also underwent a 16-min practice session prior to the pre session to become familiar with the protocol. The total duration of the experiment was approximately 90 min (Fig. 1).

2.3. Cognitive tasks

Visual VWM was assessed using a visual 3-back task similar to that used elsewhere [23]. A set of 20 letters (i.e., J) was presented pseudo-randomly for 100 ms each at a rate of 2 s per stimulus. Participants were asked to press the space key on the keyboard when the letter currently presented matched one presented 3 stimuli previously. The task consisted of 60 stimuli including 20 target stimuli and lasted approximately 2 min. Outcome measures were the change in hit rate (H), false alarm rate (F) and reaction time for correct responses (RT) as well as statistic "A", calculated by subtracting the pre task score from the online and post task scores for each participant. A is a measure of sensitivity used in signal detection theory calculated as $A = 1/2 + (H - F)(1 + H - F)/4H(1 - F)$ [24]. Auditory VWM was assessed using an auditory 3-back task. The task was the same except for the stimulus modality. In the auditory 3-back task, a set of 20 letters (i.e., J) was aurally presented pseudo-randomly for 600 ms each at a rate of 2 s per stimulus. The task consisted of 60 stimuli including 20 target stimuli and lasted approximately 2 min. Outcome measures were the same as in the visual 3-back task.

Sustained attention was assessed using modified version of the RVIP task, in which participants perform a sustained attention task with a concurrent cognitive load. In the task, a session consisting of three phases (encoding, RVIP and recall phase) was repeated twice. In the encoding phase, participants memorized a set of 6 to 9 digits. The number of digits was determined according to their performance on the forward Digit Span from the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III). In the RVIP phase, participants were shown a sequence of digit stimuli (from 1 to 9) and asked to press the space key on the keyboard when they detected a series of three consecutive odd or three consecutive even digits. A stimulus was displayed for 600 ms without a time gap between successive stimuli. The RVIP phase consisted of 400 stimuli including 64 target stimuli and lasted approximately 4 min. During the RVIP phase, participants were asked to hold in their memory the sequence of digits memorized in the encoding phase. In the recall phase, participants were asked to write down the encoded digit sequence within 10 s. The total duration was approximately 10 min. Outcome measures were the change in hit rate and reaction time for correct responses calculated by subtracting the pre session score from the online and post session scores for each participant.

All stimuli are presented and results were recorded using Matlab R2016b (MathWorks) with Psychtoolbox [25].