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Research article

Working memory capacity differentially influences responses to tDCS and HD-tDCS in a retro-cue task

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HIGHLIGHTS

- We compared tDCS and HD-tDCS in two attentional orienting working memory (WM) tasks.
- An interaction emerged between tDCS type and high/low WM capacity groups.
- Low WM capacity participants benefited from HD-tDCS compared to tDCS.
- Group differences should be taken into account to understand the stimulation effects.

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ABSTRACT

There is growing interest in non-invasive brain stimulation techniques. A drawback is that the relationship between stimulation and cognitive outcomes for various tasks are unknown. Transcranial direct current stimulation (tDCS) provides diffuse current spread, whereas high-definition tDCS (HD-tDCS) provides more targeted current. The direction of behavioral effects after tDCS can be difficult to predict in cognitive realms such as attention and working memory (WM). Previously, we showed that in low and high WM capacity groups tDCS modulates performance in nearly equal and opposite directions on a change detection task, with improvement for the high capacity participants alone. Here, we used the retro-cue paradigm to test attentional shifting among items in WM to investigate whether WM capacity (WMC) predicted different behavioral consequences during anodal tDCS or HD-tDCS to posterior parietal cortex (PPC). In two experiments, with 24 participants each, we used different stimulus categories (colored circles, letters) and stimulation sites (right, left PPC). The results showed a significant (Experiment 1) or trending (Experiment 2) WMC x stimulation interaction. Compared to tDCS, after HD-tDCS the retro-cueing benefit was significantly greater for the low WMC group but numerically worse for the high WMC group. These data highlight the importance of considering group differences when using non-invasive neurostimulation techniques.

1. Introduction

Transcranial direct current stimulation (tDCS) usage is growing rapidly due to a strong safety profile [1,2], tolerable use [3], affordability, and ability to address structure-function and translational questions in various domains (working memory (WM): [4–17]; perception: [18,19]; motor processing: [20,21]; episodic memory: [22–24]). However, tDCS can have heterogeneous effects across participants performing cognitive tasks [5,11,12], compared to relatively predictable effects on motor tasks [25]. For example, we found that anodal tDCS to right parietal cortex paired with a change detection WM task *selectively* benefited the high working memory capacity (WMC) group [7,26]. Group differences may be an *essential* overlooked factor in recent meta-analyses of tDCS effects claiming that tDCS is ineffective on cognitive tasks [27,28]. One perceived limitation of tDCS is the distribution of current, which makes it difficult to conclusively link structure and function [29,30]. HD-tDCS is an alternative that provides focal stimulation by using smaller electrodes and configuring them in a ring-like pattern to constrain current flow [31]. Current modeling recommends HD-tDCS for more targeted neuromodulation [32–36] and suggests that it induces longer lasting effects compared to conventional tDCS [31].

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However, to our knowledge no studies employing a cognitive task compare tDCS and HD-tDCS effects. We tested if these techniques interacted with WMC. Individuals with low WMC might benefit more from focal HD-tDCS because it is more locally intense than tDCS. Feedback and financial incentive restore tDCS benefits to low WMC [26], indicating that modified tDCS paradigms can be effective in this population. HD-tDCS might also boost benefits in the high WMC group, or conversely it might impair their performance by decreasing signal-to-noise ratio in the targeted area or not change the performance as a result of the ceiling effects [37]. Comparing tDCS and HD-tDCS will provide a greater sense of what facilitates WM, and in whom. Moreover, these investigations will be translational for future training and rehabilitation approaches. To sum up, we hypothesize that high WMC participants benefit on tasks with WM demands from a diffuse, general 'boost' provided by tDCS, whereas HD-tDCS might benefit low WMC group in particular, by enhancing the activity of one node in the larger WM network. We employed a retrospective cueing (retro-cue) task that measures attentional reorienting to items currently held in WM [16,38–41]. We previously found that cathodal tDCS over frontal (F4) or parietal (P4) sites disrupted retro-cue performance [16]. Our ancillary goal was to optimize performance in low and high WMC participants via anodal tDCS/HD-tDCS.

2. Materials and methods

2.1. Stimulation protocol

Two experiments tested 24 participants each in 3 counterbalanced sessions: anodal tDCS, anodal HD-tDCS, sham. Experimental sessions were conducted at least 24 h apart. Electrode sites were chosen using HD/tDCS Explore software (Soterix Medical Inc., NY, USA). A continuous current stimulator delivered tDCS (Eldith MagStim, GmbH, Germany) through two $5 \times 7\,cm^2$ electrodes housed in saline soaked sponges. The anode sat over right (P4: Experiment 1) or left (P3: Experiment 2) posterior parietal cortex; the reference was on the contralateral cheek. HD-tDCS was delivered over these sites via ring 4×1 montage (Soterix Medical Inc., New York). The electrodes were ~0.5" in diameter. Four cathodal electrodes sat equidistantly around the anode (Experiment 1: Pz, C4, P8, O2; Experiment 2: Pz, C3, P7, O1). The ring 4×1 montage has been utilized in a study combining HD-tDCS with functional Near-Infrared Spectroscopy [42].

Before HD-tDCS, we applied 0.5 ml 0.5% Lidocaine under electrodes to reduce discomfort [43], and 1.5 ml Signagel (Parker Laboratories, NJ, USA) to improve conductance. Active stimulation was 1.5 mA for 20 min. Sham was delivered by tDCS or HD-tDCS (50%). Sham involved a 20 s ramp up/down of current at the beginning and the end of stimulation with no current during the interim to blind participants to stimulation condition.

2.2. Task design

First, to get an independent baseline measure of WMC, participants completed the computerized automated operation span (OSpan) task before the first session. It is a task of divided attention in which participants solve true/false arithmetic problems while simultaneously encoding and maintaining a letter sequence [44]. The task lasted for ~5 min. A median split of the OSpan scores determined high and low WMC groups in each experiment. Next, participants completed 20 practice retro-cue trials. Stimulation started at the beginning of the practice session and lasted 20 min. After practice participants completed the retro-cue task [16,38–41]. Trials began with fixation (1200 ms), followed by a delay (200 ms), and a 4-item stimulus array (Experiment 1: 300 ms, Experiment 2: 56 ms). In Experiment 1, the stimuli were colored circles (5.5°) drawn from a set of 10 color patches. In Experiment 2, the stimuli were letters drawn from the 21 consonants ($1° \times 1°$). Stimuli were placed in each quadrant at 6° (Experiment 1) or 3.5° (Experiment 2) from fixation. Next, a black and white noise mask (10.5° X 15°, 700 ms) appeared and then a blank screen (300 ms) before the retro-cue appeared: neutral ('X', $1.4° \times 1.4°$) or valid ('arrow', $1.4° \times 1.1°$, 100 ms). After a second delay (400 ms), the probe screen appeared. The probe screen preserved the stimulus configuration by indicating locations with empty annuli (Experiment 1) or parentheses (Experiment 2); the probe location contained either an old or a new stimulus item. Participants reported whether the probe stimulus matched the object-location conjunction shown at encoding ('O': match, or 'N': non-match, 50% each). Participants received visual feedback (correct/incorrect) and initiated the next trial via key press. The task began after 5 min of stimulation and lasted ~15 min (200 trials, rest after each block of 50), meaning the end of the task coincided with the end of stimulation. Participants repeated a new three-letter word during Experiment 1 to prevent verbal rehearsal of the color patches for each block. Verbal rehearsal of the letters was not prevented in Experiment 2.

2.3. Analysis

For both experiments, we conducted a repeated measures of 3-way ANOVA with 2 cue-type (Valid, Neutral) X 3 stimulation (tDCS, HD-tDCS, sham) X 2 WMC group (High, Low) on WM raw accuracy and median response times (RT). To further understand the attentional reorienting interaction, we calculated the retro-cue benefit (RCB accuracy: valid trial% – neutral trial%; RCB RT: neutral trial RT – valid trial RT) and conducted a repeated measures of 2-way ANOVA with the between-subjects factor of WMC group (High, Low) and the within-subjects factor of stimulation (tDCS, HD-tDCS, sham).

3. Results

To test for fatigue, we compared performance on the first and second halves of the experiments for each stimulation condition. A 2-way ANOVA on raw accuracy with within factors of cue-type (Valid, Neutral) and half (First, Second) showed the expected main effect of cue-type (p's < 0.001), but no main effect of experimental half or interaction (all p's > 0.226), suggesting fatigue was not a concern.

High and low WMC groups were based on median OSPAN scores per experiment (Experiment 1: low WMC: 6–20; high WMC: 24–43; Experiment 2: low WMC: 4–26; high WMC: 27–43). Raw accuracy scores are given in Table 1. In Experiment 1, the 3-way ANOVA on raw accuracy showed a significant main effect of cue-type such that performance benefited from a valid cue ($F_{1,22} = 118.86$, $p < 0.001$; $\eta p^2 = 0.84$; valid Mean (Standard Error) = 85.69 (1.55); neutral: M = 76.45 (1.57)). The significant main effect of group ($F_{1,22} = 7.40$, $p = 0.01$; $\eta p^2 = 0.25$) showed worse performance in the low WMC group (M = 76.97 (2.12)) compared to the high WMC group (M = 85.17 (2.12)). The main effect of stimulation was not significant ($F_{2,44} = 0.53$, $p = 0.59$). Importantly, the 3-way interaction of stimulation x WMC group x cue-type reached significance ($F_{2,44} = 4.01$, $p = 0.025$; $\eta p^2 = 0.15$). To characterize this interaction two 2-way ANOVAs (cue-type x stimulation) are conducted. The results yielded significant cue-type effects for both WMC groups (p's < 0.001), but no main effects of stimulation (both p's > 0.20). A significant cue-type and stimulation interaction emerged for the low WMC group only (low WMC p = 0.012, high WMC p = 0.65). No other interactions reached significance (all p's > 0.26). A 2-way ANOVA on RCB accuracy data showed that there were no main effects of stimulation ($F_{2,44} = 1.39$, $p = 0.26$) or WMC