Transcranial Direct Current Stimulation Modulates Pattern Separation

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Abstract

Maintaining similar memories in a distinct and non-overlapping fashion, known as pattern separation, is an important mnemonic process. The medial temporal lobe (MTL), especially hippocampus, has been implicated in this crucial memory function. The present study thus examines whether it is possible to modulate pattern separation using bilateral transcranial direct current stimulation (tDCS) over the temporal lobes. Specifically, in this study, pattern separation was assessed using the Mnemonic Similarity Task (MST) following 15-minute offline bilateral temporal lobe tDCS (left cathode and right anode or left anode and right cathode) or sham stimulation. In the MST, participants studied a series of sequentially presented visual objects. In the subsequent recognition memory test, participants viewed a series of sequentially presented objects that could be old images from study, novel foils, or lures that were visually similar to the studied images. Participants reported whether these images were exactly the same as, similar to, or different from the studied images. Following both active tDCS conditions, participants were less likely to identify lures as "similar" compared to the sham condition, indicating a reduction in pattern separation resulting from temporal lobe tDCS. In contrast, no significant difference in overall accuracy was found for participants' discrimination of old and new images. Together these results suggest that temporal lobe tDCS can selectively modulate pattern separation function without changing participants' baseline recognition memory performance.

Keywords: pattern separation, non-invasive brain stimulation, transcranial Direct Current Stimulation, medial temporal lobe, recognition memory

Introduction

Maintaining specific and exclusive memories for similar external events is crucial for one to navigate in an ever-changing environment. This capability to store similar memory representations in a non-overlapping fashion is known as pattern separation [1]. A growing body of literature suggests the involvement of medial temporal lobe (MTL) structures, such as hippocampus, perirhinal cortex, and parahippocampal gyrus, in pattern separation [2-4]. For instance, a recent high-resolution neuroimaging study demonstrates that perirhinal and parahippocampus are involved in pattern separation for domain-selective information (e.g., perirhinal for object information and parahippocampus for spatial information) [4]; whereas hippocampus serves as a general hub in separating mnemonic representations across domains [4; 5]. More importantly, pattern separation deficits often occur following hippocampus lesions [6] or psychiatric conditions that produce hippocampal abnormality, such as schizophrenia [7]. These empirical findings suggest that MTL structures, especially hippocampus, are causally associated with pattern separation. In the current study, we therefore examine whether it is possible to modulate pattern separation using non-invasive stimulation of the temporal lobe with transcranial direct current stimulation (tDCS) in healthy observers.

A typical tDCS setup delivers a weak current to the brain via two electrodes, an anode and a cathode, placed on the scalp that are presumed to increase (anode) and decrease (cathode) the excitability of underlying cortex [8]. tDCS effects are often attributed to modulation of the superficial cortex; however, the physics of current flow mandate that current crossing grey matter will continue through the brain to the return electrode. As a result deep brain structures will also be polarized [9]. Imaging studies (not restricted to a cortical region of interest) suggest comparable neuromodulation of superficial and subcortical structures [10], such as hippocampus

as well as increased connectivity between hippocampus and other brain regions [11]. The regions of cortical current flow, as well as the degree of deep penetration during tDCS, is dependent on the electrode montage [9]. Positioning electrodes lateralized across the head preferentially modulates the underlying cortex, and also optimizes deep current flow to structures such as the hippocampus [12]. We therefore applied tDCS bilaterally across the temporal lobes in the present study.

Recent research demonstrated significant modulation of memory functions, which may critically depend on the MTL [13], using tDCS administered over temporal lobes [14]. For example Chi et al. [14] demonstrated that temporal lobe tDCS improved participants' memory accuracy. In this study, participants remembered sets of simple objects of varying shapes, sizes and orientations. Items in each set were related by particular themes (e.g., combinations of small and large circles). In the test phase, items that were related to studied items (e.g., recombination of features from different studied items), but were not included in the study set, were presented as critical lures. The application of temporal lobe tDCS led to an improvement in participants' discrimination of studied items from critical lures. In this study, it is crucial for participants to encode proper relational information (e.g., a small circle on the left and a right circle on the right) to distinguish studied items from lures (e.g., a small circle on the right and a right circle on the left). Failure in encoding relational memory will lead to falsely remembering critical lures as studied items. Given memories for relational information are critically dependent on hippocampus and surrounding structures in MTL (for review, see [13]), these results seem to suggest that temporal lobe tDCS may modulate MTL functions.

To directly assess pattern separation, items bearing more visual similarities to studied items, instead of recombining features from previous studied items as in Chi et al. [14], should

be used as lures. Correspondingly, a response option where participants may report lure items as "similar" to studied items should be included in addition to "old" and "new" response options [15]. The stimuli and tasks from Chi et al. [14] did not satisfy these requirements, given that experiments in Chi et al. [14] were designed to test relational memory and false memory. Therefore, we adopted the Mnemonic Similarity Task (MST; formerly known as the Behavioral Pattern Separation Task-Object Version, see Figure 2) to directly investigate pattern separation for real world objects [15]. In this task, participants' pattern separation performance is evaluated using the pattern separation index (PSI), calculated as the difference between "similar" responses on the lure trials and "similar" responses on the foil trials [15]. This index has been shown to reliably capture individual differences in pattern separation ability across healthy and clinical populations [15].

The present study therefore investigated effects of bilateral temporal lobe tDCS on pattern separation of real world objects using the MST task. Assessment of pattern separation with the MST task was conducted offline after a 15-minute tDCS session. Bilateral stimulation, instead of unilateral stimulation, was chosen because its effectiveness in polarizing superficial and deep MTL structures on the base of computational modeling of current flow with tDCS (see Methods for details). We thus adopted similar stimulation montage, duration, and current intensity, as used in previous studies [14; 16]. Although we predict that temporal lobe tDCS will perturb MTL functions, there is no general consensus on which polarity will lead to the strongest effect [14; 16]. Therefore, left cathode right anode (L-R+), left anode right cathode (L+R-), and sham conditions are all included and compared using a within-subject design. We hypothesize that bilateral temporal lobe tDCS should modulate pattern separation relative to sham stimulation. Given the difficulties to determine whether these tDCS montages will exert

excitatory or inhibitory effects on MTL deep structures without neural imaging data (see Method section for details), the current tDCS protocol could lead to increase or decrease in pattern separation.

Methods

Participants

Twenty volunteers (20.0 ± 1.1 years old, 10 female) participated in the experiment for course credit at the University of California, Riverside. All had normal or corrected-to-normal visual acuity and reported having normal color vision. Informed consent was obtained at the beginning of the experiment.

Transcranial Direct Current Stimulation (tDCS)

Prior to the study phase of the MST task in each session, participants received either a 15-minute bilateral tDCS across the anterior temporal lobes (for L+R- and L-R+ conditions) or a 15-second sham stimulation using a neuroConn DC-Stimulator Plus (GmbH, Germany). Stimulation protocols (stimulation montage, duration, and intensity) were modified from Chi et al. [14]. Direct current at 1.5 mA was delivered with two 5 × 5 cm saline-soaked surface sponge electrodes (yielding an average electrode current density of 0.06 mA/cm^2). Participants received three bilateral stimulations over the anterior temporal lobes (see Figure 1a) in three sessions separated by at least one day. For each session, participants received stimulation under one of three conditions. In the L+R- condition, the anode electrode was placed midway between T7 and FT7 (International 10-20 EEG System) and the cathode electrode was placed midway between T8 and FT8. The polarity of the electrodes was switched for the L-R+ condition (the cathode electrode was placed midway between T7 and FT7 and the anode electrode was placed midway between T8 and FT8). In the sham condition, the placement of the electrodes was counter

balanced matching either the L-R+ condition or the L+R- condition. The order of the three tDCS conditions was counterbalanced across subjects. During stimulation, participants sat quietly for the entire 15-min period (including the sham condition).

The Human Research Review Broad of University of California, Riverside approved the tDCS stimulation protocol in the present study. No adverse effects were reported by the subjects or observed by the experimenters during or after the stimulation.

Modeling of tDCS

To demonstrate the current tDCS montage could be effective in delivering stimulation to deep MTL structures, two finite element models simulating bilateral stimulation of the temporal lobes were developed based on previously described protocols [17; 18]. A 3-D 1mm isotropic T1 MRI of an adult male was segmented into 20 different head regions using both automated and manual techniques. The electrodes were initially modeled as vertically aligned 5 × 5 cm saline-soaked surface sponge electrodes in a computer-aided design format and placed midway between FT7 and T7 and midway between FT8 and T8. They were imported into the segmentation model where a volumetric mesh was then generated.

For both active stimulation conditions, the boundary conditions as electrically insulated was applied surrounding the head and the 20 segmented regions were assigned one of seven possible conductivities: skin, fat, skull, cerebral spinal fluid, gray matter, white matter, or air. For the first active condition, an inward current density of 0.06mA/cm^2 was applied to the electrode between FT7 and T7, and ground was applied to the return. For the second active condition, an inward current density of 0.06mA/cm^2 was applied to the electrode between FT8 and T8, with ground applied to the return. The Laplace equation was solved with these conditions using COMSOL Multiphysics 4.3 (COMSOL, Inc., Burlington, MA) to a relative

tolerance of $1x10^{-6}$. Cortical and deep structure electric field magnitudes and cortical radial electric field were plotted for the resulting solutions of each model (see Figure 1b & 1c).

As expected, symmetric bilateral stimulation across the head produced a symmetric pattern of current flow intensity (Figure 1b), primarily in the temporal lobe. The direction of cortical flow depended on proximity to the anode (inward current) or cathode (outward current flow [19]. Consistent with prior models of tDCS using pad-electrodes, current flow was distributed across the cortex but the lateralized montage produce maximal concentration (peak ~0.7 V/m) under the electrodes. Inverting the polarity of stimulation (from L-R+ to L+R-) reversed the direction of current flow across the cortex, but did not change peak intensity in any region due to the linearity of the electric current distribution (not shown).

Significant electrical stimulation was also estimated in both hippocampi (peak ~0.24 V/m) with clustering within the hippocampi (Figure 1c). Note whereas cortical current flow was represented as either inward (positive, excitatory) or outward (negative, inhibitory) using a bipolar scale, current flow in across the hippocampus was represented as electric field magnitude [19]. With typical tDCS montages, including the one used in the present study, electrical current predominately flows in tangential direction (relative to the cortical surface) in the cortex, so the polarity of the tangential field can be determined. However, only the intensity of radial current flow, which is perpendicular to tangential field, can be modeled in deep structures [19]. Consequently the activation seen in Figure 1c & 1d represented the magnitude of the stimulation, ranging from 0 to 0.5V/m.

Several additional deep structures in the medial temporal lobes, including those traditionally considered as parts of the limbic system, such as amygdala, thalamus, hypothalamus, and basal ganglia, are also being stimulated using the present stimulation

parameters (Figure 1c). However, these structures are not involved in tasks targeting pattern separation as demonstrated in a previous whole-brain neuroimaging study [20]. The present study thus focused on the effects of tDCS on MTL structures that are implicated in pattern separation, specifically hippocampus.

Stimuli

Three separate sets of images of everyday objects (see Figure 2) from the standard MST task [15] were used for three sessions for each participant. The order of the three image sets was counterbalanced across participants. Each image subtended visual angle of 2.9° to 12.9° in width and 4.0° to 12.8° in height. All stimuli were presented on a LCD monitor (calibrated with a X-Rite I1Pro spectrophotometer) at a viewing distance of 57 cm, using the Psychtoolbox in Matlab (Mathworks).

Procedure

Participants came in for three one-hour sessions at least one day apart. Following the 15-minute offline temporal lobe tDCS at the beginning of each session, electrodes were removed and participants immediately began the MST task. As seen in Figure 2, the MST task consisted of two separate phases given in immediate succession: a study phase and a test phase. In the study phase, 128 images were sequentially displayed at the center of the screen for 2,000 ms per image with a 500-ms inter-stimulus interval. Participants reported whether the image contained an indoor object or an outdoor object by pressing the “V” and “N” buttons on a standard keyboard, respectively. They were allowed up to 2,500 ms to make such a response following the presentation of the object. Participants were asked to respond as accurate as possible within the given time window. If the participant was unsure, they were instructed to make the best guess possible and to try to make a response for each image. No performance feedback was given.

In the test phase, 192 images were sequentially displayed at the center of the screen for 2,000 ms per image with a 500-ms inter-stimulus interval. One-third of these images were exact repetitions of images presented in the study phase (targets); one-third of the images were new images not previously seen (foils); and one-third of the images were similar to those seen during the study phase, but not identical (lures). Participants responded to whether they saw the image during the study phase (old), whether the image was similar to one seen in the study phase (similar), or whether the image was not seen in the study phase (new) by pressing the "V", "B", and "N" keys, respectively. Accuracy was stressed as long as participants responded within the appropriate time window (2,500 ms). A computer generated beep was played as feedback when no response was made. On average the MST task was about 20 minutes across sessions and participants.

Data analyses

Pattern separation was assessed using pattern separation index (PSI), calculated as the difference between "similar" responses on the lure trials and "similar" responses on the foil trials [6], which has also been named BPS score [15]. A high PSI indicates that participants often respond "similar" on lure trials, showing a propensity for pattern separation (i.e., the ability to distinguish between the old image and a lure that is similar to the old image).

Results

Based on previous literature implicating the hippocampus in pattern separation [2], if the estimated electric current distribution in the hippocampus is large enough, we expect to see a pattern separation modulation. As shown in Figure 3, bilateral temporal lobe tDCS indeed reduced pattern separation assessed as PSI, relative to the sham stimulation. Repeated measures ANOVA yielded a significant difference in PSI across the three bilateral temporal lobe tDCS

stimulation conditions (L-R+: 0.34 ± 0.15 [*Mean* ± *SD*], L+R-: 0.38 ± 0.17, sham: 0.45 ± 0.19, $F_{(2,38)} = 5.59, p = .007, \eta^2_p = .23$). Planned comparisons showed significantly lower PSI for the L-R+ condition ($t_{(19)} = 2.93, p = .009$, Cohen's $d = 0.67$) and L+R- condition ($t_{(19)} = 2.15, p = .045$, Cohen's $d = 0.49$), compared to the sham condition. No significant difference in PSI was found between the L-R+ and L+R- conditions ($t_{(19)} = 1.25, p = .23$, Cohen's $d = 0.29$).

No significant difference was found in overall recognition memory accuracy (percent correct: L-R+: 86.9 ± 10.8%, L+R-: 86.7 ± 8.0%, sham: 86.7 ± 9.2%, $F(2,38) = 1.06, p = .36, \eta^2_p = .053$). Planned comparisons verified that recognition memory accuracy was comparable between the L-R+ condition and sham condition ($t_{(19)} = 1.28, p = .22$, Cohen's $d = 0.29$), between the L+R- condition and sham condition ($t_{(19)} = 1.60, p = .13$, Cohen's $d = 0.37$), and between the L-R+ and L+R- conditions ($t < 1$). Percent endorsed for each stimulus and response type was listed separately for each stimulation condition in Table 1. Taken together, these results suggested that bilateral temporal lobe tDCS degraded pattern separation without affecting overall recognition memory accuracy.

Discussion

The present study tested the causal relationship between the temporal lobes, presumably medial temporal lobes, and pattern separation with temporal lobe tDCS. We found bilateral tDCS over the temporal lobes (both L-R+ and L+R-) decreased pattern separation performance relative to sham stimulation. Specifically, temporal lobe tDCS decreased participants' ability to correctly identify similar lures as similar to studied items, relative to sham stimulation, even though participants' ability to correctly identify objects as old or new was comparable across the three conditions.

Although the stimulation used in the present study most likely affected temporal lobe tissues directly beneath the electrodes, some remote structures in MTL could also been affected by temporal lobe tDCS based on the modeling data. These remote MTL structures have been implicated in pattern separation. For example, hippocampal activities for lure and target items seemed to be more distinctive in CA3 and dentate gyrus of hippocampus than other sub regions of hippocampus [2]. Complimentary to previous lesion studies [6], the specific effect of anterior temporal lobe tDCS on pattern separation in the present study thus provided further support for the causal role of the MTL in pattern separation in normal brain. To further establish more exclusive roles of the MTL in pattern separation, an active stimulation over another area (e.g., posterior parietal cortex) could be used as an active control condition to be compared with the anterior temporal lobe tDCS effects from the present study.

Two primary approaches are typically used in tDCS studies: a combination online/offline approach (continues stimulation into the task), or a purely offline approach (all stimulation occurs prior to the task). The combination online/offline approach makes it difficult to determine exactly what mechanism is behind any observed effects. Therefore, for the current study we adopted a pure offline approach, so the mechanism behind the decreased pattern separation performance is only due to after-effects of tDCS. These after-effects have been demonstrated in human cortex, as probed with non-invasive techniques [8]. As for deeper structures, tDCS cannot have substantial effects unless the current penetrates the cortex immediately beneath the stimulation sites and continue through the cortex [9]. As demonstrated in Figure 1d, the bilateral stimulation in the present study maximizes the likelihood that deep MTL structures, including hippocampus, are modulated by tDCS.

The offline tDCS protocol combined with the short duration (about 20 minutes) of the MST memory task in the present study make it possible that both memory encoding and retrieval are affected by tDCS. To isolate encoding effects [21], a sufficiently long delay between study and test could be introduced in future studies to ensure the effects of tDCS wear off before the test starts. To isolate retrieval effects, tDCS could be applied between study and test so that memory encoding is not affected by tDCS.

Due to the limited understanding of the neural mechanisms and effects of tDCS, it is difficult to know exactly what anatomical structures the stimulation is affecting and how they are affected based on computational modeling of tDCS effects alone [9]. Therefore, it remains possible that the decreased pattern separation may directly result from the modulation of anterior temporal lobe activities by bilateral tDCS. This alternative interpretation is in line with the functional roles of anterior portion of temporal lobe in long term memory in general [22] and specifically in representing fine-grained details of complex objects [23]. Further research using deep brain stimulation or combined temporal lobe tDCS and functional neuroimaging is needed to determine a more definitive mechanism behind the observed effects. Nonetheless, the present study has established that it is possible to change pattern separation function using non-invasive brain stimulation, which may have implications in applied settings such as eyewitness memory.

Previous studies showed that temporal lobe tDCS improved visual memory by reducing false memory [14], which may seem to contradict the current finding of pattern separation impairment. However, these studies used a false memory paradigm in which all items in the memory sets were related to some extent [24]. In this task, a relational scheme across the whole study set has been learned and subsequently affects recognition. Specifically, the presence of the critical lure in the test that is consistent with the relational scheme allows for the provocation of

false memories. In sharp contrast, there is no relationship between the memory items presented in the current study using the MST, and the lures are visually similar to one of the studied items. Therefore performance in this task should be largely determined by item memory, specifically the participant's ability to distinguish between memory representation of a studied item and a visually similar lure. As associative memory and item memory are dissociable [13], effects of temporal lobe tDCS on associative memory in the two previous studies [14] and item memory in the current study could also be dissociable. Similar improvements were previously observed in verbal memory using bilateral anterior temporal lobe tDCS [25], supporting the functional role of anterior temporal lobe as the semantic hub. Given the current study's focus on visual memory and MTL, it is not straightforward to make direct comparisons between those previous studies on verbal memory and the present study. Further research is needed to understand the relationship between these effects of anterior temporal lobe tDCS on memory across paradigms and modalities.

To conclude, the present study demonstrated that pattern separation, an essential mnemonic process that was indexed by PSI in the MST task, decreased in the L-R+ and L+R- temporal lobe tDCS conditions relative to the sham condition, adding to the growing literature on modulation of memory functions using non-invasive brain stimulation.

References

1. Marr D. Simple Memory: A Theory for Archicortex. *Philos T Roy Soc B* 1971; **262** (**841**): 23–81.

2. Yassa MA, Stark CEL. Pattern separation in the hippocampus. *Trends Neurosci* 2011; **34** (**10**): 515–525.

3. Bussey TJ, Saksida LM, Murray EA. Perirhinal cortex resolves feature ambiguity in complex visual discriminations. *Eur. J. Neurosci.* 2002; **15** (**2**): 365–374.

4. Reagh ZM, Yassa MA. Object and spatial mnemonic interference differentially engage lateral and medial entorhinal cortex in humans. *P Natl Acad of Sci USA* 2014; **111** (**40**): E4264–E4273.

5. LaRocque KF, Smith ME, Carr VA, Witthoft N, Grill-Spector K, Wagner AD. Global similarity and pattern separation in the human medial temporal lobe predict subsequent memory. *J Neurosci* 2013; **33** (**13**): 5466–5474.

6. Kirwan CB, Hartshorn A, Stark SM, Goodrich-Hunsaker NJ, Hopkins RO, Stark CEL. Pattern separation deficits following damage to the hippocampus. *Neuropsychologia* 2012; **50** (**10**): 2408–2414.

7. Das T, Ivleva EI, Wagner AD, Stark CEL, Tamminga CA. Loss of pattern separation performance in schizophrenia suggests dentate gyrus dysfunction. *Schizophr Res* 2014; **159** (**1**): 193–197.

8. Brunoni AR, Nitsche MA, Bolognini N, Bikson M, Wagner T, Merabet L, et al. Clinical research with transcranial direct current stimulation (tDCS): Challenges and future directions. *Brain Stimul* 2012; **5** (**3**): 175–195.

9. Bikson M, Rahman A, Datta A. Computational models of transcranial direct current stimulation. *Clin EEG Neurosci* 2012; **43** (**3**): 176–183.

10. Chib VS, Yun K, Takahashi H, Shimojo S. Noninvasive remote activation of the ventral midbrain by transcranial direct current stimulation of prefrontal cortex. *Transl Psychiatry* 2013; **3** (**6**): e268.

11. Lindenberg R, Nachtigall L, Meinzer M, Sieg MM, Flöel A. Differential effects of dual and unihemispheric motor cortex stimulation in older adults. *J Neurosci* 2013; **33** (**21**): 9176–9183.

12. Sadleir RJ, Vannorsdall TD, Schretlen DJ, Gordon B. Target optimization in transcranial direct current stimulation. *Front. Psychiatry* 2012; **3**: 90.

13. Eichenbaum H, Yonelinas AP, Ranganath C. The medial temporal lobe and recognition memory. *Annu Rev Neurosci* 2007; **30** (**1**): 123–152.

14. Chi RP, Fregni F, Snyder AW. Visual memory improved by non-invasive brain stimulation. *Brain Res.* 2010; **1353** (**C**): 168–175.

15. Stark SM, Yassa MA, Lacy JW, Stark CEL. A task to assess behavioral pattern separation (BPS) in humans: Data from healthy aging and mild cognitive impairment. *Neuropsychologia* 2013; **51** (**12**): 2442–2449.

16. Boggio PS, Khoury LP, Martins DCS, Martins OEMS, de Macedo EC, Fregni F. Temporal cortex direct current stimulation enhances performance on a visual recognition memory task in Alzheimer disease. *J Neurol Neurosurg Psychiatry* 2008; **80** (**4**): 444–447.

17. Truong DQ, Magerowski G, Pascual-Leone Á, Alonso-Alonso M, Bikson M. Finite Element study of skin and fat delineation in an obese subject for transcranial Direct Current Stimulation. San Diego, California USA: IEEE; 2012. pp. 6587–6590.

18. Truong DQ, Datta A, Xu J, Fregni F, Bikson M. Prefrontal Cortex transcranial direct current stimulation via a combined high definition and conventional electrode montage: A FEM modeling studying. San Diego, California, USA: 2012. pp. 6608–6611.

19. Rahman A, Reato D, Arlotti M, Gasca F, Datta A, Parra LC, et al. Cellular effects of acute direct current stimulation: somatic and synaptic terminal effects. *J Physiol* 2013; **591** (**10**): 2563–2578.

20. Motley SE, Kirwan CB. A parametric investigation of pattern separation processes in the medial temporal lobe. *J Neurosci* 2012; **32** (**38**): 13076–13084.

21. Javadi A-H, Cheng P. Transcranial Direct Current Stimulation (tDCS) enhances reconsolidation of long-term memory. *Brain Stimul* 2013; **6** (**4**): 668–674.

22. Wong C, Gallate J. The function of the anterior temporal lobe: A review of the empirical evidence. *Brain Res.* 2012; **1449** (**C**): 94–116.

23. Kriegeskorte N, Formisano E, Sorger B, Goebel R. Individual faces elicit distinct response patterns in human anterior temporal cortex. *P Natl Acad Sci USA* 2007; **104** (**51**): 20600–20605.

24. Roediger HL, McDermott KB. Creating false memories: Remembering words not presented in lists. *J Exp Psychol Learn* 1995; **21** (**4**): 803–814.

25. Ross LA, McCoy D, Wolk DA, Coslett HB, Olson IR. Improved proper name recall by electrical stimulation of the anterior temporal lobes. *Neuropsychologia* 2010; **48** (**12**): 3671–3674.

Table and Figure Captions

Table 1. Mean (SD) percentage of different responses for each experimental condition.

Figure 1. The bilateral temporal lobe tDCS montage (a) and estimated brain electric field amplitude distribution on the surface of the cortex including temporal lobes (b), estimated electric field amplitude distribution within deeper bran structures including hippocampus (c), and estimated current flow through the hippocampus and amygdala. Only the L-R+ polarity condition is shown for illustrative purposes. a) Positions of tDCS electrodes are shown for L-R+ condition on a 10-20 system diagram (left) and a 3D model of a male brain (right). The cathode (blue) is placed between T7-FT7 and anode (red) is placed between T8-FT8. Another stimulation condition, L+R-, consisted of the opposite polarity, with the anode placed between T7-FT7 and the cathode placed between T8-FT8 (not shown). b) Predicted current distribution on the temporal cortex for L-R+ condition is broadly distributed and clustered. Bidirectional current bar (-0.5 to 0.5 V/m) shows currents are dominantly inward (positive) under the anode and outward (negative) under the cathode. The densest condensation of unidirectional peaks is in the temporal lobes. c) Predicted electrical flow distribution in deep structures, including hippocampus, transparently plotted beneath temporal lobes (top row) and in isolation with the temporal lobes removed (bottom row). Displayed electrical flow intensity represents the unidirectional magnitude of current (0 to 0.5 V/m). Predicted electrical flow distribution in the hippocampus suggests peaks approximately 75% of maximum cortical intensity with local clustering. d) The flux lines represent current flow through the hippocampus and amygdala from a lateral view (left) and a front view (right).

Figure 2. Task structure of the Behavioral Pattern Separation Task-Object version. Participants first performed an encoding phase in which they responded "indoor" or "outdoor" to a series of images. They were then given a recognition memory test in which they responded "old", "new", or "similar" to a series of images that were the exact old images from study, novel foils, or lures that were visually similar to the studied images.

Figure 3. Pattern Separation Index (PSI) for each stimulation condition. Error bars represent standard error. (* $p < .05$)

413 *Table 1*. Mean (SD) percentage of different responses for each experimental condition.

Stimuli Type	Response Type	Stimulation Conditions (%)		
		L-R+	L+R-	Sham
Targets	Old	74.9 (13.3)	76.6 (8.8)	80.3 (8.3)
	New	6.2 (3.9)	8.4 (4.0)	7.15 (3.8)
	Similar	16.2 (11.2)	12.6 (6.1)	10.9 (6.4)
Lures	Old	37.8 (10.9)	32.9 (7.5)	25.5 (10.5)
	New	12.3 (9.2)	12.7 (6.4)	16.1 (9.5)
	Similar	46.7 (9.7)	51.8 (8.8)	56.1 (12.5)
Foils	Old	2.5 (1.9)	3.28 (2.5)	3.4 (4.9)
	New	76.3 (11.0)	77.7 (7.3)	83.1 (7.7)
	Similar	12.9 (5.3)	14.4 (5.9)	10.8 (5.2)

414 Note: No-response trials were not included.

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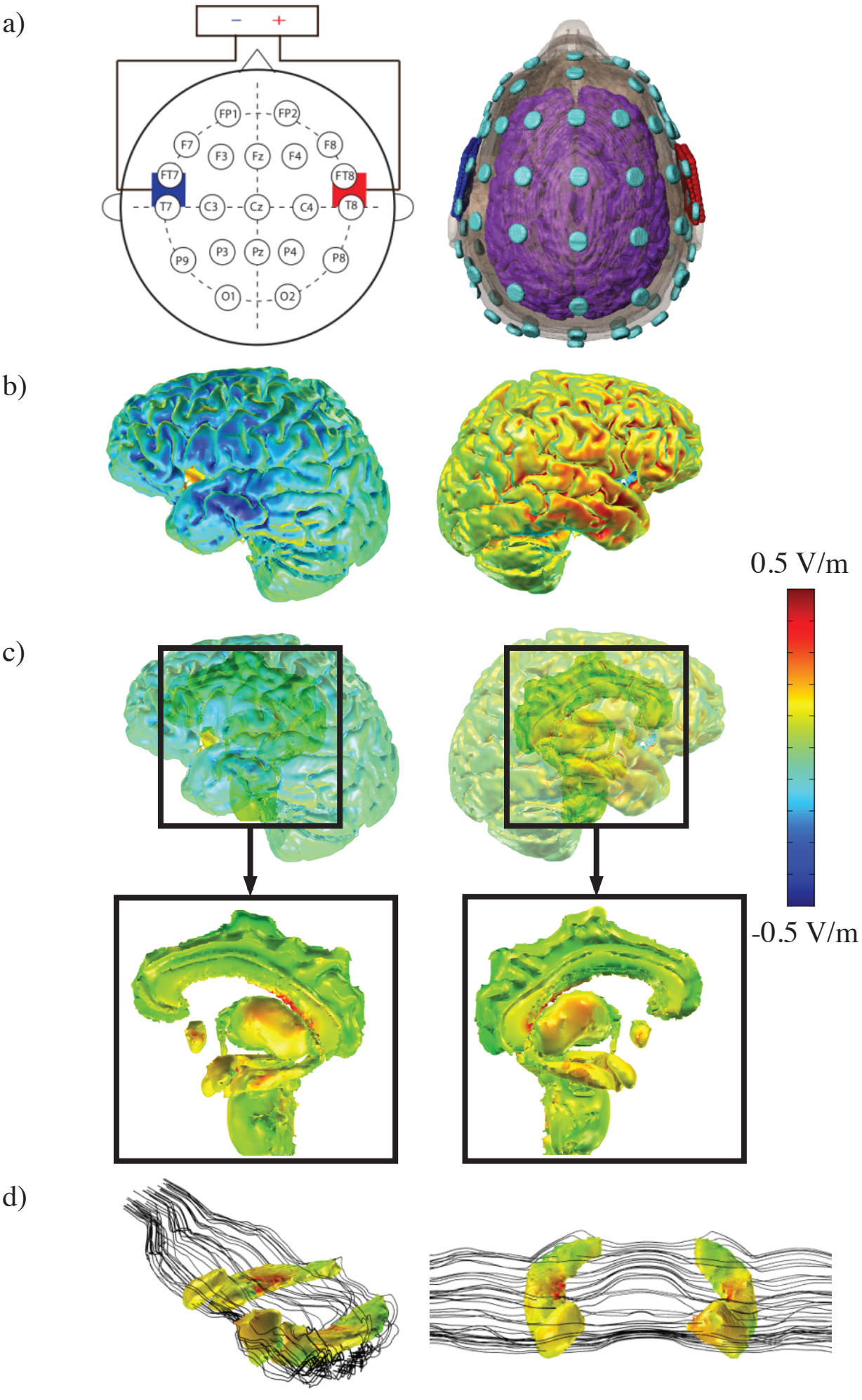
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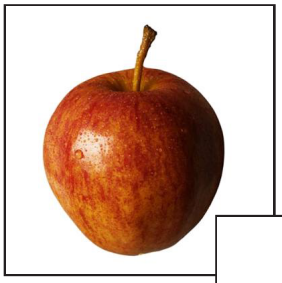
Study Phase
Indoor/Outdoor?

Test Phase
Old/Similar/New



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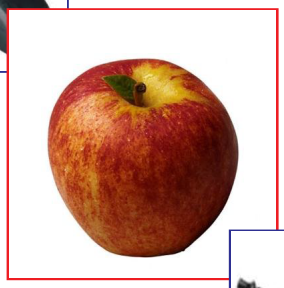
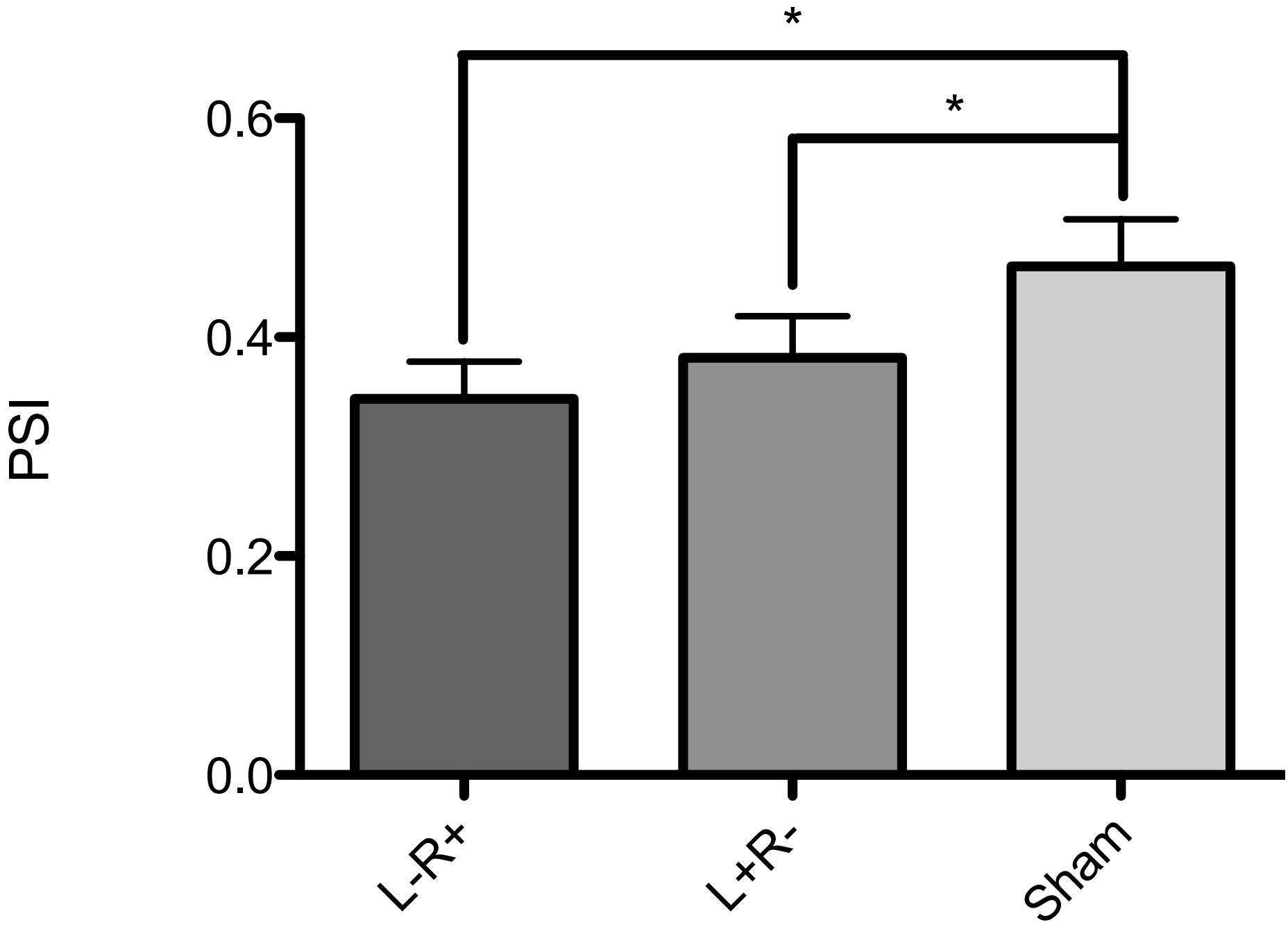
0.5 s ISI

Foil



Lure


*
*
0.6
0.4
0.2
0.0
PSI
L-R+
L+R-
Sham