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Interference with episodic memory retrieval following transcranial stimulation of the inferior but not the superior parietal lobule

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ABSTRACT

Although posterior parietal cortex (PPC) has been traditionally associated with spatial attention and sensorimotor functions, recent neuroimaging evidence has suggested the involvement of regions of left PCC (LPPC) in memory retrieval. Yet, the role of the parietal lobe in memory-related functions is still controversial. Here we investigated the causal involvement of different LPPC regions in episodic memory retrieval using repetitive transcranial magnetic stimulation (rTMS) during a task that provided both objective and subjective measures of item recognition and source memory. Stimulation sites were identified on the basis of a recent fMRI study showing the involvement of regions of the default mode network (DMN), such as the angular gyrus (AG) in the inferior parietal lobule (IPL), during search for relevant information in episodic memory, and regions of the dorsal attention network (DAN), such as the superior parietal lobule (SPL), during perceptual search. We predicted a selective disruption of memory performance following rTMS stimulation of the left AG relative to a sham condition or stimulation of the left SPL. We found a modest but significant decrease of sensitivity for item recognition when AG was directly compared to SPL, but not to sham stimulation. A stronger effect was however observed for the criterion of source memory judgments when comparing AG with both SPL and sham stimulation, suggesting that the rTMS over AG affects subjective aspects of source monitoring associated with the weighing of relevant retrieved information for source attribution.

1. Introduction

The observation that left posterior parietal cortex (LPPC) is typically activated by episodic memory retrieval in human fMRI studies has generated many hypotheses concerning its role in the retrieval process (Cabeza, Ciaramelli, Olson, & Moscovitch, 2008; Vilberg & Rugg, 2008; Wagner, Shannon, Kahn, & Buckner, 2005). However, the validity of these theories is complicated by two factors: the correlational nature of fMRI, which precludes any firm conclusion about causal relationships between brain activity and cognitive functions, and the observation that lesions of PPC are commonly associated with visuo-spatial attention rather than memory deficits (Corbetta & Shulman, 2011; Mesulam, 1999).

Recent neuropsychological investigations have revealed that parietal patients do show subtle memory deficits that can go unnoticed during standard neuropsychological evaluations. Specifically, patients tend to have problems with subjective (e.g., less vividness/richness; less confidence, reduced sense of recollection) rather than objective (accuracy) aspects of recollection (Berryhill, Phuong, Picasso, Cabeza, & Olson, 2007; Davidson et al., 2008; Simons et al., 2008; Simons, Peers, Mazuz, Berryhill, & Olson, 2010). These clinical observations, however, appear quite modest if compared with the robust activation of LPPC in fMRI studies on healthy subjects, which would predict a more significant memory disruption. This apparent inconsistency may be explained by methodological differences across studies. Lesion studies have typically involved few patients with lesions of different size, location and degree of white matter damage, and the resulting inter-subject variability may have considerably weakened the possibility to isolate more objective memory deficits in these patients. This issue appears crucial when considering the high functional heterogeneity of this portion of cortex (Nelson et al., 2010; Sestieri, Corbetta, Romani, & Shulman, 2011). In addition, since most of the lesion studies have been conducted 6 months or

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more after the injury, the degree of functional reorganization in these patients is unknown (Schoo et al., 2011).

Transcranial magnetic stimulation (TMS) studies offer a potential solution to these problems, as this method can produce transient behavioral deficits that are thought to be associated with the function of the stimulated cortex or connected regions. The present rTMS study was designed to address several outstanding issues concerning the causal relationship between left parietal cortex and episodic retrieval.

First, it is currently unknown whether rTMS stimulation of LPPC produces deficits in paradigms assessing source memory, i.e., the memory for specific details of the context in which an item or event was previously encountered (Johnson, Hashtroudi, & Lindsay, 1993 for a review). Whereas item recognition memory is generally considered to depend on contributions from both recollection and familiarity (Yonelinas & Levy, 2002), source memory is considered a better test of recollection because success requires retrieval of the encoding context (Simons et al., 2008). The neuroimaging literature indicates that regions of the LPPC, and especially of the IPL, show stronger BOLD response for recollection, compared to familiarity (Cabeza et al., 2008; Vilberg & Rugg, 2008; Wagner et al., 2005). This may explain why previous rTMS studies (Manenti, Tettamanti, Cotelli, Miniussi, & Cappa, 2010; Rossi et al., 2006), which have used item recognition paradigms, have failed to reveal memory deficits comparable to those observed during stimulation of the prefrontal cortex (Manenti et al., 2010; Rossi et al., 2001; Wais, Kim, & Gazzaley, 2011).

Second, neuropsychological studies (i.e., (Simons et al., 2010)) suggest that rTMS stimulation may selectively affect subjective measures of memory performance. Whereas objective measures assess performance in terms of accuracy (sensitivity) and speed (reaction times), subjective measures reflect, for example, how participants evaluate their performance (confidence), or what criterion (bias) they adopt during both old/new and taskA/taskB source memory decisions. For instance, during item recognition, subjects can differently weigh information about familiarity or recollection to indicate that they have seen an item before. In a similar vein, during source monitoring, subjects may have a bias toward a particular source category (criterion shift) because they weigh more one kind of information over another (e.g., semantic vs. visual) when attributing a memory detail to a particular source (Johnson et al., 1993).

A final issue concerns the spatial specificity of the potential rTMS effects. Consistent with previous studies (reviewed in (Vilberg & Rugg, 2008; Wagner et al., 2005), we have recently shown (Sestieri, Shulman, & Corbetta, 2010) that search for relevant information in episodic memory evokes significant BOLD responses in posterior nodes of the default mode network (DMN) (Raichle et al., 2001; Shulman et al., 1997), especially in the left angular gyrus (AG). We also reported the existence of a dynamic competition between this set of regions and an other set of parietal regions, included in the dorsal attention network (DAN), which are involved in perceptual search (SPL, posterior intraparietal sulcus). Importantly, this push–pull relationship was related to behavioral performance, as better performance at one task was associated with both greater BOLD activation in the set of task specific regions and greater deactivation in the other set of regions (Sestieri et al., 2010). This finding may reflect the existence of a mechanism of mutual suppression between functionally specialized parietal regions, based on task demands.

The present study aimed at fully characterizing the pattern of behavioral effects induced by rTMS interference on LPPC activity during a memory task that assessed both objective and subjective measures of item recognition and source memory using signal detection theory (SDT, (Green & Swets, 1966)). In order to increase the topographic precision of our rTMS procedure, we targeted specific sub-regions within LPPC. The first region (AG) has been shown to be specifically involved in searching for task-relevant information in episodic memory (Sestieri et al., 2010). To assess the topographic specificity of potential memory effects following AG stimulation, we also selected a region (SPL) that has been shown to be involved in perceptual search. Because previous fMRI have mainly reported left-lateralized parietal activations during memory retrieval (Wagner et al., 2005), we focused our investigation on stimulation sites in the left hemisphere.

2. Methods

2.1. Subjects

Sixteen right-handed (Oldfield, 1971) volunteers (age range: 20–38 years old; seven males) with normal or corrected to normal vision and no previous psychiatric or neurological history participated in the experiment. The experiment was conducted in accordance with the Code of Ethics of the World Medical Association, and with standards of the University of Chieti Institutional Review Board and Ethics Committee.

2.2. Experimental paradigm

Fig. 1 illustrates the TMS sites (A) and the experimental design ((B) and (C)). The experiment involved two sessions performed in two consecutive days. During the first day (encoding), subjects performed two intermixed encoding tasks. Approximately 24 h later (retrieval), they were asked to provide item-recognition decisions combined with a source-recollection judgment (Kahn,

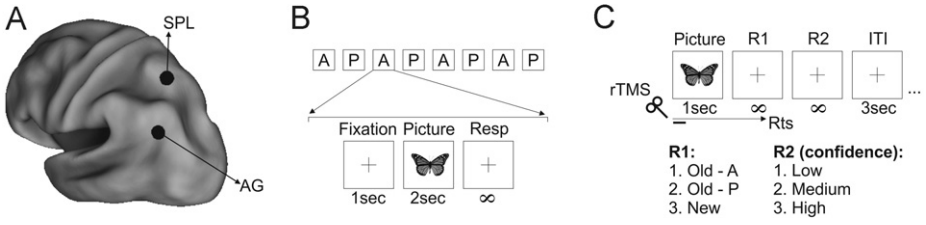

Fig. 1. Paradigm and rTMS stimulation sites. (A) The LPPC sites where rTMS was delivered in separate blocks. The spheres indicate the Talairach coordinates of the two active stimulation sites (AG: $x=-42$, $y=-68$, $z=+27$; SPL: $x=-23$, $y=-58$, $z=+49$) and are superimposed on the inflated representation of the left hemisphere (PALS Atlas, Caret 5.61) (Van Essen, 2005). (B) Trial structure of the encoding task. A 1 s fixation display was followed by the presentation of a colour picture that lasted on the screen for 2 s. Depending on the specific block, subjects were instructed to provide either an animacy (A, natural vs. manmade) or a pleasantness (P, like vs. dislike) judgment. At picture offset, subjects indicated their answer by pressing one of two keys. Each block included 34 trials. (C) Trial structure of the retrieval task. An old or a new picture was presented on the screen for 1 s, rTMS was delivered at the beginning of picture presentation and lasted for 150 ms. Subjects were asked to provide item recognition combined with source memory judgments (R1) by pressing one of three keys with their left hand, as accurately and as fast as they could, starting from picture onset. After the first response, subjects provided a confidence rating of the previous source memory judgment by pressing one of three keys with their right hand (R2). The subsequent trial was preceded by a fixation display lasting for 3 s. Each condition included 90 trials.