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Research report

Electrically stimulating prefrontal cortex at retrieval improves recollection accuracy

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ABSTRACT

Neuroimaging and brain damage studies suggest that dorsolateral prefrontal cortex (dlPFC) is involved in the cognitive control of episodic recollection. If dlPFC is causally involved in retrieval, then transcranial direct current stimulation (tDCS) of this brain region should increase recollection accuracy, especially when recollection is difficult and requires cognitive control. Here, we report the first brain stimulation experiment to directly test this hypothesis. We administered tDCS to dlPFC immediately after studying to-be-learned material but just prior to recollection testing, thereby targeting retrieval processes. We found that stimulation of dlPFC significantly increased recollection accuracy, relative to a no-stimulation sham condition and also relative to active stimulation of a comparison region in left parietal cortex. There was no significant difference in the size of this increase between hemispheres. Moreover, these dlPFC stimulation effects were behaviorally selective, increasing accuracy only when participants needed to recollect difficult information. Electrically stimulating dlPFC allowed people to more accurately recollect specific details of their experiences, demonstrating a causal role of dlPFC in the retrieval of episodic memories.

1. Introduction

Neuroimaging and brain damage studies have implicated dorsolateral prefrontal cortex (dlPFC) as a key brain region for our ability to recollect specific details about past experiences (Hayama & Rugg, 2009; Mitchell & Johnson, 2009). While the exact role of this region in episodic memory is still unknown, it is often assumed that dlPFC is involved in cognitively controlled aspects of retrieval, such as the strategic search for information (e.g., pre-retrieval orientation) and the evaluation of information that comes to mind (e.g., post-retrieval monitoring). For example, lesions to dlPFC and other frontal areas are more likely to impair performance on memory tests involving the effortful recollection of specific details compared to easier memory tests that require less cognitive control (e.g., source *vs* recognition memory, see Simons & Spiers, 2003). Neuroimaging techniques further reveal that dlPFC activity increases when participants need to make more demanding memory decisions (e.g., Cruse & Wilding, 2009; Henson, Shallice, & Dolan, 1999), ostensibly because these decisions require more cognitive control. Yet,

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because these approaches have interpretative limitations (e.g., brain damage can affect both encoding and retrieval; neuroimaging is correlational), there is little direct evidence that dlPFC is causally involved in the retrieval of episodic memories.

Electrically stimulating the brain with transcranial direct current stimulation (tDCS) can more directly test causal hypotheses about cortical functions during episodic memory. Research shows that tDCS can temporarily boost performance on tasks involving cognitively controlled processes, such as working memory (for review, see Coffman, Clark, & Parasuraman, 2014). While there are relatively fewer studies of tDCS on episodic memory, emerging research indicates tDCS of dlPFC during encoding or retrieval also can boost performance (for a partial review, see Manenti, Cotelli, Robertson, & Miniussi, 2012). These studies have demonstrated that tDCS to dlPFC can increase the *quantity* of information retrieved from memory, operationalized as the number of studied items correctly retrieved on traditional recall or recognition memory tasks. Critically, if dlPFC subserves the cognitively controlled aspects of episodic recollection, then tDCS also should increase the *quality* of memories (Koriat, Goldsmith, & Pansky, 2000), enabling people to more accurately recollect specific details associated with studied items and to avoid false recollection of erroneous details. To our knowledge, no prior brain stimulation studies – using tDCS or other brain stimulation techniques – have investigated the role of dlPFC on objective measures of recollection accuracy for specific details.

Here, we report the first brain stimulation experiment to test the hypothesis that dlPFC is causally involved in the cognitively controlled aspects of episodic recollection, specifically targeting retrieval processes by administering tDCS to dlPFC immediately after the to-be-remembered materials had been encoded and just prior to taking the memory tests. Memory was tested using the criterial recollection task, which is a special kind of source memory task designed to objectively measure recollection accuracy for specific details (for review see Gallo, 2013). In the study phase of this task, participants attempt to memorize words (concrete nouns) that are associated either with a specific font color or with a picture of the object. In the test phase, participants are presented with the studied words as retrieval cues, and they must recollect the previously associated information (font color or a picture). Unlike traditional recognition memory tasks, which benefit from feelings of familiarity as well as specific recollections (see Yonelinas, 2002), a key feature of this task is that participants must rely on the recollection of specific information. Another key feature of this task is that recollection demands can be experimentally manipulated across test blocks. For example, participants might be required to selectively recollect font color on one test block and to recollect pictures on the other test block. Although both of these tests require the recollection of specific information, recollection demands would be greater on the font test than the picture test, because pictures are more perceptually distinctive than font color and hence easier to recollect.

To the extent that dlPFC is causally involved in recollection, we predicted that tDCS at retrieval would improve recollection accuracy relative to a no-stimulation sham condition. Further, to the extent that dlPFC drives the cognitively controlled aspects of recollection (e.g., effortful search or evaluation processes), this tDCS effect should be greater on more difficult recollection tests. These predictions were motivated by previous fMRI work using this same recollection task, which has consistently found lower recollection accuracy, coupled with greater activation of dlPFC, when testing recollection for font color compared to pictures (Gallo, Kensinger, & Schacter, 2006; Gallo, McDonough, & Scimeca, 2010; McDonough, Wong & Gallo, 2013). These fMRI results suggest that attempting to retrieve less distinctive font information is more demanding of dlPFC resources than picture information, and hence should benefit more from dlPFC stimulation. As described in the methods section, we administered three different recollection test blocks to manipulate different aspects of cognitive control at retrieval.

In addition to investigating the behavioral specificity of tDCS across different recollection tests, we also explored regional specificity by separately stimulating left or right dlPFC. Neuroimaging studies have consistently implicated dlPFC in episodic memory retrieval, but there is debate as to whether the two hemispheres play different roles and, if so, what those roles might be (for discussion see Mitchell & Johnson, 2009). With respect to the recollection task used here, Gallo (2013) reanalyzed the brain damage data from Hwang et al. (2007), and found that participants with right dlPFC damage were more impaired on the more difficult recollection task than were participants with left dlPFC damage. Similarly, Gallo et al. (2010) found that right dlPFC was more strongly activated than the left dlPFC as a function of recollection demands, in keeping with an emphasis on right dlPFC in cognitively controlled aspects of retrieval from the earlier neuroimaging literature (e.g., Rugg, 2004). However, bilateral activity of dlPFC is often found in this recollection task and related fMRI studies, so we consider this prior evidence for laterality of function as tentative. By separately stimulating left and right dlPFC with tDCS in the current study, we aimed to provide a more direct test of the lateralization of prefrontal function during episodic recollection.

To further explore regional specificity, we also administered active tDCS to a more posterior region in left parietal cortex. Left parietal cortex was chosen as a comparison site because, much like dlPFC, neuroimaging studies often report activity in left parietal cortex region during episodic memory tasks, but unlike dlPFC regions, damage to left parietal cortex has not been consistently associated with robust episodic memory impairment (e.g., Simons et al., 2008). These patterns have led to the suggestion that left parietal cortex directs attention or awareness towards recollected information *after* it has been retrieved (Cabeza et al., 2011; Yazar, Bergstrom, & Simons, 2012), but is not necessarily involved in the search or evaluation processes that characterize the cognitively controlled aspects of recollection. If this hypothesis is correct, then stimulation of this parietal region should not increase recollection accuracy to the same extent (if at all) compared to stimulation of dlPFC.

2. Materials and method

The relevant Internal Review Board of the University of Chicago approved all study procedures, and all participants gave informed consent prior to the study. The participants were 96 right-handed University students (18–30 years, 48 females). The procedures of the behavioral task were modeled after Gallo et al. (2010). During each trial of the encoding phase, participants first passively read object words presented in black font (500 msec), and then immediately saw either the same word in red font or a picture of the object. Each study trial was always initiated by the presentation of the item as a word in black font, because black words were later used as retrieval cues in all testing conditions, and we wanted this aspect of study presentation to be held constant for all of the red font and picture items. Each item was presented twice at study (nonconsecutively and randomly intermixed), with 90 items associated only with a red font at study, 90 items associated only with a picture at study, and 60 items associated with a red font on one presentation and a picture on the other presentation (nonconsecutively). To help participants pay attention during encoding, they were prompted to make a semantic judgment for each red words ("Is this item typically made in a factory?") and a perceptual judgment for each picture ("Is this picture a relatively detailed image?"). Participants were given up to 1200 msec to make this judgment to the corresponding word in larger red letters or picture.

Participants received tDCS immediately after encoding. In the dlPFC stimulation conditions, a 2 mA current was delivered for 20 min using 2 electrodes in 5 × 7 cm saline-dampened sponges (Soterix Medical, New York, NY). The anodal electrode was placed over areas F3 (left, $n = 24$) or F4 (right, $n = 24$) according to the 10–20 EEG-system, with the cathodal electrode on the contralateral supraorbital region. The sham condition ($n = 24$) used the same prefrontal montage (12 left, 12 right), but current only was administered during the first and last 30 sec. This is a common sham condition in the tDCS literature, and was designed to yield some electrical stimulation sensations without stimulating the brain for the full 20 min. The parietal tDCS condition ($n = 24$) used the same 20 min stimulation procedure as the left dLPFC stimulation conditions, except the anodal electrode was placed approximately over area P5 (as in the tDCS study by Manenti, Brambilla, Petesi, Ferrari, & Cotelli, 2013).

Immediately after tDCS we administered three memory tests. To ensure that the three tests would be evenly distributed across the testing period, each of the three tests was divided into thirds, and we administered a third of each test during the first, middle, and last third of the testing phase for each participant. The order of these mini-blocks was counterbalanced across participants. Before each mini-block, participants were given a prompt indicating the test they were about to take (Font Test, Picture Test, or Exclusion Test), and a prompt also remained on the computer screen for each test item.

Each test used black words as retrieval cues but had different instructions for making the yes/no response. On the two criterial recollection tests (Font Test, Picture Test), 30 items from each study format (red font, pictures, both) were intermixed with 30 nonstudied items. On the Font Test participants pressed "yes" whenever they recollected studying the item in red font, whereas on the Picture Test they pressed "yes" whenever they recollected a picture. Participants were told that one format was not predictive of the other (i.e., some test items were studied in both formats), so they should focus only on recollecting the criterial format for each test (e.g., red font on the Font Test, pictures on the Picture Test). As outlined in the Introduction, we predicted tDCS would increase accuracy on the Font Test more than the Picture Test, due to greater recollection demands.

The third test was similar to the Font Test, except it did not include test items that had been studied in both formats, so that the red font (30 items) and picture items (30 items) were rendered mutually exclusive at test (Exclusion Test). Because there were no test items that had been studied in both formats on this test, an additional 30 nonstudied items (60 total) were included as lures on this test (thereby keeping this test length consistent with the other two tests). Participants were instructed to press "yes" if they recollected that the test item had been studied with a red font, but in contrast to the Font Test instructions, where participants were told to focus only on recollecting font information, the Exclusion Test instructions emphasized that recollecting a picture now ensured that the test item was not studied in red font (i.e., an exclusion process, see Brainerd, Reyna, Wright, & Mojardin, 2003). Gallo et al. (2010) found that this exclusion procedure selectively reduced false recollection errors to picture items on the Exclusion Test relative to the Font Test, implicating the use of more distinctive picture recollections to help monitor retrieval (i.e., an exclusion process). They also linked this exclusion process to dlPFC activity. With respect to the current study, this link between the exclusion process and dlPFC activity suggests that performance on the Exclusion Test might benefit from tDCS. However, the reduction in errors on the Exclusion Test relative to the Font Test suggests that recollection was more demanding on the Font Test, which could not benefit from distinctive picture recollections. To the extent that the Font Test was more difficult and hence required more cognitively controlled search and evaluation processes than the Exclusion Test, the Font Test again would be expected to benefit the most from the performance-enhancing effects of tDCS.

3. Results

3.1. Recollection accuracy scores

Our primary analysis compared accuracy scores for each of the three recollection tests in each dlPFC stimulation condition (i.e., left, right, and sham, see Fig. 1). This accuracy score (hits minus false alarms) reflected participants' ability to discriminate between target words that had been associated with the criterial format at study (e.g., picture items on the Picture Test) and lure words that had been associated with the other format at study (e.g., red font items on the Picture Test), while disregarding responses to items that had been associated with both formats as well as nonstudied items. As discussed by Gallo (2013), the targets and the lures used in this

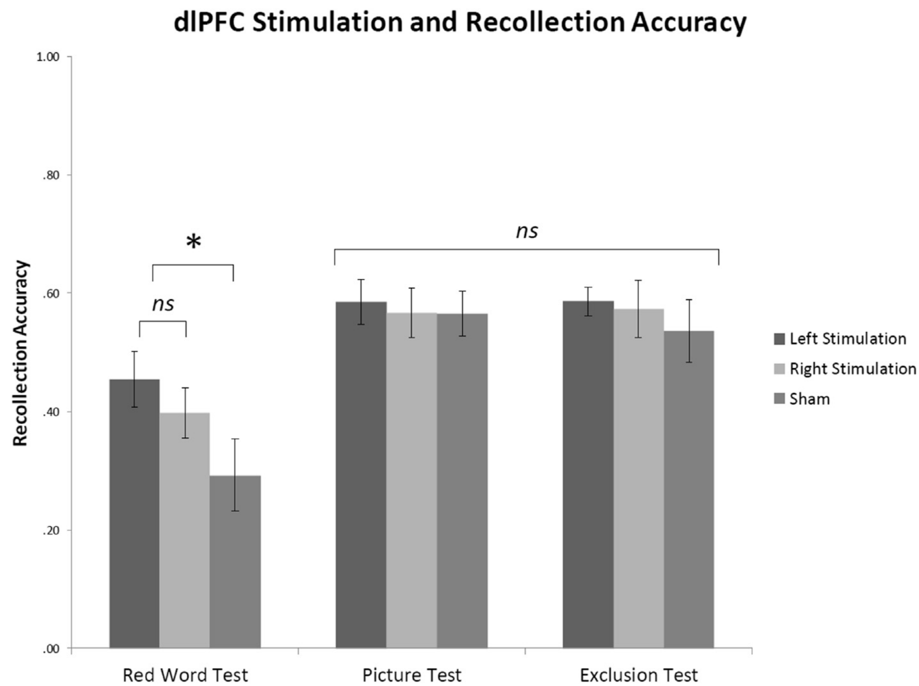

Fig. 1 – Stimulation of dlPFC significantly increased recollection accuracy relative to sham on the Font Test, but not the other tests. For accuracy scores (% target hits − % lure false alarms), items studied as red words were targets and pictures were lures (Font Test, Exclusion Test), or vice versa (Picture Test). Bars represent the standard error of the mean. The * represents significance at the $\alpha = .05$ level, two-tailed.

accuracy measure should have been similar in familiarity from the study phase, so participants needed to use recollection to differentiate them at test.[1] Moreover, because this recollection accuracy score reflects participants' ability to discriminate between the same kinds of red font and picture items on each of the three recollection tests, differences in this accuracy score across tests can be attributed to differences in recollection demands across the three tests. Consistent with these assumptions, overall accuracy (collapsing across dlPFC stimulation conditions) was lower on the Font Test than the Picture Test, $t(71) = 6.90$, $p < .001$, $d = .854$, demonstrating the expected advantage of distinctive picture recollections on performance. Accuracy also was lower on the Font Test than the Exclusion Test, $t(71) = 7.41$, $p < .001$, $d = .764$, demonstrating the advantage of using picture recollections in an exclusion process. There was no accuracy difference between the Picture Test and the Exclusion Test ($t < 1$), as each of these tests benefited from distinctive picture recollections.

To evaluate the effects of stimulating dlPFC on recollection accuracy, we first ran a 2 (stimulation: active, sham) × 2 (hemisphere: left, right) ANOVA on each of the three recollection tests, considering only the conditions with electrodes placed on dlPFC sites. This analysis revealed that recollection accuracy on the Font Test was improved by tDCS, as there was a main effect of Stimulation (active > sham), $F(1, 68) = 4.65$, $p = .035$, $\eta^2 p = .064$, but no main effect of Hemisphere (left, right), and no interaction (p's > .25). By contrast, stimulation had no significant effects on the Picture Test or the Exclusion Test (all p's > .19). Thus, as predicted by the hypothesis that dlPFC is causally involved in the cognitively controlled aspects of recollection, stimulation of dlPFC increased recollection accuracy on the Font Test more than the other two tests, which were less cognitively demanding.

As an additional test of regional specificity, we compared recollection accuracy scores in the parietal stimulation condition to the sham stimulation condition (see Fig. 1). Unlike our analysis of dlPFC stimulation, this analysis of parietal stimulation revealed no significant differences in accuracy scores on any of the three tests relative to the sham condition (all p's > .29). Moreover, a direct comparison between the parietal stimulation condition and the dlPFC stimulation conditions (collapsing hemispheres) revealed that recollection accuracy on the Font Test was significantly greater with dlPFC stimulation than parietal stimulation, $t(70) = 2.51$, $p = .01$, $d = .62$, with no differences in accuracy on the other two tests (both p's > .14). Taken together, these analyses demonstrate that parietal stimulation did not yield the same performance benefit as did dlPFC stimulation.

[1] By design, the ability to discriminate between these particular item types should have relied on recollection of the criterial information on each test, but it is important to note that responses to other items may have relied on other kinds of information. Items that were studied in both formats may have elicited the retrieval of either format when encountered at test (and alternating formats also may have been noticed during encoding), and nonstudied lures could have been rejected based on a lack of familiarity. Because of these design features, our primary analyses focused only on the aforementioned items that could elicit the recollection of criterial information.

3.2. Hits and false alarms

In addition to recollection accuracy scores, we also analyzed performance separately for targets and lures in each of the brain stimulation conditions (see Table 1). Unlike recollection accuracy scores, which theoretically represent the ability to discriminate between targets and lures independent from overall response bias effects, a separate analysis of hits and false alarms might be affected by unintended differences in response bias across brain stimulation conditions and so should be interpreted with caution. Nevertheless, a separate analysis of targets and lures can potentially inform different cognitively controlled aspects of retrieval. If tDCS primarily increases the effectiveness of pre-retrieval search processes, then it should increase the correct recollection of target information in our task, with little effect on responses to lures that were not associated with target information. By contrast, if tDCS primarily increases the effectiveness of post-retrieval monitoring or evaluation processes, then it should facilitate participants' ability to reject lures associated with the retrieval of noncriterial information.

In order to help interpret stimulation effects on targets and lures, we first describe the behavioral results to targets and lures from our sham (no stimulation) condition, which replicated four key results from Gallo et al. (2010) and other work with this task. First, on each of the three tests, participants responded "yes" more often to targets than to lures (all p's $< .01$), demonstrating that they used recollection to differentially respond to test items that had been associated with red font or pictures at study. Second, on each of the three tests, participants made significantly more false alarms to lures that were studied in the incorrect format (e.g., picture items on the Font Test and Exclusion Test; Red Words on the Picture Test) compared to nonstudied items, demonstrating an effect of stimulus familiarity on false recollection errors (all p's $< .05$). Third, false alarms to studied lures and nonstudied lures were each greater on the Font Test than on the Picture Test (both p's $< .01$), demonstrating a distinctiveness effect on false recollection errors and that retrieval-monitoring demands were greater on the Font Test than the Picture Test. Fourth, participants made significantly fewer false alarms to studied lures on the Exclusion Test compared to the Font Test, $t(23) = -5.33$, $p < .01$, $d = -.95$, but there was no reduction in false alarms to nonstudied lures, $t(23) = 1.44$, $p = .16$, $d = .26$. This selective reduction in false alarms on the Exclusion Test demonstrates that participants had used picture recollections to reduce recollection errors via an exclusion process, again implicating increased recollection demands on the Font Test.

To investigate brain stimulation effects on targets and lures separately, we compared hits and false alarms across the dlPFC stimulation conditions. As with our recollection accuracy scores, this analysis focused on items that had been associated with one of the two studied formats (e.g., red font or pictures). For the Font Test, this comparison revealed that the left dlPFC stimulation significantly boosted hits to red font items compared to sham stimulation, $t(46) = 2.46$, $p = .02$, $d = .71$, with no effect on false alarms to picture items, $t(46) < 1$. Similarly, right dlPFC stimulation significantly boosted hits to red font items compared to sham stimulation, $t(46) = 2.77$, $p = .01$, $d = .80$, with no effect on false alarms to picture items, $t(46) < 1$. In contrast, there were no significant differences in these hit or false alarm rates between stimulation and sham conditions for the other two tests (all p's $> .22$), nor did parietal stimulation significantly affect these hit or false alarm rates relative to sham (both p's $> .30$). These analyses indicate that the benefits of dlPFC stimulation on recollection accuracy on the Font Test was driven primarily by a significant increase in hit rates to targets, as opposed to a reduction in false alarms to studied lures.[2] These data support the idea that brain stimulation increased the effectiveness of a pre-retrieval search process, primarily helping participants to recollect the targeted information.

Table 1 – Mean Proportion of "Yes" responses on each recollection test as a function of Brain stimulation conditions.

	Sham	Left dlPFC	Right dlPFC	Left Parietal
Font test				
Both hits	.69 (.04)	.74 (.03)	.72 (.03)	.69 (.04)
Red word hits	.65 (.04)	.77 (.03)	.79 (.03)	.67 (.05)
Picture HIts	.35 (.04)	.31 (.03)	.40 (.04)	.39 (.05)
Nonstudied FAs	.10 (.02)	.08 (.01)	.16 (.02)	.18 (.03)
Picture test				
Both hits	.79 (.04)	.84 (.03)	.82 (.03)	.73 (.04)
Picture hits	.14 (.04)	.14 (.03)	.17 (.03)	.15 (.05)
Red word FAs	.70 (.03)	.73 (.03)	.74 (.03)	.65 (.04)
Nonstudied FAs	.05 (.01)	.04 (.01)	.05 (.01)	.06 (.02)
Exclusion test				
Red word hits	.72 (.03)	.74 (.03)	.77 (.03)	.68 (.04)
Picture hits	.18 (.03)	.16 (.02)	.19 (.03)	.18 (.03)
Nonstudied FAs	.13 (.02)	.11 (.02)	.25 (.04)	.25 (.05)

Notes: Standard errors of each mean are in parenthesis. Red words were targets on the font test and exclusion test, and lures on the picture test. Pictures were targets on the picture test, but lures on the font test and exclusion test. Nonstudied items were always lures.

4. Discussion

This is the first experiment to show that electrically stimulating prefrontal cortex increases recollection accuracy, allowing people to more accurately retrieve the details of their experiences. These tDCS effects were behaviorally selective, as stimulating dlPFC boosted performance on the Font Test, where recollection demands were greatest, but not on the Picture of Exclusion tests. These tDCS effects also were regionally selective, as stimulating dlPFC boosted recollection accuracy but stimulating left parietal cortex did not, even though both regions have been associated with memory retrieval. Taken together, these results provide strong evidence that dlPFC plays a causal role in episodic memory

[2] In fact, out of all of the target and lure comparisons, the only other dlPFC stimulation effect that differed significantly from sham was a significant increase in false alarms to nonstudied items on the exclusion test with right dlPFC stimulation, $t(46) = 2.43$, $p = .02$, $d = .70$. We did not expect this effect, and caution must be made to avoid Type 1 error with many multiple comparisons, but this increase in false alarms clearly is inconsistent with the idea that brain stimulation boosted post-retrieval evaluation.

retrieval, increasing the effectiveness of the cognitively controlled processes that are required when recollection is difficult.

Our finding dlPFC stimulation benefitted the Font Test but not the Picture Test is consistent with several neuroimaging studies using this task, which have repeatedly shown that dlPFC is more active on the Font Test than the Picture Test (e.g., Gallo et al., 2010, 2006; McDonough et al., 2013). We also found that tDCS stimulation to left or right dlPFC increased recollection accuracy on the Font Test, but there was no significant difference in the size of this increase between hemispheres. As discussed in the Introduction, prior fMRI work has focused on right dlPFC activity during the Font Test (Gallo et al., 2010), but the Font Test often activates both left and right dlPFC relative to the Picture Test. More generally, neuroimaging and brain damage studies have yielded mixed evidence on the laterality of retrieval processes (e.g., Dobbins & Han, 2006; Hwang et al., 2007; Ranganath, Heller, & Wilding, 2007). In the current study we were able to differentially target each of the two hemispheres with tDCS, and our findings suggest that each hemisphere is likely to be involved.

In contrast to the stimulation effects we observed on the Font Test, we found that dlPFC stimulation did not significantly benefit performance on the Exclusion Test. As discussed in the Methods section, the use of distinctive picture recollections in the exclusion process reduces recollection difficulty relative to the Font Test, so that stimulating dlPFC was not expected to benefit performance on the Exclusion Test as much as the Font Test. However, the fMRI study of Gallo et al. (2010) associated the Exclusion Task with dlPFC activity, suggesting that this test might have benefitted from tDCS to some extent. Indeed, the use of a recollection-based exclusion process typically is considered a cognitively controlled process in the behavioral literature (for a review, see Gallo & Lampinen, 2015). It may be that the dlPFC is causally involved in the exclusion process, but that using picture recollections in this exclusion process is not too demanding of dlPFC resources, so that dlPFC stimulation does not yield additional performance benefits. Alternatively, it may be that the dlPFC activity observed with fMRI was not causally linked to the use of an exclusion process, but instead reflected some correlated aspect of processing. Either of these interpretations is currently viable.

Our primary analysis of brain stimulation effects focused on recollection accuracy scores, because this measure is designed to control for familiarity effects as well as differences in response bias that may affect responding to both targets and lures across conditions. Nevertheless, it also is informative that the effects of dlPFC stimulation on the Font Test were primarily driven by increased hit rates to targets as opposed to reduced false alarm rates to lures. This pattern suggests that dlPFC stimulation primarily increased the effectiveness of a pre-retrieval search process, or the ability to successfully recollect the criterial information at test (which by definition was associated with targets but not lures). In contrast, this pattern is less consistent with the idea that dlPFC stimulation increased the effectiveness of post-retrieval evaluation process, or the ability to match what is retrieved with one's expectations, as this aspect of retrieval tends to affect false alarms to lures.

Recent behavioral work indicates that people attempt to mentally reinstate (or imagine) encoding conditions at test, as a way to strategically constrain retrieval when searching memory for specific information (Alban & Kelley, 2012; Halamish, Goldsmith, & Jacoby, 2012). Moreover, our own work indicates that this search process is engaged on the kind of task used here (e.g., recollecting words that were studied with semantic judgments, see Gray & Gallo, 2015). The current results suggest that tDCS to dlPFC can temporarily enhance this aspect of cognitive control, helping people search memory for information that is difficult to recollect. Regardless of whether the dlPFC is ultimately found to be involved in this or other cognitively controlled aspects of retrieval, our results provide strong evidence that dlPFC is causally involved in the recollection of episodic memories.

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