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Effects of HD-tDCS on memory and metamemory for general knowledge questions that vary by difficulty

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ABSTRACT

Background: The ability to monitor one's own memory is an important feature of normal memory and is an aspect of 'metamemory'. Lesion studies have shown dissociations between memory and metamemory, but only single dissociations have been shown using transcranial direct current stimulation (tDCS). One potential reason that only single dissociations have been shown is that tDCS effects may be moderated by task difficulty.
Objective/Hypothesis: We used high definition (HD) tDCS to test for dissociable roles of the dorsolateral prefrontal cortex (DLPFC) and anterior temporal lobe (ATL) in semantic long-term memory and metamemory tasks. We also tested whether general knowledge question difficulty moderated the effects of HD-tDCS.
Methods: Across 3 sessions, participants received active HD-tDCS over the left DLPFC or left ATL, or sham HD-tDCS during general knowledge recall and recognition tests, and a 'feeling-of-knowing' metamemory task. General knowledge questions were blocked by difficulty. Repeated measures ANOVAs were used to examine the effects of HD-tDCS on memory and metamemory tasks by memory question difficulty.
Results: HD-tDCS over the ATL led to improved recall compared to DLPFC and sham HD-tDCS, and this occurred only for medium difficulty questions. In contrast, for non-recalled questions, HD-tDCS over the DLPFC led to improved recognition accuracy and improved feeling-of-knowing accuracy compared to ATL and sham HD-tDCS, and this was not moderated by memory question difficulty.
Conclusion (s): HD-tDCS can be used to dissociate the roles of the ATL and DLPFC in different memory and 'metamemory' tasks. The effects of HD-tDCS on task may be moderated by task difficulty, depending on the nature of the task and site of stimulation.

1. Introduction

When asked a general knowledge question, people either know or do not know the answer, but even when they cannot access the answer, they might nevertheless have a 'feeling' that the answer is available in their semantic long-term memory [1]. This 'feeling-of-knowing' (FOK) is the result of monitoring our memory, and is an important feature of 'metamemory', which has been broadly defined as knowledge about our memory [2]. These FOK judgments are often predictive of memory performance such that items given a higher FOK are more likely to be remembered than items given a lower FOK [3]. In terms of the brain regions supporting metamemory and semantic memory, the frontal lobes are thought to be critical for metamemory [5] and the anterior temporal lobes are thought to be critical for semantic memory [6–8]. We recently showed the accuracy of FOK judgments (i.e., how related the judgments are to memory accuracy) can be enhanced by increasing excitability of the dorsolateral prefrontal cortex (DLPFC) via high definition transcranial direct current stimulation (HD-tDCS), whereas there was no significant effect of increasing excitability of the anterior temporal lobe (ATL) via HD-tDCS on semantic long-term memory or metamemory [9]. However, it is unknown whether these effects are consistent across different levels of general knowledge question difficulty. This is important because tDCS effects on cognition have been shown to vary based on task difficulty, at least in working memory tasks [10,11]. The present study tested whether our previous results were replicable [9] and

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also examined the effects of HD-tDCS over the DLPFC and ATL on a semantic long-term memory and metamemory task where general knowledge questions varied based on difficulty.

When using a general knowledge paradigm, typical FOK tasks ask participants to attempt to recall the answer to a general knowledge question, and if they fail to recall the answer, they are asked to predict the likelihood that they would recognize the answer on a later test (i.e., to make a FOK judgment), which is then followed by a recognition test [3]. Several behavioral studies have indicated that question difficulty and metamemory performance are linked [12–14]. For example, when general knowledge questions are divided by difficulty, there are more and/or higher feelings-of-knowing for more difficult questions compared to easier questions [12] and there is overconfidence in answers to hard questions [14]. Furthermore, previous work examining metamemory accuracy, which is evaluated by determining how well each participant's subjective FOK rating relates to their objective memory performance, has shown that participants have the best metamemory accuracy for the easiest general knowledge questions, the worst metamemory accuracy for the hardest questions, and an in between level for medium difficulty questions [13]. Because metamemory accuracy can be affected by question difficulty, we tested whether or not HD-tDCS effects on metamemory were also moderated by question difficulty.

In the present study, we targeted the ATL and DLPFC: 1) to replicate our previous work [9], and 2) based on previous work showing their roles in memory and metamemory [15]. We chose to stimulate the ATL because ERP studies using the general knowledge task have shown memory effects over inferior-temporal electrode sites [16–18]. The ATL is also thought to be a “hub” for semantic memory [19]. Furthermore, patients with semantic dementia show significant atrophy in the ATL and the extent of atrophy correlates with the extent of semantic memory impairment [6], demonstrating that the ATL plays a critical role in semantic memory. Turning to metamemory, several fMRI studies have shown that the DLPFC modulates based on the level of FOK expressed [20–23]. The left DLPFC, in particular, showed similar FOK-related activity for episodic and semantic memory tasks [24]. Additionally, several lesion studies have shown deficits in metamemory with frontal lobe damage in different kinds of memory and metamemory tasks [5,25–27]. Although no lesion studies have directly tested for a dissociation between memory and metamemory in individuals with ATL versus DLPFC lesions in a semantic memory task, findings in the episodic memory domain have shown that temporal lobe epilepsy patients show intact metamemory and impaired memory [4,28], whereas patients with frontal lobe damage have shown intact memory and impaired metamemory [5]. Taken together, these findings suggest that memory and metamemory may be at least partially dissociable and that the ATL and DLPFC are involved in these processes.

Although lesion and neuroimaging studies are informative, issues with recovery/compensation for patients [29,30] and the correlational nature of neuroimaging are limiting factors when making inferences. Non-invasive brain stimulation is well-suited to answer questions about the brain regions that subserve cognitive processes. TDCS is a non-invasive brain stimulation technique in which electrodes are placed on the scalp and deliver a constant current of low-amperage (usually 1–2 mA) to reach the cortex [31]. Conventional tDCS typically places two large electrodes, one stimulation electrode often referred to as the “anode” and one return electrode often referred to as the “cathode,” on the scalp that are spaced somewhat far apart. It is generally assumed that the area under the anode shows enhanced cortical excitability (often referred to as “anodal stimulation”), whereas the area under the cathode shows inhibition (often referred to as “cathodal stimulation”), but this appears to hold true in studies of the motor cortex and less so for cognitive studies [32]. Thus, it is not always easy to predict the direction of change in cortical excitability or behavior with tDCS and it has been noted that “anodal” vs. “cathodal” stimulation may be misleading terms when referring to the desired effects on the brain and behavior [33]. An additional challenge with conventional tDCS is that because it uses large electrodes that are spaced far apart, both the region of interest and surrounding structures are stimulated [34]. To address this issue, more focal methods of tDCS have been created, termed High Definition tDCS (HD-tDCS), which uses a 4×1 ring electrode configuration that restricts the area of stimulation [35]. In the present study, we used HD-tDCS with one central stimulating electrode (i.e., anode) and 4 return electrodes (i.e., cathodes) to increase excitability of the ATL and DLPFC, and could be referred to as “anodal stimulation”. Although some questions remain about the underlying biological mechanisms responsible for tDCS-induced changes in behavior, online tDCS (i.e., the actual stimulation period) is thought to modify neural activity via altering the resting potential [36] and/or inducing surges in astrocytic calcium signaling [37]. In addition to online effects, there are thought to be longer lasting “after effects” or “offline” effects that induce changes in synaptic plasticity [38].

The ability of conventional tDCS to alter neural firing rates and/or plasticity, and to lead to reliable effects on behavior, has been a subject of recent debate [39–41]. One possible explanation for why conventional tDCS effects appear unreliable [41], is that previous work using other cognitive tasks has shown conventional tDCS effects are seen only on appropriately challenging tasks [10,11,42,43]. For example, both “anodal” and “cathodal” stimulation of the parietal cortex led to improvements in a change detection working memory task, but only for individuals with high working memory capacity and only in the most difficult change detection task (set size 8) [11]. In another example, “anodal” tDCS over the prefrontal cortex led to improvements in sentence processing and n-back tasks, but only in the more difficult conditions [43]. There have been numerous published papers using conventional tDCS [for review, see 40,41], but there are fewer studies that have tested the effects of HD-tDCS on cognition [9,44–47]. We previously showed that HD-tDCS over the DLPFC improved metamemory accuracy [9], but did not show the expected increase in recall with ATL stimulation. Therefore, the aims of this experiment were to replicate those findings and examine whether the effects of HD-tDCS were moderated by question difficulty.

Given the relative paucity of published HD-tDCS studies, there could be some concern that it is “too focal” to exert its effects, which has been a potential issue with transcranial magnetic stimulation (TMS) [48–50]. However, several HD-tDCS studies targeting the prefrontal cortex have reported effects across a variety of cognitive tasks, ranging from memory to impulsivity [9,44–46,51]. Although even fewer published studies have targeted regions in the temporal lobe, there have been a few findings showing improvements in behavior [44,51,52] and our own data showing no significant effect on memory [9]. Thus, extant research indicates that HD-tDCS has the potential to demonstrate changes in behavior and is not “too focal” for all cognitive tasks.

We previously used HD-tDCS to test the roles of the ATL and DLPFC in memory and metamemory accuracy using a general knowledge FOK task during which participants attempted to recall the answer to a general knowledge question, made a FOK judgment, and then completed a recognition task for the correct answer to the question [9], but did not examine effects of question difficulty. We chose to stimulate the left DLPFC because it has modulated by the level of FOK in both episodic and semantic memory tasks [24] and chose the left ATL because it has been shown to be