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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.

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Keywords

Transcranial direct current stimulation; dorsolateral prefrontal cortex; anterior temporal lobe; feeling-of-knowing; recall; recognition

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 [4,5] 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 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 to: 1) 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 that temporal lobe epilepsy patients show intact metamemory and impaired memory [4,28], whereas patients with frontal lobe damage show 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 induce 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 25, 29], 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 critical for semantic memory [6,53]. HD-tDCS over the DLPFC improved metamemory accuracy, but there were no significant effects of ATL stimulation on recall, recognition, or FOK judgments [9]. Because replication is critical [41,54,55], one aim of the present experiment was to replicate our previous work [9]. The HD-tDCS montages, duration of stimulation, stimuli, task, and population (i.e., Brooklyn College students) in the present study are the same as in our previous work. A second aim was to examine the role of question difficulty as moderator of the effects of HD-tDCS on semantic memory and metamemory. Previously, we did not show the expected effects of HD-tDCS over the ATL improving semantic memory [9], and we reasoned that perhaps the questions were not appropriately difficult. Thus, the only change from our previous work

was that we previously used one test with questions of varying difficulty intermixed, and in this experiment we blocked the test into 3 blocks of varying difficulty (1 easy block, 1 medium block, and 1 hard block). Our third aim was to test for dissociable roles of the ATL and DLPFC in semantic memory and metamemory accuracy. We expected to replicate and extend our previous work showing that DLPFC stimulation improved metamemory accuracy, and tested whether or not this occurred across different levels of question difficulty. Our previous work did not show effects of HD-tDCS over the ATL, but based on neuropsychological studies showing the ATL plays a critical role in semantic memory [6,53], we expected that question difficulty would moderate the effects of HD-tDCS on memory performance.

Materials and methods

Participants

39 healthy, English speaking, Brooklyn College students consented to participate in this 3-session, research study for course credit (1 credit per hour) or for pay (\$15/hour). Two participants failed to return for the third visit and 1 participant withdrew after receiving the “pre-stim tickle” and finding HD-tDCS unpleasant, so data from the 36 participants (12F/7M/17 undisclosed, ages 18–27, Mean $\pm$ SEM: 21.42 $\pm$ 0.32 years) who completed the study were analyzed. Participants were screened before each experiment to ensure they were eligible to participate and had no contraindications to tDCS. Participants were free from any self-reported neurologic and psychiatric illness, and none had any open wounds on the scalp and/or face. Each participant provided written consent in a manner approved by the Human Research Protection Program at the City University of New York (CUNY).

High Definition Transcranial Direct Current Stimulation (HD-tDCS)

HD-tDCS was administered using the Soterix 1×1 tDCS Low-Intensity Stimulator (Model 1224-B, Soterix Medical, New York, NY) with a Soterix 4×1 adaptor. For DLPFC stimulation, the stimulating electrode (anode) was placed at the F3 position (using the 10–20 system) and 4 return electrodes (cathodes) were placed at positions AF3, F1, F5, and FC3. The same montage was used for the sham condition. For ATL stimulation, the stimulating electrode (anode) was placed at T7 and 4 return electrodes were placed at FT7, FT9, C5, and TP7. The electrodes were sintered Ag/AgCl ring electrodes (outer radius: 12mm; inner radius 6mm). The electrodes were fixed on an EEG cap with HD Electrode holders (Soterix Medical, New York, NY) and filled with Signa Gel to ensure electroconductivity. In all montages, the anode was set to deliver a total current of 2 mA, and the return electrodes shared the same current intensity (0.5 mA each). We chose 2mA because HD-tDCS has been shown to be safe and tolerable for up to 2mA [44,56,57] and it is the most commonly used strength [38–46, but see 47–50]. Furthermore, in a study that manipulated current intensity (1 mA vs. 2mA) and stimulation duration (10 min vs. 20 min), 2mA for a duration of 20 min was more effective [51]. The montages were chosen based on computational models that generated simulated current maps using HDExplore (Soterix Medical, New York, NY) that showed good current flow in the left DLPFC or left ATL, respectively. During active DLPFC or ATL stimulation, participants received 2mA of stimulation for 20 minutes, plus a 30 sec ramp up time at the start of stimulation and a 30 sec ramp down time at the end of

stimulation. During sham HD-tDCS [61], the current ramped up to 2 mA and then back down during the first 30 sec, remained at 0.1 mA for 20 minutes, and then ramped up to 2mA and down again at the end of the sham period for the last 30 seconds. Participants completed 3 sessions (~1 week apart), with separate DLPFC, ATL, and sham HD-tDCS sessions; sessions were counterbalanced for stimulation and order across subjects (Figure 1).

2.4 Stimuli and Procedure

Stimuli consisted of 300 general knowledge questions that we used in our previous study [9] and that had previously been normed using a CUNY sample (the Baruch Knowledge Norms; <http://www.mangelslab.org/bknorms>). Questions spanned a wide variety of disciplines, including arts and culture, geography, history (American and World), mathematics, natural and social sciences, and technology. Questions had a single correct answer that consisted of a single word, 3–12 letters long. There were 4 additional questions used in a practice task to familiarize participants with the task. To manipulate question difficulty [13,14], questions were classified as “Easy”, “Medium” and “Hard” questions based on the proportion of CUNY students who recalled the answers correctly in prior studies, with 1/3 of the questions in each category. An example of an “Easy” question is: “What is the name of the supposedly unsinkable ship that sunk on its maiden voyage in 1912” [Answer: Titanic]. An example of a “Medium” question is: “What is the largest organ of the human body?” [Answer: skin]. An example of a “Hard” question is: “What is the name of the food storage organ found in many birds” [Answer: Crop]. The questions were broken down into 3 sets of 100 questions, and one unique set of questions was used for each HD-tDCS session. Questions were presented using Psychopy [64].

HD-tDCS began at the start of the general knowledge task (Figure 1). The task was divided into three separate test blocks and subjects were told that they would complete 3 distinct tests. At the start of each block subjects viewed a screen that read, “You are now starting a new test. Press the space bar when you are ready to continue.” Each block contained questions of a single difficulty. Order of question difficulty by block was counterbalanced across participants, but each participant received the same block order for each visit. In other words, a participant who completed the blocks in the order Medium, Easy, Hard, would have that same block order, but with different questions, for DLPFC, ATL, and sham HD-tDCS. A different subject might have the order Hard, Medium, Easy, for all three sessions.

After the instructions, participants first viewed a general knowledge question on the screen and were instructed to type in the answer if they could recall it, and to type “idk” to indicate “I don’t know” if they did not know the answer. Subjects had a maximum of 45 seconds to answer the question. The trial advanced after a subject typed in an answer and hit the ‘enter’ key, or after 45 seconds. This was followed by a FOK judgment, in which they had a maximum of 30 seconds to indicate the likelihood that they would recognize the correct answer on a 1–10 scale, with each number representing 10% increments in the likelihood of later recognition, with 1 representing 0–10% and 10 representing 90–100%. This was then followed by a recognition judgment in which they had a maximum of 15 seconds to choose which among 4 answers was the correct answer to the general knowledge question. One of the answers was correct and the three incorrect answers were the most frequently given

incorrect responses provided by other CUNY students. Participants completed FOK judgments and recognition questions for all questions, not just questions for which they could not recall the answer. The average duration of the memory and metamemory task was 26 min 40 s ($\pm$ 55 s) during sham stimulation, 26 min 12 s ($\pm$ 58 s) during DLPFC stimulation, 26 min 17 s ($\pm$ 58 s) during ATL stimulation. A mixed ANOVA on task duration with HD-tDCS as a within subjects factor (HD-tDCS: Sham, DLPFC, ATL) and block order as a between subject showed no main effect of HD-tDCS [$F(2,60)=0.22$, $p>0.8$], block order [$F(5,30)=1.63$, $p>0.18$], and no HD-tDCS by block order interaction [$F(10,60)=0.67$, $p>0.7$].

Following HD-tDCS, participants were given a questionnaire asking about whether specific side effects were absent, mild, moderate, or severe, and were also asked whether they believed these side effects were related to HD-tDCS. The side effects were: headache, neck pain, scalp pain, tingling, burning sensation, skin redness, sleepiness, trouble concentrating, and mood. For one subject, in the ATL session, the post-stimulation questionnaire was lost, and the ratings are reported for the remaining sessions. Participants were also asked to guess if they received “active” or “sham” stimulation for each session.

2.5 Data Analysis

FOK accuracy was assessed in two ways: 1) calculating the levels of FOK ratings given for both correct and incorrect memory, and 2) using d_a , a trial-by-trial measure of monitoring resolution based in signal detection theory which is thought to be superior to other measures of metamemory accuracy [65–67]. To compute d_a , we used the procedure described by Benjamin and Diaz (2008), using the formula $2y_0/(1+m^2)$, where y_0 is the y intercept and m^2 is the slope of a normal deviate isosensitivity function.

The relationships between memory, the level of FOK expressed, FOK accuracy, question difficulty and HD-tDCS were analyzed using repeated measures ANOVAs and post-hoc t-tests in SPSS 22.0. Mauchly’s test of sphericity was used to determine whether or not the assumption of sphericity was met. If the assumption was violated, the Greenhouse-Geisser correction was applied and the epsilon (ϵ) is reported. As a measure of effect size, partial eta squared (ηp^2) values are reported. Results were considered significant at $p<0.05$. Post-hoc tests were Bonferroni adjusted for multiple comparisons.

Results

Tolerability and Blinding of HD-tDCS

We first examined the side effects and sensations of HD-tDCS that participants reported as related to HD-tDCS. The only side effect reported as not related to HD-tDCS was sleepiness. Overall, most participants tolerated HD-tDCS rather well and experienced only mild and moderate side effects of stimulation (Table 1). Although most side effects were reported as “mild” or “moderate”, some were occasionally rated as “severe.” During sham HD-tDCS, there were 2 reports of a severe burning sensation. During DLPFC stimulation, there was 1 report of a severe headache, 4 reports of severe tingling, 6 reported of severe burning, and 1 report of severe redness. During ATL stimulation, there were 2 reports of severe tingling, 1 report of severe burning, and 1 report of severe sleepiness. All participants

were told they were free to stop at any time. Only one participant withdrew after experiencing HD-tDCS.

Friedman tests were used to assess any differences in sensations for the HD-tDCS conditions. There were no significant differences between stimulation conditions in reports of headaches, neck pain, scalp pain, sleepiness, concentration, or mood. It is worth noting that differences in neck [$X^2(2)=5.25$, $p<0.08$] and scalp pain [$X^2(2)=5.51$, $p<0.07$] approached significance. There were significant differences in tingling [$X^2(2)=6.86$, $p<0.05$], burning sensations [$X^2(2)=11.90$, $p<0.005$], and skin redness [$X^2(2)=11.84$, $p<0.005$]. Post hoc analyses with Wilcoxon signed rank tests were conducted and were Bonferroni corrected, resulting in a significance level of $p<0.017$. There was more tingling with DLPFC compared to sham stimulation ($Z=2.50$, $p<0.012$), marginally more tingling with ATL compared to sham stimulation ($Z=2.33$, $p<0.02$), and no difference between DLPFC and ATL stimulation ($Z=0.43$, $p>0.66$). There were more burning sensations with DLPFC ($Z=2.82$, $p<0.005$) and ATL ($Z=2.57$, $p<0.011$) compared to sham stimulation, and no difference between DLPFC and ATL stimulation ($Z=1.35$, $p>0.17$). There was more redness with DLPFC compared to ATL ($Z=2.51$, $p>0.012$) and sham stimulation ($Z=2.86$, $p>0.005$), and no difference between ATL and sham stimulation ($Z=0.83$, $p>0.4$). Overall, DLPFC and ATL stimulation were better matched in terms of side effects than DLPFC and sham or ATL and sham.

To assess participant blinding, we examined participants' guesses about whether they received active or sham stimulation. In the sham condition, 18 participants incorrectly guessed they received active stimulation, 17 correctly guessed they received sham stimulation, and 1 person didn't respond. In the DLPFC condition, 27 participants correctly guessed they received active stimulation, 8 participants incorrectly guessed they received sham stimulation, and 1 person didn't respond. In the ATL condition, 21 participants correctly guessed they received active stimulation, 13 participants incorrectly guessed they received sham stimulation, and 1 person didn't respond, and data were missing for 1 participant. To test if the belief about stimulation differed between conditions, we excluded blank responses, and used repeated measures logistic regression with DLPFC stimulation as the reference. Blinding was imperfect for the sham condition; significantly more participants guessed that active stimulation was applied in the DLPFC condition compared to the sham condition (Wald Chi-Square=6.34, $p<0.02$). However, there was no significant difference in guessing that active stimulation was applied between the DLPFC and ATL sessions (Wald Chi-Square=1.82, $p>0.17$). Similar to the side effects, DLPFC and ATL stimulation were better matched in terms of participants guessing the stimulation condition than DLPFC and sham or ATL and sham.

Memory Accuracy: Recall

To test for the effects of HD-tDCS to the ATL and DLPFC on semantic memory and whether question difficulty was a moderator, we first examined the effect of question difficulty and HD-tDCS on the number of answers to general knowledge questions that were correctly recalled (Figure 2). A 3 (HD-tDCS: Sham, DLPFC, ATL) $\times$ 3 (Question Difficulty: Easy, Medium, Hard) repeated measures ANOVA showed a main effect of difficulty [$F(1.61$,

56.37)=552.60, $p<0.00001$, $\epsilon=0.81$, $\eta_p^2=0.94$], a main effect of HD-tDCS [$F(2, 70)=7.55$, $p<0.001$, $\eta_p^2=0.18$], and a significant interaction [$F(3.12, 109.21)=3.61$, $p<0.02$, $\epsilon=0.81$, $\eta_p^2=0.093$]. Because we were mainly interested in effects of HD-tDCS, we followed up this interaction with repeated measures ANOVAs that tested for effects of HD-tDCS (Sham, DLPFC, ATL) within each level of question difficulty (Easy, Medium, Hard). A repeated measures ANOVA comparing the effect of HD-tDCS (Sham, DLPFC, ATL) on recall of answers to easy questions showed no difference in recall [$F(2, 70)=1.99$, $p>0.1$, $\eta_p^2=0.054$], with a slight trend of ATL HD-tDCS showing better recall than sham HD-tDCS ($p<0.12$). Similarly, a repeated measures ANOVA comparing the effect of HD-tDCS (Sham, DLPFC, ATL) on recall of answers to hard questions showed no difference in recall [$F(2, 70)=0.26$, $p>0.75$, $\eta_p^2=0.018$]. In contrast, a repeated measures ANOVA comparing the effect of HD-tDCS (Sham, DLPFC, ATL) on recall of answers to medium difficulty questions was significant [$F(1.46, 51.01)=9.81$, $p<0.001$, $\epsilon=0.73$, $\eta_p^2=0.22$]. For questions in the medium difficulty block, ATL stimulation showed better recall than sham ($p<0.005$, 95% CI of the difference in the means [1.04, 6.18]) and DLPFC stimulation ($p<0.02$, 95% CI of the difference in the means [0.41, 4.87]). These analyses provide evidence that the ATL is involved in recall of general knowledge questions, and that question difficulty is a moderator of the effects of HD-tDCS on recall of semantic information.

Memory Accuracy: Recognition

In addition to recall, we also tested semantic memory via recognition tests. Therefore, we next examined the effect of question difficulty and HD-tDCS on the number of answers to general knowledge questions that were correctly recognized (Table 2). A 3 (HD-tDCS: Sham, DLPFC, ATL) $\times$ 3 (Question Difficulty: Easy, Medium, Hard) repeated measures ANOVA showed a main effect of question difficulty [$F(2, 70)=575.80$, $p<0.00001$, $\eta_p^2=0.94$], a main effect of HD-tDCS [$F(2, 70)=3.29$, $p<0.05$, $\eta_p^2=0.086$], but no interaction [$F(3.27, 114.58)=0.733$, $p>0.5$, $\epsilon=0.82$, $\eta_p^2=0.021$]. The main effect of difficulty indicated that, even though question difficulty was classified based on recall, the questions still varied by difficulty during recognition. To follow up on the main effect of HD-tDCS, we examined the effect of HD-tDCS on recognition across all questions; although no post hoc t-tests survived Bonferroni correction, the main effect appears to be driven by DLPFC stimulation leading to marginally more correctly recognized answers compared to sham HD-tDCS ($p<0.09$, 95% CI of the difference in the means [-0.004, 0.081]).

Because participants completed the recognition task for all questions, including those that they recalled, we next examined the effect of question difficulty and HD-tDCS on the number of answers to general knowledge questions that were correctly recognized, conditionalized such that they were not recalled (Table 2). A 3 (HD-tDCS: Sham, DLPFC, ATL) $\times$ 3 (Question Difficulty: Easy, Medium, Hard) repeated measures ANOVA showed a main effect of difficulty [$F(2, 70)=78.72$, $p<0.00001$, $\eta_p^2=0.69$], a main effect of HD-tDCS [$F(2, 70)=7.95$, $p<0.001$, $\eta_p^2=0.19$], but no interaction [$F(3.11, 108.69)=2.09$, $p>0.15$, $\epsilon=0.78$, $\eta_p^2=0.056$]. To follow up on the main effect of HD-tDCS, Bonferroni-corrected post hoc t-tests showed that DLPFC stimulation led to more of the non-recalled answers being subsequently recognized compared to sham HD-tDCS ($p<0.05$, 95% CI of the difference in the means [0.015, 0.15]) and ATL stimulation ($p<0.005$, 95% CI of the

difference in the means [0.022, 0.13]). These results suggest that the DLPFC plays a role in recognition, and that question difficulty does not moderate the effects of HD-tDCS in this task.

Feeling-of-Knowing Ratings

The feeling-of-knowing is defined as occurring after a failed attempt at recall [2], so our metamemory analyses are confined to non-recalled trials. Because a large proportion of questions in the easy block were recalled, only 29 participants had enough non-recalled trials to calculate the average FOK rating across all 3 levels of question difficulty. A 2 (recognition accuracy: hits, misses) $\times$ 3 (HD-tDCS: Sham, DLPFC, ATL) $\times$ 3 (Question Difficulty: Easy, Medium, Hard) repeated measures ANOVA on FOK ratings showed a significant main effect of accuracy [$F(1, 28)=35.50$, $p<0.00005$, $\eta_p^2=0.56$], difficulty [$F(1.57, 44.04)=12.81$, $p<0.0005$, $\epsilon=0.79$, $\eta_p^2=0.31$], and an accuracy $\times$ HD-tDCS [$F(2, 56)=43.95$, $p<0.00001$, $\eta_p^2=0.61$] and an accuracy $\times$ difficulty $\times$ HD-tDCS interaction [$F(4, 112)=2.58$, $p<0.05$, $\eta_p^2=0.084$], with no other significant main effects or interactions. We followed up the three-way interaction with repeated measures ANOVAs that tested for effects of HD-tDCS (Sham, DLPFC, ATL) and question difficulty (Easy, Medium, Hard) for correct and incorrect recognition separately. A follow up 3 (HD-tDCS: Sham, DLPFC, ATL) $\times$ 3 (Question Difficulty: Easy, Medium, Hard) repeated measures ANOVA on FOK ratings for correct responses showed a main effect of difficulty [$F(2, 56)=9.73$, $p<0.0005$, $\eta_p^2=0.26$], and a main effect of HD-tDCS [$F(2, 56)=14.79$, $p<0.00001$, $\eta_p^2=0.35$], but the difficulty $\times$ HD-tDCS interaction did not quite reach significance [$F(3.14, 87.92)=2.5$, $p<0.065$, $\epsilon=0.79$, $\eta_p^2=0.082$]. Related to HD-tDCS, there were higher FOK ratings for correct responses with DLPFC stimulation (6.60 ± 0.30) compared to ATL (5.55 ± 0.30 ; $p<0.0005$, 95% CI of the difference in the means [0.72, 2.33]) and sham stimulation (5.07 ± 0.32 ; $p<0.003$, 95% CI of the difference in the means [0.38, 1.76]). The follow up 3 (HD-tDCS: Sham, DLPFC, ATL) $\times$ 3 (Question Difficulty: Easy, Medium, Hard) repeated measures ANOVA on FOK ratings for incorrect responses also showed a main effect of difficulty [$F(2, 70)=8.15$, $p<0.001$, $\eta_p^2=0.23$] and a main effect of HD-tDCS [$F(2, 70)=8.90$, $p<0.0005$, $\eta_p^2=0.24$] on FOK ratings, and no difficulty $\times$ HD-tDCS interaction [$F(3.18, 89.00)=0.64$, $p<0.6$, $\epsilon=0.80$, $\eta_p^2=0.022$]. Related to HD-tDCS, there were lower FOK ratings for incorrect responses with DLPFC stimulation (4.55 ± 0.19) compared to ATL (5.30 ± 0.30 ; $p<0.001$, 95% CI of the difference in the means [-1.20, -0.30]) and sham stimulation (5.27 ± 0.29 ; $p<0.011$, 95% CI of the difference in the means [-1.30, -0.14]). Thus, DLPFC stimulation led to higher FOKs for subsequently recognized answers and lower FOKs for answers that were not subsequently recognized, with minimal to no effect of question difficulty, suggesting that DLPFC stimulation increased FOK accuracy.

We also conducted similar analyses on FOK ratings that were restricted to medium and hard question blocks so that data from all 36 participants were used. A 2 (recognition accuracy: hits, misses) $\times$ 3 (HD-tDCS: Sham, DLPFC, ATL) $\times$ 3 (Question Difficulty: Medium, Hard) repeated measures ANOVA showed main effects of accuracy [$F(1, 35)=31.84$, $p<0.00005$, $\eta_p^2=0.48$], difficulty [$F(1, 35)=11.45$, $p<0.005$, $\eta_p^2=0.25$], and HD-tDCS [$F(2, 70)=3.86$, $p<0.05$, $\eta_p^2=0.10$], and an accuracy $\times$ HD-tDCS interaction [$F(1.62, 56.82)=48.67$, $p<0.000001$, $\epsilon=0.81$, $\eta_p^2=0.58$], with no other significant interactions. Bonferroni corrected

post-hoc tests showed that there were higher FOKs given for correct answers with DLPFC stimulation (6.64 ± 0.30) compared to ATL stimulation (5.45 ± 0.26), and higher FOKs for correct responses with ATL stimulation compared to sham HD-tDCS (4.81 ± 0.30), all p 's < 0.05. For incorrect responses, Bonferroni corrected post-hoc tests showed that there were lower FOKs given for incorrect answers with DLPFC stimulation (4.49 ± 0.20) compared to both ATL stimulation (5.20 ± 0.28) and sham HD-tDCS (5.16 ± 0.29), all p 's < 0.05, and sham and ATL HD-tDCS did not differ. Thus, similar to our earlier analyses with 29 participants, DLPFC stimulation led to higher FOKs for subsequently recognized answers and lower FOKs for answers that were not subsequently recognized, and this was consistent across different question difficulties.

Metamemory Accuracy

Because DLPFC stimulation led to an increase in recognition of non-recalled answers, one possibility was that the bigger difference in FOK ratings between correct and incorrectly recognized answers was driven by the difference in recognition accuracy. Therefore, we next examined whether HD-tDCS affected metamemory accuracy, which accounts for differences in memory performance. We first examined metamemory accuracy in the 29 participants who had enough incorrect trials to compute metamemory accuracy across all three levels of difficulty (Figure 3). A 3 (HD-tDCS: Sham, DLPFC, ATL) $\times$ 3 (Question Difficulty: Easy, Medium, Hard) repeated measures ANOVA on metamemory accuracy, as measured by d_a , showed a main effect of HD-tDCS [$F(2, 56)=19.77$, $p<0.00001$, $\eta_p^2=0.41$], but no effect of difficulty [$F(2, 56)=0.49$, $p>0.6$, $\eta_p^2=0.017$], or difficulty $\times$ task interaction [$F(2.44, 68.36)=1.32$, $p>0.25$, $\epsilon=0.61$, $\eta_p^2=0.045$]. Bonferroni corrected post-hoc t-tests showed that the main effect of HD-tDCS was driven by better metamemory accuracy under DLPFC stimulation compared to sham ($p<0.00005$, 95% CI of the difference in the means [0.29, 0.69]) and ATL stimulation ($p<0.0003$, 95% CI of the difference in the means [0.20, 0.69]). The pattern was similar when analyses were confined to medium and hard blocks and all 36 participants' data were used. A 3 (HD-tDCS: Sham, DLPFC, ATL) $\times$ 2 (Question Difficulty: Medium, Hard) repeated measures ANOVA on metamemory accuracy showed a main effect of HD-tDCS [$F(2, 70)=25.94$, $p<0.00001$, $\eta_p^2=0.43$], but no effect of difficulty [$F(1, 35)=0.50$, $p>0.45$, $\eta_p^2=0.014$], or difficulty $\times$ task interaction [$F(2, 70)=0.12$, $p>0.8$, $\eta_p^2=0.003$]. These data indicate

Discussion

We used HD-tDCS to test for different roles of the dorsolateral prefrontal cortex (DLPFC) and anterior temporal lobe (ATL) in memory and metamemory tasks. We also tested whether question difficulty moderated the effects of HD-tDCS on memory or metamemory. Consistent with a role in semantic knowledge, ATL stimulation showed improved recall of answers to general knowledge questions, but only in the medium difficulty test. In contrast, consistent with a role in monitoring, DLPFC stimulation led to improved recognition accuracy and metamemory accuracy regardless of test question difficulty. Taken together, these results show that difficulty may be a moderator for effects of HD-tDCS, and that this depends on the site of stimulation and the task.

Whether or not the effects of HD-tDCS were moderated by question difficulty depended on the task. For the recall task, HD-tDCS over the ATL led to increased recall, but only in the medium difficulty block, which is consistent with the ATL playing a direct role in semantic memory [6,53,68]. Thus it appears that HD-tDCS effects were only seen at levels that were appropriately challenging [10,11]; easy blocks were too easy, hard blocks were too hard, but the medium difficulty question were optimal for HD-tDCS effects. As a caveat, we may have been limited by floor effects in the hard condition and ceiling effects in the easy condition. In fact, it is possible that, in the hard block, we included questions that tested knowledge that individuals had never learned and thus it was impossible to retrieve the answer from semantic memory.

Interestingly, in the recognition task, despite performance differences based on question difficulty, question difficulty was not a moderator for effects of HD-tDCS, suggesting that not only does a task have to be appropriately challenging [10], but the nature of the task matters. The differential effects of HD-tDCS over the ATL and DLPFC likely relates to the different ways that recall and recognition probe memory. In the forced choice recognition test, participants could choose the correct answer because they recalled it, it was familiar, or they may have also used a recall-to-reject or process of elimination strategy. In contrast, recall tasks require participants to generate the correct answer. Indeed recall, recollection-based recognition, and familiarity-based recognition rely on different neural substrates [72,73]. Our data are consistent with previous work implicating the ATL in long-term memory [74] and that enhancing ATL activity via tDCS can lead to improved recall [75,76]. In contrast, the prefrontal cortex has been associated with familiarity-based recognition [77,78] and with memory monitoring [79], which may explain why HD-tDCS over the DLPFC led to improvements on the recognition test.

Alternatively, the fact that different factors make recall and recognition tasks difficult could explain why HD-tDCS effects based on question difficulty were only seen in the recall task. For example, recall questions may be difficult because no response is generated, whereas the recognition task may be difficult because there may be many plausible responses. Indeed, the incorrect response choices reflected the most frequent incorrect responses given by other CUNY students in a recall task (<http://www.mangelslab.org/bknorms>). The left prefrontal cortex (BA 9/10) has previously been associated with difficulty in response selection [82], and it is possible that by using frequently given incorrect response as lures for all trials that we minimized the effects of question difficulty in the recognition task.

Similar to recognition, neither the metamemory ratings nor metamemory accuracy showed question difficulty as a moderator of HD-tDCS effects. Metamemory ratings were lower for harder questions, but this did not interact with HD-tDCS. Despite other research showing that improving memory performance improves FOK accuracy [80,81], differences in performance across the blocks did not lead to changes in FOK accuracy. Note that manipulating question difficulty does not necessarily make the feeling-of-knowing task more metacognitively demanding; even if an individual is performing poorly on the general knowledge test, he or she may still be aware of not knowing the answer. It is possible that if the metacognitive demands were manipulated, HD-tDCS effects would be moderated by question difficulty.

We can only speculate as to why question difficulty was a moderator for ATL stimulation during recall, and not the other tasks. Difficulty was manipulated based on recall, so it is possible that differences in difficulty were large enough to see moderating effects only in recall. We think this is unlikely because the effects of difficulty were quite large in recall ($\eta_p^2=0.94$) and overall recognition ($\eta_p^2=0.94$), and were still large, albeit lower, for non-recalled recognized trials ($\eta_p^2=0.69$). It is worth acknowledging that recall tasks are typically viewed as more difficult than recognition tasks [69], and thus the Recall-Judgment-Recognition paradigm used here included a manipulation of task difficulty (i.e., recall vs. recognition) in addition to question difficulty. This is relevant because it has been proposed that tDCS has bigger effects on more cognitively demanding tasks [70] and other studies have shown effects on recall and not recognition using conventional tDCS [71]. It has been proposed that task difficulty matters because the extra stimulation provided by tDCS acts as a ‘tipping factor’ [10]. The ATL is thought to play a role in semantic representations [6], and perhaps HD-tDCS provides just the boost that answers close to threshold (i.e., medium difficulty questions) need to surpass threshold. Indeed, recent work showed improved face-name recall with conventional tDCS over the ATL, but only for names that were not immediately recalled [75,76]. Thus, one possibility is that effects of difficulty are seen when tasks are appropriately challenging, and there is a clear ‘tipping factor’, such as when the region is thought to play a key role in representation.

HD-TDCS over the DLPFC improved both recognition accuracy and FOK accuracy in this experiment, and neither of these effects differed by question difficulty. As a note, the findings that DLPFC stimulation led to higher FOKs for correct trials and lower FOK trials is interpreted as improving FOK accuracy rather than a separate FOK signal. The finding that DLPFC stimulation improved both recognition accuracy and FOK accuracy represents a replication from Chua & Ahmed (2016) in terms of FOK accuracy, but diverges in that there was no effect of DLPFC stimulation on recognition in our earlier work. There were more subjects in the current experiment than in Chua & Ahmed (2016), giving us increased power to detect differences. Interestingly, inspection of the means showed performance in the sham condition was lower in the current study than in the Chua & Ahmed (2016), whereas the DLPFC condition had numerically similar performance. Blocking tests by difficulty may have had an effect on baseline (sham) recognition performance, resulting in differences in the DLPFC condition compared to sham and ATL.

The finding that DLPFC stimulation led to increased FOK accuracy and recognition accuracy raises the possibility that the effect of DLPFC stimulation on FOK accuracy is due to improved recognition accuracy. However, metamemory accuracy measures, as opposed to metamemory ratings, control for differences in accuracy [65,83]. Although metamemory accuracy measures control for performance, it is possible that with better memory the basis of the metamemory judgment changes. Indeed, several studies have shown that improving memory can lead to improved metamemory accuracy, likely because with more available mnemonic information, individuals rely more on the mnemonic information rather than on other non-diagnostic cues [80,84]. However, we did not see effects of difficulty on FOK accuracy, suggesting that memory performance alone is insufficient to cause changes in FOK accuracy. Thus, the increased FOK accuracy in our study is unlikely to be due solely to increases in recognition accuracy.

Considering the overall Recall-Judgment-Recognition task, the present results showed ATL stimulation affected recall whereas DLPFC stimulation affected recognition and the FOK judgments. The finding that ATL stimulation led to improved recall is consistent with the widespread agreement that the ATL is involved in semantic memory. However, there is considerable debate about the nature of that role [8,85]. Some accounts posit that the ATLs are amodal hubs linking together distributed information, whereas others posit that the ATLs are particularly important in social concepts and others that the ATLs store knowledge about familiar people and landmarks. Our experiment was not designed to test these alternatives, but instead tests for a more general role in semantic retrieval. Our results suggest that increased excitability of the ATL leads to better recall, and this could be via increased activation of specific knowledge stored within the ATL or through increased excitation of the hub that propagates to more distributed representations.

Once information is retrieved from semantic memory via the ATL (either directly or indirectly), that information is available for monitoring by the DLPFC. The finding that DLPFC stimulation led to improvements in both recognition accuracy and feeling-of-knowing accuracy is consistent with a role for the DLPFC in memory monitoring accuracy, which is broadly related to executive functioning. It is worth noting that the DLPFC is large and is thought to consist of at least two subregions: an anterior-ventral region (BA46/9) and a posterior-dorsal region (BA 9/8) [86], and F3 (the center of our HD-tDCS montage) is over the more posterior-dorsal region [87], and thus our findings may best be interpreted as related to excitation of the more posterior-dorsal aspect of the DLPFC. The more posterior-dorsal region of the DLPFC is functionally connected to the posterior parietal cortex and has been implicated in executive functions, which includes monitoring [86]. Indeed, several fMRI studies have shown that activity in the DLPFC increases with demands on memory monitoring [88,89]. Feeling-of-knowing tests provide a direct test of memory monitoring because participants are explicitly asked to monitor their memory and decide whether any retrieved information satisfies the current task demands, and rate how likely they believe they are to recognize the answer in the future [2]. Similarly, recognition tests, especially forced choice recognition tests, also require memory monitoring. In this case, participants consider whether retrieved information related to any of the choices is sufficient for choosing that answer. This is consistent with data from patients with frontal lesions whose poorer memory performance is thought to result from monitoring difficulties, as evidenced by higher false alarm rates [90,91]. Given that HD-tDCS delivers continuous stimulation over a period of time, it is reasonable that memory monitoring would improve across tasks, and in the present study HD-tDCS over the DLPFC appeared to improve memory monitoring across different tasks.

We have framed our results in terms of stimulation to the ATL and DLPFC, but due to functional connections between brain regions, it is unlikely that the effects of HD-tDCS are confined solely to the regions of interest. Indeed, multimodal studies combining neuroimaging with conventional tDCS over the DLPFC have shown increased perfusion in the cingulate and parietal cortices [92] and changes in the default mode and frontoparietal networks [93,94], indicating that, at least with conventional tDCS, the effects may span multiple brain regions and networks. It is therefore worth considering whether or not there is evidence for effects of stimulating the ATL or DLPFC on other regions of interest.

Participants received ATL stimulation in one session and DLPFC stimulation in another session in a different week. If HD-tDCS over the ATL or DLPFC exerted downstream effects on the other region, we would expect to see similar effects on behavior across the active stimulation sessions. However, any improvements in recall with ATL stimulation did not lead to improvements in recognition or FOK accuracy for non-recalled items, suggesting that the effects of ATL stimulation were relatively specific. Similarly, DLPFC stimulation led to improvements in recognition and FOK accuracy, but did not influence recall performance.

TDCS is known to exert “online” effects during stimulation and “offline” effects after stimulation [38]. In this experiment, HD-tDCS was applied at the start of the task and some individuals finished the task by the end of stimulation whereas others continued the task beyond the stimulation period. Given this variability in task time, we are limited in our inferences and cannot make strong claims about whether the effects in this experiment are due to online vs. offline effects. The variability in task time in our experiment also raises the possibility that some blocks may have been disproportionately affected by online vs. offline effects of HD-tDCS. To minimize the likelihood of this, block order was counterbalanced across subjects. Additionally, there were no differences in task duration based on stimulation condition, block order, or a stimulation×block order interaction, making it unlikely that certain blocks were disproportionately affected by online vs. offline HD-tDCS effects.

One potential criticism of this work is that sham HD-tDCS may not have resulted in adequate participant blinding. Indeed, participants experienced fewer side effects and were more likely to guess “sham” in the sham condition. If participants had expectations about the effects of HD-tDCS, this could have led to differences in behavior. However, this is unlikely to change our inferences because this experiment contained two active stimulation conditions (i.e., ATL and DLPFC) and side effects and sensations were similar for both. Even if participants had expectations about HD-tDCS, it is less likely that they had montage-specific expectations or could distinguish the montages used during active HD-tDCS. Importantly, different behavioral effects were shown for ATL stimulation and DLPFC stimulation. These results suggest that including an active control (i.e., another stimulation site) is important for within subject HD-tDCS studies to increase the likelihood of participant blinding.

Conclusions

The present study provides evidence that HD-tDCS is capable of producing significant effects on cognition. Whether or not HD-tDCS leads to improved memory performance depends on the site of stimulation and the type of task and difficulty of the task, as evidenced by ATL stimulation leading to improved recall for medium difficulty questions and DLPFC stimulation leading to improved overall recognition. Note that this does not preclude tDCS over other regions showing an impact on memory performance [95,96]; indeed several studies have shown that tDCS over the parietal cortex can alter retrieval. Future work may want to investigate the role of the parietal cortex in this paradigm. Turning to metamemory, HD-tDCS over the DLPFC also showed reliable effects on feeling-of-knowing accuracy, with similar results in the present study and our previous work [9], and

this replication is important in light of recent criticisms of tDCS [41]. We interpret these findings as consistent with a broader role of the DLPFC in monitoring. Taken together, we showed a role of the ATL in recall for general knowledge when questions were of medium difficulty and a role for the DLPFC in memory monitoring accuracy. These findings suggest that HD-tDCS over the ATL or DLPFC may be useful as potential sites for developing interventions for impairments in memory monitoring and memory, as long as task difficulty is taken into account. However, further research is needed to determine whether these effects extend to clinical populations, and how long any effects of HD-tDCS would last.

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- Anterior temporal lobe stimulation improved recall only for medium difficulty
- Prefrontal excitation led to improved recognition memory for all difficulty levels
- Prefrontal excitation led to improved memory monitoring for all difficulty levels
- Effects of difficulty on behavioral changes due to HD-tDCS vary by region and task

Figure 1. Experimental Design. Participants completed 3 separate sessions (~1 week apart) with DLPFC (top), ATL (middle) and sham (bottom) HD-tDCS for 20 min. Stimulation order was counterbalanced across participants. In this example, a participant received DLPFC stimulation at Visit 1 (top), ATL stimulation at Visit 2 (middle), and sham stimulation at Visit 3 (bottom). The behavioral task was completed during HD-tDCS and consisted of 3 blocks, with easy, medium, and hard general knowledge questions. Block order was counterbalanced across participants, but each participant received the same block order

across sessions. In this example, a participant had the following block order: easy, medium, hard. For each trial, participants first attempted to recall the answer to the general knowledge question, then made a feeling-of-knowing judgment, then completed a four alternative forced choice recognition task. A sample trial is given for the easy block (top), the medium block (middle), and the hard block (bottom). Note that some participants took longer than 20 minutes to complete the task and the results may be due to both online and offline effects.

Figure 2.

HD-tDCS effects on Recall. ATL stimulation led to more answers to general knowledge questions being recalled, but this was driven by increased recall in the medium difficulty block. Error bars represent within-subjects standard errors of the mean [97].

Figure 3. HD-tDCS effects on Metamemory Accuracy (d_a). DLPFC stimulation led to increased metamemory accuracy, and this was consistent across all levels of question difficulty. Error bars represent within-subjects standard errors of the mean [97].

Table 1

Number of subjects who self-reported the expected side-effects of HD-tDCS in a post-stimulation questionnaire and believed they were related to receiving HD-tDCS.

	Sham	Dorsolateral Prefrontal Cortex	Anterior Temporal Lobe
Headache	4	2	5
Neck Pain	0	5	4
Scalp Pain	9	15	12
Tingling	21	27	25
Burning	12	25	21
Skin Redness	7	17	8
Sleepiness	6	2	3
Trouble concentrating	5	4	3
Changes in Mood	1	1	2

Table 2

Memory performance (Mean $\pm$ SEM) for recognition (proportion correct), for overall recognition and for non-recalled trials, based on stimulation condition for all questions and for blocks that differ in difficulty.

	Sham	Dorsolateral Prefrontal Cortex	Anterior Temporal Lobe
Overall Recognition	0.56 $\pm$ 0.014	0.60 $\pm$ 0.017	0.59 $\pm$ 0.015
Easy	0.79 $\pm$ 0.017	0.84 $\pm$ 0.016	0.82 $\pm$ 0.016
Medium	0.56 $\pm$ 0.020	0.57 $\pm$ 0.020	0.59 $\pm$ 0.022
Hard	0.35 $\pm$ 0.023	0.39 $\pm$ 0.022	0.36 $\pm$ 0.019
Non-recalled Recognized	0.34 $\pm$ 0.013	0.41 $\pm$ 0.015 *	0.33 $\pm$ 0.013
Easy	0.44 $\pm$ 0.035	0.59 $\pm$ 0.033 *	0.50 $\pm$ 0.031
Medium	0.38 $\pm$ 0.021	0.44 $\pm$ 0.019 *	0.34 $\pm$ 0.022
Hard	0.27 $\pm$ 0.018	0.32 $\pm$ 0.019 *	0.27 $\pm$ 0.014

* p<0.05, Bonferroni corrected for multiple comparisons