A selective working memory impairment after transcranial direct current stimulation to the right parietal lobe

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A R T I C L E  I N F O

Article history:
Received 22 April 2010
Received in revised form 27 May 2010
Accepted 28 May 2010

Keywords:
Working memory
tDCS
Parietal
Internal attention
Recognition
Recall

Abstract

Functional neuroimaging studies have consistently reported that portions of the posterior parietal cortex (PPC) are active during a wide variety of working memory (WM) tasks [reviewed in (35,43)]. Similarly, neuropsychological studies have also shown that damage to portions of the PPC lead to WM impairments [reviewed in (35)]. The springboard for the current study is a recent finding by our laboratory in which we showed a dissociation in WM performance following PPC damage. Patients with PPC damage have intact performance when WM is tested by recall, but abnormally low performance when WM is tested by old/new recognition. This surprising recall/recognition dissociation was observed across several stimulus types, set sizes, and maintenance durations [7,5]. Likewise, several older fMRI studies of verbal WM in which the effects of different retrieval conditions were compared found that portions of the PPC were activated when memory was probed by old/new recognition, but not when probed by recall [4,11,16,20,24].

These findings may be interpreted in several ways. For instance, the PPC may subserve certain retrieval processes required only by recognition trials, or may have functions related to making an old/new decision. Our favored interpretation is that the observed recall/recognition dissociation is due to the employment of distinct maintenance strategies. Recall WM paradigms may encourage participants to engage an active rehearsal strategy. PPC patients can adopt this maintenance process and perform normally. Recognition WM paradigms may encourage a less active strategy since participants know that they can rely on familiarity, rather than production, at the retrieval stage. Presumably, this strategy requires attentional refreshing of the items stored in WM, a process that may be damaged after PPC lesions [7,5].

This distinction between strategies and attentional demands is consistent with a larger theoretical framework termed the internal attention (IA) account. The IA account holds that portions of the PPC contain a domain-general attentional mechanism. This mechanism revives WM representations, a process referred to as attentional refreshing [29,12]. According to the IA account, WM representations can be “boosted” by returning them to the focus of attention. The notion that attention plays an active role in covert maintenance is consistent with several recent attention-based models of WM (e.g. [13,3,28]). These models assume the existence of two alter-

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native covert maintenance mechanisms: a material-specific (e.g. verbal) mechanism that relies on rehearsal rather than on attention, and an attentionally mediated refreshing mechanism.

Although this explanation is compelling in its alignment with well-known attentional functions of the parietal cortex, there is one weakness: the data and interpretations depend primarily on lesion studies. Neuropsychological research provides causal links between brain structure and cognitive function. However, the technique suffers from certain limitations. For instance, lesion patients are generally older and may experience additional health problems, experience progressive disease processes, or lesions impinging on multiple brain regions. Perhaps of greatest concern with regard to cognitive performance, patients’ brains may reorganize following trauma and adopt alternative strategies. These factors reduce the ability to generalize findings to the general population and temper our inferential power.

The purpose of the present study was to counter these concerns by replicating our finding of a recall/recognition dissociation in a young healthy population using a different experimental technique: transcranial direct current stimulation (tDCS). In tDCS, a low, safe level of current is transmitted through the scalp to inhibit (cathodal stimulation) or enhance (anodal stimulation) the likelihood of firing in underlying neural populations [1,32,37]. Performance on cognitive tasks may be disrupted or enhanced depending on the stimulation parameters and the task demands.

Based on our lesion findings, we predicted that active tDCS (e.g. when compared to sham stimulation) to the right PPC would selectively affect WM performance on blocks of recognition, but not recall, trials. A secondary prediction was that cathodal tDCS would impair recognition WM performance whereas anodal tDCS would improve recognition WM performance [17,34].

Eleven neurologically normal young adults (age = 25.0, 6 males) participated. Three additional subjects’ data were not included because they performed at ceiling (N=2) or at floor (N=1). All experimental protocols were approved by the Hospital of the University of Pennsylvania Internal Review Board. Participants provided informed consent and they received reimbursement for their time.

There were three stimulation conditions: anodal, cathodal, and sham. No separate baseline condition was included as identical results between sham and baseline have previously been reported [14]. Conditions were tested on different days and order was counterbalanced between subjects. In all conditions one electrode was placed on the scalp over the right inferior parietal cortex at position P4 (International 10-20 EEG system) while the reference electrode was placed over the left cheek. This site was chosen because it is off of the head and thus less likely to affect a response in the brain. For anodal stimulation, the anode electrode was placed over P4 and for cathodal stimulation the electrodes were reversed, such that the cathode was placed over P4. During sham stimulation, anodal or cathodal placement was randomly applied to the P4 location. Participants were unaware of the polarity of stimulation [19] and the experimental predictions. During debriefing, several participants incorrectly guessed which day they received sham stimulation, suggesting the polarity of the stimulation was blinded.

Stimulation consisted of single continuous direct current delivered by a battery-driven continuous current stimulator (Magstim Eldith 1 Channel DC Stimulator Plus, Magstim Company Ltd., Whitley, England). Current was delivered through two electrodes housed in 5 cm × 7 cm saline-soaked sponges. During cathodal and anodal sessions, 1.5 mA current was applied for 10 min. During sham sessions, participants received pseudo-stimulation in which the current lasted for 20 s at the beginning and at the end of the stimulation time. The sham condition provides the temporary itching sensation but little actual current. Immediately following the stimulation, the electrodes were removed and participants began performing the task.

The visual stimuli were 20 colorized drawings of common objects (e.g. nail, pig, clock) [38]. The stimuli were approximately 20 cm × 10 cm.

The session began with a practice block of 30 old/new recognition WM trials during stimulation. Recognition trials alone were practiced because only a button press response was required. This eliminated any articulatory movements required by the verbal recall response that might have displaced the electrodes. After 10 min of stimulation the electrodes were removed and the four experimental trial blocks began. The beginning of recognition and recall trials began identically (see Fig. 1A). A series of six images was presented sequentially (1000 ms/image) at central fixation. Next, a checkerboard mask was presented for 1000 ms, during which time the memory set was maintained. At this point, recall and recognition trials diverged. During recall blocks, participants were required to verbally report the names of the items they had observed. Responses were recorded using GarageBand software (Apple Inc., Cupertino, CA) and transcribed off-line. During recognition blocks a seventh probe image appeared and the task was
to make an old/new button press response based on whether the probe had been in the memory set or not.

There were two 20-trial blocks of recognition trials alternating with two 10-trial blocks of recall trials per session (see Fig. 1B). The order of recognition and recall blocks was counterbalanced across sessions; each block lasted 3–5 min. After each block of trials, participants provided a confidence judgment on a scale of 1–6.

Our primary dependent measure was accuracy. Corrected recognition (hit rate minus false alarm rate) was the measure used on old/new recognition trials; raw accuracy was the measure used on recall trials. Initial analyses used separate repeated measures analysis of variance for recognition and recall with two factors: block (first, second) and stimulation session (anodal, cathodal, sham). Data were examined with separated repeated measures analysis of variance (ANOVA) for recognition and recall blocks with one factor: stimulation session (anodal, cathodal, sham).

Since no differences were observed between the first and second blocks of each task (accuracy: recognition; $F_{1,10} = 0.1, p = 0.99$, recall; $F_{1,10} = 1.52, p = 0.25$; reaction time: recognition; $F_{1,10} = 2.37, p = 0.16$, recall: $F_{1,10} = 9.3, p = 0.016$) the data were collapsed across block. Reaction time data were examined and no significant effects were observed (recognition: $F_{2,20} = 1.2, p = 0.89$; recall: $F_{2,20} = 0.47, p = 0.63$). No subject reported mental fatigue or an inability to concentrate throughout the study.

There was a significant main effect of stimulation session on recognition WM performance ($F_{2,20} = 3.46, p = 0.05$); see Fig. 2. Pairwise comparisons found that the main effect was driven by the significant WM impairment under cathodal stimulation relative to sham ($p = 0.016$). Anodal stimulation did not significantly impair recognition WM performance relative to sham ($p = 0.12$). There was no statistically significant difference between the anodal and cathodal sessions ($p = 0.37$). Participants appeared to be unaware of the deleterious effects of stimulation on performance: when confidence ratings were assessed, there were no significant differences between stimulation conditions ($F_{2,20} = 0.39, p = 0.68$).

Hit rates and false alarm rates were subjected to separate ANOVAs to determine whether the significant effect of cathodal tDCS was due to shifting hit or false alarm rates. There was a marginal effect of session (cathodal, sham) on hit rate ($F_{1,10} = 3.98, p = 0.07$) but no effect of session on false alarm rate ($F_{1,10} = 1.64, p = 0.23$). Instead, tDCS stimulation of the right PPC appears to cause an effect by reducing the hit rate during the cathodal stimulation session.

In contrast to the recognition data, there was no main effect of stimulation session on recall performance ($F_{2,20} = 0.25, p = 0.78$, see Fig. 2). Confidence ratings were similarly unaffected by stimulation ($F_{2,20} = 0.71, p = 0.51$).

We applied tDCS over the right inferior parietal cortex while subjects performed an object WM task probed by recall or recognition. Our primary prediction was confirmed: tDCS to right inferior parietal cortex selectively impaired WM probed by old/new recognition whereas recall WM performance was unaffected. A more specific prediction based on previous tDCS studies of WM was partially confirmed. We predicted that anodal stimulation would improve recognition WM and cathodal stimulation would impair recognition WM. We observed that cathodal stimulation did impair recognition, but anodal stimulation had no significant effect on recognition performance.

This prediction was shaped by a range of motor and cognitive findings showing that anodal tDCS can improve performance in healthy and patient groups. For example, in the motor literature, anodal stimulation of primary motor cortex decreases inhibition and enhances cortical excitability [10,42], even improving motor function in Parkinson’s disease patients [18]. In the depression literature, anodal stimulation of left dorsolateral prefrontal cortex temporarily alleviated symptoms in the clinically depressed [9,15]. However, anodal and cathodal effects do not always oppose each other in the motor literature. There are examples from the motor literature demonstrate effects isolated to anodal or cathodal stimulation. First, anodal stimulation to primary motor cortex improved performance on a serial reaction time task whereas no effects were observed following cathodal stimulation or stimulation of premotor or prefrontal cortex sites [33]. Second, cathodal stimulation alone to area V5 improved performance in a visuomotor tracking task [1]. It has also been shown that the task itself (e.g. passive, cognitive, motor) may shape and influence tDCS effects [2]. In short, it is simplistic to expect cathodal-impairment, anodal-improvement in tDCS paradigms.

The small WM-tDCS literature is also inconsistent. Several studies have reported that anodal tDCS to the left dorsolateral prefrontal cortex (DLPFC) improves performance on verbal n-back tasks [17,34,9,23,8]. However, two studies using Sternberg WM tasks and bilateral DLPFC stimulation reported impaired performance after either anodal or cathodal stimulation [15,30]. In sum, the WM literature indicates that anodal stimulation of the left DLPFC can improve accuracy on verbal n-back WM tasks but other WM tasks and stimulation sites are not associated with WM improvement.

Our study is the first to assess the effects of tDCS stimulation of the right PPC on WM performance. However, there are several WM studies in which transcranial magnetic stimulation (TMS) was used to disrupt superior PPC function. These studies reported decreased WM for letter alphabetization [36] and spatial location WM [22,21,25,44]. Our study is the first to show that object recognition WM is impaired following cathodal stimulation to the PPC.

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2 In these cases the reference electrode was on the right prefrontal cortex, thus each participant received bilateral stimulation.
The IA account discussed earlier predicts that damaging portions of the PPC will impair WM performance on tasks taxing the attentional functions of the PPC. Several categories of WM tasks meet this criteria: (1) most old/new recognition tasks [5,6]. Likewise, transcranial magnetic stimulation (TMS) designed to disrupt the superior parietal lobe can reduce WM for both passively maintaining letters and when manipulating letters in an alphabetization task as tested by old/new recognition [36]. The present iDCS data show that a second type of disruptive stimulation, cathodal iDCS, to the right PPC decreased WM performance for objects when tested by old/new recognition.

Second, TMS disruption of the superior parietal lobe can impair WM on tasks requiring information manipulation [36]. Consistent with these findings, patients with unilateral superior parietal lobe lesions are impaired on tasks requiring manipulation of information such as the backward digit span, or n-back tasks, but they perform normally on WM tasks requiring the maintenance of easily rehearsed information, such as forward digit span [26].

Third, numerous studies of patients with right PPC lesions have reported the existence of spatial WM deficits on both recall and recognition tasks (reviewed in [35]). Spatial attributes are difficult to verbalize and rehearse thus, patients with PPC damage may be impaired for poor recognition WM performance in the cathodal condition, while we would have anticipated observing altered performance for the anodal recognition condition as well – and this was not found.

In summary, we successfully replicated the intact WM recall/impaired WM recognition dissociation first observed in patients with parietal lesions [5,6]. This replication assuages concerns that our previous results were due to a peculiar patient group or due to brain reorganization following trauma.

Acknowledgments

We are grateful to Jennifer Benson for administrative help. We thank Jason Chein, Roy Hamilton, Peter Turkeeltaub, and Jared Medina for helpful comments and suggestions. This research was supported by NRSA NS059093 to Marian Berryhill.

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