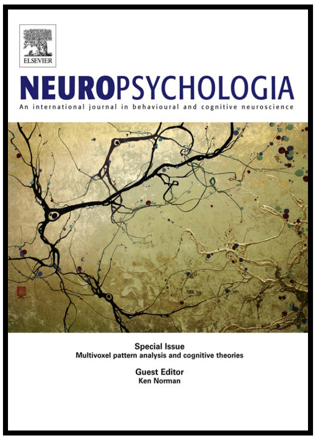
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Superior parietal cortex and the attention to delayed intention: An rTMS study

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Abstract

Prospective memory (PM) is the ability to remember to carry out an intention when the appropriate cue occurs. This study aimed to investigate whether the superior parietal cortex is causally involved in PM and, if so, what is its functional role. We applied repetitive transcranial magnetic stimulation (rTMS) to the left and right superior parietal cortex, and we evaluated the TMS effects on two different PM tasks that required to direct the attention towards either the external stimuli ('Monitoring-load' task) or the intention in memory ('Retrospective-load' task).

rTMS of left parietal cortex produced a facilitation of PM performance in both tasks. This was coupled by slower responses to the ongoing activity, for left and right parietal stimulation, but selectively in the 'Retrospective-load' condition.

The present results suggest that superior parietal cortex is causally involved in biasing top-down attentional resources between the external, ongoing stimuli and the internal, PM intentions. The possible physiological mechanisms underlying the TMS-related improvement in PM performance are discussed.

Keywords: prospective memory; intentions; parietal; superior parietal cortex; TMS; transcranial magnetic stimulation; attention; top-down; bottom-up; monitoring

1. Introduction

Survage: Why did you paint a portrait of me with only one eye?
Modigliani: Because you look at the world with one eye; with the other, you look into yourself.
(Dan Frank, 2001)

Prospective memory (PM) consists in remembering to execute delayed intentions when the appropriate moment or event – the PM cue – occurs, carrying out such intentions in coordination with other ongoing activities. PM is considered to be a multi-phase process, comprising the phases of intention encoding, intention maintenance, intention retrieval and execution (Marsh, Hicks, & Watson, 2002; Kliegel et al., 2002). Furthermore, PM relies upon multiple processes, which can be clustered under the terms 'strategic monitoring' and 'spontaneous retrieval'. Strategic monitoring consists of a set of top-down attentional and memory processes needed to monitor the environment for the presence of the PM cue and to maintain the intention active and refreshed in memory. Spontaneous retrieval consists of bottom-up processes, such as the automatic capture of attention by the PM cue and the activation of intention from memory (Einstein & McDaniel, 2005). Many factors were shown to modulate the extent to which the two kinds of processes are recruited. For example, strategic monitoring is particularly recruited when the PM cues are nonfocal (i.e., when PM cue features are not easily extracted from processing of the ongoing stimuli) or nonsalient, whereas spontaneous retrieval occurs when the PM cues are focal (i.e., when processing of the PM cue features is stimulated by processing of the ongoing stimuli) or salient (Einstein et al., 2005).

In recent years, there has been a growing interest in understanding the neural mechanisms of PM and in identifying the brain regions involved in each phase and process of PM (e.g., Gilbert et al., 2012; Rusted et al., 2011; Burgess et al., 2011; Cona et al., 2015, 2016, *for recent reviews*).

One of the key regions supporting PM is the anterior prefrontal cortex (aPFC; Brodmann Area, BA 10), which acts as a gateway mechanism between stimulus-independent and stimulus-oriented thoughts (Burgess et al., 2007, 2011; Gilbert et al., 2005). More specifically, the lateral parts of the aPFC mediate stimulus-independent processes, which include maintaining the PM intention active in memory, whereas the medial parts of the aPFC support stimulus-oriented processes, such as processing of the ongoing stimuli (Barban et al., 2013; Benoit et al., 2012; Burgess et al., 2007, 2011; Gilbert et al., 2005, 2006). In such a way, aPFC regions orchestrate and distribute the resources allocated for the PM task and the ongoing activity, allowing an individual to perform both tasks simultaneously.

Two recent meta-analyses showed that, aside from the aPFC, the frontoparietal networks are crucially involved in PM tasks (Cona et al., 2015, 2016). In particular, the dorsal frontoparietal network (i.e., dorsolateral prefrontal cortex (DLPFC), premotor regions, frontal eye fields (FEF), superior parietal lobule and precuneus) was found to be involved mainly in the maintaining phase, whereas the ventral frontoparietal network (i.e., ventrolateral prefrontal regions, inferior parietal lobule and supramarginal gyrus) was found to be more active during the retrieval phase. According to the Attention to Delayed Intention (AtoDI) model, the dorsal frontoparietal network would support the allocation of top-down attention, which would be directed both externally, towards the environment for monitoring the presence of the PM cue, and internally, towards the representation of intention for keeping it active in memory. By contrast, the ventral frontoparietal network would underpin the bottom-up attention, which would be captured externally, by the PM cue, and internally, by the representation of the associated intention (Cona et al., 2015). Several other works found consistent activations of the frontoparietal regions (e.g., Barban et al., 2014; Beck et al., 2014; Landsiedel & Gilbert, 2015). The AtoDI account is also supported by the findings of recent PM studies, which proposed that strategic monitoring – consisting of top-down attentional and memory processes – are supported mainly by dorsal frontoparietal regions (Beck et al., 2014; Gonneaud et al., 2014). Also, a transcranial magnetic stimulation (TMS) study showed that the right DLPFC is causally involved in strategic monitoring whereas the left inferior parietal lobule is involved in retrieval of intention (Bisiacchi et al., 2011).

So far, no study has ever investigated whether the superior parietal cortex causally contributes to PM and, if so, what is its functional role. In order to answer these questions, we applied off-line repetitive TMS over the left and right superior parietal cortex and we evaluated the possible TMS effects on the performance in two PM tasks that vary for the type of load required, in line with the logic underlying the study by Meier and Zimmermann (2015). One of the PM tasks used in our study was indeed characterized by high monitoring load (i.e., 'Monitoring-load' PM task). The PM cue was nonfocal and nonsalient compared to the ongoing stimuli, thus a great amount of top-down attentional resources towards the external stimuli was required to accomplish this task. The other PM task was instead characterized by high retrospective load (i.e., 'Retrospective-load' PM task), as it comprised multiple intentions to remember. In this condition, the attention was required to be directed mainly toward the internal intentions stored in memory. Moreover, in order to minimize the monitoring load, the PM cues were very salient and distinctive compared to the ongoing stimuli.

Based on the AtoDI model, we can make some predictions: if the superior parietal cortex mediates the allocation of attention towards the external stimuli, we should expect to observe an effect of superior parietal cortex stimulation mainly in the Monitoring-load PM task. By contrast, if the superior parietal cortex supports the allocation of attention towards the internal representation of the intention, we should expect to observe an effect of TMS mainly in the Retrospective-load PM task.

Importantly, the investigation of the TMS effects on the performance in the ongoing task executed concurrently with the two types of PM tasks helped us to better disentangle these two types of attention.

2. Materials and Method

2.1 Participants

Twenty-two students of the University of Padua took part in the experiment (14 females; mean age: 23.6; range: 21-28).

Participants had normal or corrected-to-normal vision, and were all right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971). All were healthy, with no history of head injury or physical, neurological, or psychiatric illness. They were all checked for TMS exclusion criteria (Rossi et al., 2009). They gave informed written consent before participating in the experiment. The study was carried out in accordance with the guidelines of the Declaration of Helsinki and was approved by the ethical committee of the Department of General Psychology, University of Padua.

2.2. Stimuli and Apparatus

Participants seated in front of a color monitor screen at a distance of about 60 cm. The experiment was run using the E-Prime software system. An ongoing task and a PM task were administered. The ongoing task was a lexical decision task (LTD).

Stimuli were valid Italian words and pronounceable nonwords. Word stimuli were selected from the “Corpus e Lessico di Frequenza dell'Italiano Scritto” (CoLFIS) database (http://linguistica.sns.it/CoLFIS/Formario.htm) and could range from 5 to 9 letters in length. Nonwords were pseudo-word stimuli, created from the used words by changing one or two letters.

In the ongoing task, participants were required to decide whether each string of letters presented on the screen was a word or a nonword, by pressing the “N” key with the right index finger or the “M” key with the right middle finger, respectively. All participants were instructed to respond as quickly and accurately as possible.

The psycholinguistic variables of words (mean length and mean frequency) were matched across all the experimental sessions and stimulus types (e.g., ongoing words *versus* PM trials). The stimuli were presented in black in the center of a white screen.

Together with the ongoing task, participants were asked to accomplish a PM task. More specifically, the participants were instructed that, when a particular stimulus occurred, i.e. the PM cue, they had to make a PM response instead of pressing the keys for the ongoing lexical decision task. Two different PM conditions were designed, which vary as a function of the type of load allocated for the PM task (monitoring load versus retrospective load). Half the participants underwent the Monitoring-load condition, whereas the other half underwent the Retrospective-load condition.

In Monitoring-load condition, participants were required to press the ‘Z’ key with their left index finger whenever they saw a pre-selected syllable (e.g., ‘sti’) within the string of letters. This task is indeed typically known as effective in emphasizing monitoring processes (e.g., Einstein et al., 2005; Scullin et al., 2010). In Retrospective-load condition, participants were given three distinct PM cue-intention associations to remember. For example, they were instructed to remember to press, using their left hand, the ‘Q’ key if they saw the word ‘marrone’ (brown), the ‘W’ key for the word ‘giallo’ (yellow) and the ‘E’ key for the word ‘viola’ (violet).

Notably, in order to minimize the monitoring load, participants were informed that these words were always underlined, thus they were more salient compared to the other strings of letters. Each session comprised 150 ongoing trials and 10 PM trials (frequency of the PM cue: 6.25%).

As each participant underwent three separate sessions – one for each TMS condition – three different versions of the PM plus ongoing task were created (version A, version B, and version C). The words across the mappings were equated on word frequency and number of letters, therefore the ongoing and the PM tasks across the versions were equally difficult[1]. The three versions were counterbalanced across participants.

The PM cues in the other two versions of the Monitoring-load conditions were ‘pra’ in version A, and ‘gli’ in version B, whereas the PM cues for the Retrospective-load conditions were: ‘grigio’ (grey), ‘azzurro’ (light blue), ‘rosso’ (red) in version A, and ‘verde’ (green), ‘arancione’ (orange), ‘bianco’ (white) in version B. In version C, the PM cues were those already mentioned above for the examples.

A practice block comprising only the ongoing task was administered at the beginning of the experiment. The instructions for the PM task were given immediately after the TMS, and there was no interval between the PM instructions and the administration of the tasks.

2.3. TMS protocol

Repetitive TMS pulses (rTMS) were applied using a Magstim 200 magnetic stimulator model (Magstim, UK) with a figure-of-eight coil (70 mm outer diameter).

Stimulation sites (i.e., right and left superior parietal regions) were identified on the participants' structural magnetic resonance imaging (MRI) scan. Scanning was executed at the Neuroradiology Unit (Azienda Ospedaliera di Padova) on a 3T Ingenia Philips whole-body scanner with a 32-channel head-coil. The details of the anatomical T1-weighted images were the following: TR/TE = 8.1/3.7, 180 sagittal slices; flip angle = 8°; voxel size = $1 \times 1 \times 1$ mm^3; FOV = 24 cm; acquisition matrix = 240×240).

The anatomical MRI images were incorporated into Brainsight stereotaxic neuronavigation system (Rogue Research, Inc., Montreal, Canada) coupled with a Polaris Vicra infrared camera system (NDI, Waterloo, Canada) to guide coil placement and to monitor the coil position during the experimental session. Participants also wore a swimming cap on which a colored dot was positioned in order to mark the "hotspot". Moreover, to reduce head movements, a chin support was provided.

The stimulation sites were the right and left superior parietal cortex. The identification of the stimulation sites was based on the superior parietal coordinates found in the meta-analysis by Cona and collaborators (2015), which were: $x = \pm 26$, $y = -56$, $z = 66$, and then slightly adjusted on the basis of each participant's MRI scan (which means that, if the position of the identified site was over a sulcus, this position was slightly moved).

A sham stimulation condition was included. In this condition, the coil was positioned on a posterior site over the interhemispheric fissure (site Pz according to the 10-20

System), but angled slightly off the head, with the two wings of the figure-eight coil touching the scalp at 45° respect to the scalp (Lisanby et al., 2001). This has been demonstrated to be an effective sham condition since it can simulate the proprioceptive and acoustic sensation produced by TMS without stimulating brain regions (Correa et al., 2014). The participants underwent the three TMS conditions in separate days. In each session, a different site was stimulated. The order of the TMS conditions was counterbalanced across participants.

Each TMS session consisted of the application of off-line, low frequency TMS (i.e., 1 Hz) for 20 minutes at 100% of each participant's motor threshold at rest. Motor threshold was determined at the optimal scalp position corresponding to the right and left primary motor cortices, and was defined as the minimum intensity that can elicit a reliable twitch in the contralateral hand in five of ten consecutive trials when the hand muscles were completely relaxed. For our group of participants, the mean stimulation intensity was 60 % (range 52 - 66%) of the maximum output of the stimulator, which is within the guidelines on safety of rTMS (Rossi et al., 2009). No adverse effects of TMS were reported.

2.4. Data analysis

Mean accuracy and mean reaction times (RTs) were measured, for the PM task and the ongoing task. Such behavioral measures were analyzed by means of separate ANOVAs, including Type of load as between-subject variable (monitoring-load and retrospective-load) and TMS condition as within-subject variable (right parietal site, left parietal site, sham). Significant effects were further explored by Newman–Keuls post hoc comparisons. Partial eta squared (η_p^2) values were calculated for all ANOVAs as an effect size index.

3. Results

3.1. PM task

The analysis of accuracy in the PM task revealed a significant main effect of TMS condition [$F(2,40) = 4.63$; $p < .05$; $\eta_p^2 = .18$]. Post-hoc comparisons showed that performance was significantly better after left parietal stimulation than after the right parietal stimulation and the sham stimulation (all *p*s < .05), for both the monitoring-load and retrospective-load PM tasks (Figure 1).

The effect of Type of load was not significant [$F(1,20) = 4.03$; $p = .058$; $\eta_p^2 = .16$] and did not interact with the TMS condition [$F(2,40) = 0.68$; $p > .05$; $\eta_p^2 = .03$].

The analysis of RTs showed a significant effect of Type of load, with RTs being slower in Retrospective-load PM task than in Monitoring-load PM task [$F(1,20) = 24.71$; $p < .01$; $\eta_p^2 = .55$] (Figure 1). The main effect of TMS and the TMS × Type of load interaction were not significant [*F*s < .54; *p*s > .05].

3.2. Ongoing task

The analysis of accuracy in the ongoing task did not show significant effects [all *F*s < 1.62; all *p*s > .05], thus the level of accuracy in the ongoing task was not influenced either by the TMS condition or the type of load allocated to the PM task.

The analysis of RTs revealed a significant main effect of TMS [$F(2,40) = 3.39$; $p > .05$; $\eta_p^2 = .14$] and a significant TMS × Type of load interaction [$F(2,40) = 3.40$; $p > .05$; $\eta_p^2 = .14$]. Post-hoc comparisons exploring the interaction revealed that in the Retrospective-load condition, the RTs in the ongoing task were significantly slower after the left and right parietal stimulation than after the sham stimulation (both *p*s <

.05; Figure 2). In the Monitoring-load condition, no significant differences were observed across the TMS conditions (all *p*s > .05; Figure 2). The main effect of Type of load was not significant [$F(1,20) = .69$; $p > .05$; $\eta_p^2 = .03$].

4. Discussion

The present study aimed to investigate the contribution of superior parietal cortex to PM. Our data showed that TMS applied over the left superior parietal cortex facilitated PM performance, in both Monitoring-load and Retrospective-load tasks. This finding may appear odd given that low frequency TMS typically interferes with cognitive performance, but becomes clearer when looking at the TMS effect on the ongoing performance. Indeed, a slowing of RTs in the ongoing task was observed following the left or right parietal stimulation (compared to sham stimulation), but selectively in the Retrospective-load condition. This pattern of results suggests that stimulation of superior parietal cortex would have biased the attentional resources from the ongoing activity in favor of the PM task. More specifically, one possible explanation is that after parietal stimulation, top-down attention would have been directed away from the external stimuli towards the representations of the intentions, and this could have interfered with the ongoing task. Notably, although there was no a baseline block consisting of the ongoing task alone, the fact that the detrimental effect of TMS on the ongoing task was observed only in the Retrospective-load condition, thus when multiple intentions needed to be maintained and refreshed in memory, seems to support this interpretation. This finding indicates indeed that the TMS did not interfere with the ongoing task per se (otherwise it would have seen also in the ongoing performance under the Monitoring-load condition), but suggests that the

TMS modulated a process particularly stressed and required in the Retrospective-load condition, namely the maintenance of the intentions. This hypothesis is also driven by a recent line of findings that suggests that the superior parietal cortex, belonging to the dorsal attention network, is implicated in the top-down allocation of attentional resources to internal representations, and thus it is involved in all those cognitive domains (e.g., working memory, episodic memory) that actually rely on such internal attention required to maintain the internal representations of stimuli (Lückmann et al., 2014, *for a review*). For example, a study developed outside the PM literature showed that the intraparietal sulcus (IPS), which is located in the dorsal part of the parietal lobe, has an internal attentional role, contributing to the attentional refreshing of items held in working memory (Killebrew et al., 2015).

The enhanced PM accuracy produced by left parietal stimulation is, however, a very surprising outcome given that 1 Hz TMS has typically an inhibitory effect on cognitive performance. Nevertheless, to date more than sixty studies have reported significant TMS-related improvements in accuracy and/or speed in a variety of cognitive tasks (Luber & Lisanby, 2014), also when using low-frequency TMS protocols (e.g., Drager et al., 2004; Hodsoll et al., 2009). Different hypotheses can be formulated to explain such performance enhancement. A possible mechanism is the entrainment of functionally-relevant EEG oscillations to TMS rhythms (Thut et al., 2011). In this regard, 1 Hz TMS could have driven the delta waves, which range from 0.5 to 3.5 Hz, causing a local entrainment of these slow brain oscillations. Interestingly, delta waves are found to be an indicator of internal attention (Harmony et al., 1996; Harmony, 2013). More specifically, the cognitive tasks requiring internal concentration or mentation were accompanied by the apparition of EEG delta waves, which inhibit the other ongoing processes that might interfere with the resolution of these cognitive tasks (Harmony, 2013). This explanation fits well with the evidence of the TMS-related PM facilitation/ongoing task inhibition: The power increase of low frequencies would be associated with the activation and refresh of the internal, to-be-remembered intentions, making such intentions more accessible and, thus, more easily retrieved, and with the inhibition of the processing for the ongoing, lexical decision task.

Another possible mechanism underlying PM enhancements produced by 1 Hz modulation is the release of the inhibition exerted by the stimulated area. Superior parietal stimulation could have produced a facilitatory effect on PM performance by modulating the competition between this region and the ventral parietal regions, such as the angular gyrus (AG), in favor of these, through the release of direct inhibition from dorsal to ventral parietal regions (Hilgetag, 2001; Kobayashi et al., 2004). Previous TMS and fMRI studies showed indeed the presence of a dynamic competition between ventral parietal regions (e.g., the AG), more related to memory retrieval, and dorsal regions, which include the superior parietal cortex (Sestieri et al., 2010, 2013). In particular, an fMRI study observed a push–pull relationship between these areas: if one cluster of regions was activated, the other was found to be deactivated, and *vice versa* (Sestieri et al., 2010). Notably, a TMS study revealed potential facilitatory effects on memory retrieval associated with left superior parietal stimulation and interpreted such effects as the result of the antagonist relationship between these two sets of regions (Sestieri et al., 2013). The same reasoning can be applied to our findings and converges with the AtoDI model, according to which dorsal parietal regions would be mainly involved during the maintenance phase, subserving strategic monitoring, whereas ventral parietal regions would be activated mainly in the retrieval of intention (Cona et al., 2015).

Importantly, the two explanations presented above are not necessarily mutually exclusive. Moreover, although our arguments about the exact mechanism need to be considered only speculative, nonetheless, both the scenarios suggest that superior parietal cortex is part of a gateway/competition mechanism between attention towards external *versus* internal stimuli. In this light, it is conceivable that the superior parietal regions interplay with the aPFC regions to manage and balance the activation of stimulus-independent processes (i.e., maintaining the intention) and stimulus-oriented processes, such as processing of the ongoing stimuli (Barban et al., 2013; Benoit et al., 2012; Burgess et al., 2007, 2011; Gilbert et al., 2005, 2006). The meta-analysis by Gilbert et al. (2010) reported indeed that the lateral aPFC regions are consistently co-activated with a network comprising the dorsolateral parietal regions.

Furthermore, this pattern of results would support two core features of the computational model of PM presented by Gilbert et al. (2013). First, the model assumed the presence of interactive, competing pathways responsible for the ongoing and PM responding. This competition was particularly emphasized in our experiment since, in PM trials, participants were required to press the key for the PM task instead of the keys for the ongoing task (and not in addition to). Following Gilbert et al.'s model, the parietal stimulation would have caused the activation of the pathway governing the PM responding at the expense of the pathway for the ongoing task. Second, such model considers the slowing of ongoing responses associated with the increased PM accuracy as the result of a top-down control mechanism. Even if our study did not include a baseline block, the comparison of the parietal TMS conditions with the sham condition allowed us to observe slower ongoing RTs (coupled by improvements in PM performance after left stimulation). Based on Gilbert et al.'s model, this TMS-related pattern of results would suggest that superior parietal cortex is a key structure of a top-down mechanism, which could be likely to support strategic monitoring, as proposed by the AtoDI model (Cona et al., 2015, 2016).

The third possible mechanism for the enhanced PM performance following left stimulation is that TMS of the left parietal cortex released the right parietal cortex from inter-hemispheric inhibition. It might be plausible that a facilitation of the PM performance emerged as a consequence of increased neural activity in the right parietal regions. This explanation seems however less likely given that the direct stimulation of the right parietal cortex did not have any effect on PM performance.

Indeed, it is also worthy of note that, while left and right parietal stimulation slowed ongoing responses, only left parietal stimulation facilitated PM performance. This finding suggests that bilateral dorsal parietal regions are involved during the maintenance phase, but the left parietal cortex uniquely contributes to PM retrieval. A recent fMRI study that has manipulated the number of PM intentions observed that when the PM cues appeared (so, in the retrieval phase), the activation shifted to a set of left-sided dorsal frontoparietal regions and the precuneus (as well as the middle temporal gyrus) (Barban et al., 2014). Interestingly, the involvement of this cluster of regions was shown when the number of PM cues was increased during high memory load and was interpreted as reflecting attention and working memory demanding processes. Furthermore, many lines of evidence revealed the special contribution of left parietal cortex to memory processes (e.g., Vilberg & Rugg, 2009; Wagner et al., 2005). In particular, a PM study showed that 10 Hz TMS applied over the left – but not right – inferior parietal cortex led to an impairment in PM retrieval and an improvement in the ongoing task, which represents the pattern opposite to that shown in the present experiment when stimulating the left superior parietal cortex (Bisiacchi et al., 2011). Taken together, these findings would corroborate the idea proposed by

Sestieri and collaborators (2010, 2013), concerning the existence of a push–pull relationship between dorsal and ventral parietal regions. Moreover, the study by Bisiacchi and collaborators (2011) used a 10 Hz stimulation protocol, thus suggesting possible frequency-dependent effects of TMS on balancing PM and ongoing processing.

Finally, according to the AtoDI model, the superior parietal regions would direct the attention toward both the external stimuli and the internal representations stored in memory (Cona et al., 2015). The PM facilitation observed under both the Monitoring- and Retrospective-load condition following left superior parietal stimulation seems to provide some evidence in favor of this idea, although this result must be interpreted with caution as the underlying physiological mechanism of such facilitation is not clear. This idea would be corroborated by a recent fMRI study showing that superior parietal cortex was activated for both memory-guided visuospatial attention and stimulus-guided visuospatial attention in a change detection task (Rosen et al., 2015).

Alternatively, it is possible that TMS has affected a process that was involved in both the conditions (although with a different extent), such as the retrieval of the intention, possibly by releasing the left inferior parietal cortex from the suppression exerted by the superior parietal cortex. The left inferior parietal cortex was indeed widely considered to support recollection (see Vilberg & Rugg, 2008, *for a review*).

In conclusion, the current study showed that the superior parietal regions are causally involved in PM tasks, and highlighted their bilateral involvement during the maintenance phase, suggesting that stimulation of either left or right superior parietal cortex might have biased processing from the external ongoing stimuli towards internal representation of the intention. On the other hand, stimulation of the left superior parietal cortex only facilitated the PM performance. Such TMS effects might be due to the release from inter-hemispheric inhibition or, more likely, from the competition exerted by dorsal to the ventral parietal cortex. Interestingly, if we take into account this work and our previous TMS study (Bisiacchi et al., 2011) together, we can conclude that the processes of directing the attention towards the external *versus* internal stimuli seem to operate in different frequency channels and are inversely modulated by interference with neural activity in different parietal sub-regions. Although the present study provides the first direct evidence for a causal role of superior parietal cortex in PM, nevertheless it leaves an open question. This concerns why the right parietal stimulation – which seems to produce a shift of attention towards the internal representation of the intention – did not lead to a PM facilitation, as instead shown after left parietal stimulation. Therefore, further studies are needed to answer this question. Moreover, the sample size used, even if comparable with that of other TMS studies, is relatively small. Future studies with larger sample sizes would be thus desirable.

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Footnotes

1 A pilot study confirmed that the ‘A’, ‘B’, ‘C’ versions of the PM tasks were equivalent in terms of difficulty.

References

Barban, F., Carlesimo, G. A., Macaluso, E., Caltagirone, C. & Costa, A., 2014. Functional interplay between stimulus-oriented and stimulus-independent attending during a prospective memory task. Neuropsychologia 53, 203–212.

Beck, S. M., Ruge, H., Walser, M. & Goschke, T., 2014. The functional neuroanatomy of spontaneous retrieval and strategic monitoring of delayed intentions. Neuropsychologia 52, 37–50.

Benoit, R. G., Gilbert, S. J., Frith, C. D. & Burgess, P. W., 2012. Rostral prefrontal cortex and the focus of attention in prospective memory. Cereb. Cortex. 22, 1876–1886.

Bisiacchi, P. S., Cona, G., Schiff, S. & Basso, D., 2011. Modulation of a fronto-parietal network in event-based prospective memory: an rTMS study. Neuropsychologia 49, 2225–2232.

Burgess, P. W., Dumontheil, I. & Gilbert, S. J., 2007. The gateway hypothesis of rostral prefrontal cortex (area 10) function. Trends. Cogn. Sci. 11, 290–298.

Burgess, P. W., Gonen-Yaacovi, G. & Volle, E., 2011. Functional neuroimaging studies of prospective memory: what have we learnt so far? Neuropsychologia 49, 2246–2257.

Cona, G., Bisiacchi, P. S., Sartori, G., & Scarpazza, C., 2016. Effects of cue focality on the neural mechanisms of prospective memory: A meta-analysis of neuroimaging studies. Sci. Rep. 6, 25983.

Cona, G., Scarpazza, C., Sartori, G., Moscovitch, M. & Bisiacchi, P. S., 2015. Neural bases of prospective memory: a meta-analysis and the “Attention to Delayed Intention” (AtoDI) model. Neurosci. Biobehav. Rev. 52, 21–37.

Correa, Á., Cona, G., Arbula, S., Vallesi, A., & Bisiacchi, P., 2014. Neural dissociation of automatic and controlled temporal preparation by transcranial magnetic stimulation. Neuropsychologia 65, 131–136.

Drager, B., Breitenstein, C., Helmke, U., Kamping, S., Knecht, S., 2004. Specific and nonspecific effects of transcranial magnetic stimulation on picture-word verification. Eur. J. Neurosci. 20, 1681–1687

Einstein, G. O. & McDaniel, M. A. 2005. Prospective memory: Multiple retrieval processes. Curr. Dir. Psychol. Sci. 14(6), 286–290.

Einstein, G. O., et al., 2005. Multiple processes in prospective memory retrieval: factors determining monitoring versus spontaneous retrieval. J. Exp. Psychol. Gen. 134, 327–342.

Gilbert, S. J., Armbruster, D. J. & Panagiotidi, M., 2012. Similarity between brain activity at encoding and retrieval predicts successful realization of delayed intentions. J. Cogn. Neurosci. 24, 93–105.

Gilbert, S. J., Frith, C. D. & Burgess, P. W., 2005. Involvement of rostral prefrontal cortex in selection between stimulus-oriented and stimulus-independent thought. Eur. J. Neurosci. 21, 1423–1431.

Gilbert, S. J., Gonen-Yaacovi, G., Benoit, R. G., Volle, E., & Burgess, P. W., 2010. Distinct functional connectivity associated with lateral versus medial rostral prefrontal cortex: A meta-analysis. NeuroImage 53(4), 1359–1367.

Gilbert, S. J., Hadjipavlou, N., & Raoelison, M., 2013. Automaticity and control in prospective memory: a computational model. PloS One 8(3), e59852.

Gilbert, S. J., Spengler, S., Simons, J. S., Steele, J. D., Lawrie, S. M., Frith, C. D., et al., 2006. Functional specialization within rostral prefrontal cortex (area 10): a meta-analysis. J. Cogn. Neurosci. 18, 932–948.

Gonneaud, J. et al., 2014. How do we process event-based and time-based intentions in the brain? an fMRI study of prospective memory in healthy individuals. Hum. Brain Mapp. 35, 3066–3082.

Harmony, T., 2013. The functional significance of delta oscillations in cognitive processing. Front. Integr. Neurosci. 7, 83.

Harmony, T., Fernández, T., Silva, J., Bernal, J., Díaz-Comas, L., Reyes, A., et al., 1996. EEG delta activity: an indicator of attention to internal processing during the performance of mental tasks. Int. J. Psychophysiol. 24, 161–171.

Hilgetag, C. C., Théoret, H., & Pascual-leone, A., 2001. Enhanced visual spatial attention ipsilateral to rTMS-induced “virtual lesions” of human parietal cortex. Nat. Neurosci. 4(9), 953–957.

Hodsoll, J., Mevorach, C., Humphreys, G.W., 2009. Driven to less distraction: rTMS of the right parietal cortex reduces attentional capture in visual search. Cereb. Cortex 19 (1), 106–114.

Killebrew, K., Mruczek, R., & Berryhill, M. E., 2015. Intraparietal regions play a material general role in working memory: Evidence supporting an internal attentional role. Neuropsychologia 73, 12–24.

Kliegel, M., Martin, M., McDaniel, M.A., & Einstein, G.O., 2002. Complex prospective memory and executive control of working memory: a process model. Psychol. Beitr. 44, 303–318.

Kobayashi, M., Hutchinson, S., Theoret, H., Schlaug, G., & Pascual-Leone, A., 2004. Repetitive TMS of the motor cortex improves ipsilateral sequential simple finger movements. Neurology 62, 91–98.

Landsiedel, J. & Gilbert, S. J., 2015. Creating external reminders for delayed intentions: dissociable influence on “task-positive” and “task- negative” brain networks. Neuroimage 104, 231–240.

Lisanby, S.H., Gutman, D., Luber, B., Schroeder, C., & Sackeim, H.A., 2001. Sham TMS: intracerebral measurement of the induced electrical field and the induction of motor-evoked potentials. Biol. Psychiatry 49 (5), 460–463

Luber, B., & Lisanby, S. H., 2014. Enhancement of human cognitive performance using transcranial magnetic stimulation (TMS). NeuroImage 85, 961–970.

Lückmann, H. C., Jacobs, H. I. L., & Sack, A. T., 2014. The cross-functional role of frontoparietal regions in cognition: Internal attention as the overarching mechanism. Progr. Neurobiol. 116, 66–86.

Marsh, R. L., Hicks, J. L. & Watson, V., 2002. The dynamics of intention retrieval and coordination of action in event-based prospective memory. J. Exp. Psychol. Learn. Mem. Cogn. 28, 652–659.

Meier, B., & Zimmermann, T. D., 2015. Loads and loads and loads: the influence of prospective load, retrospective load, and ongoing task load in prospective memory. Front. Hum. Neurosci. 9, 1–12.

Oldfield, R.C., 1971. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 9, 97–113.

Rosen, M. L., Stern, C. E., Michalka, S. W., Devaney, K. J., & Somers, D. C., 2015. Cognitive Control Network Contributions to Memory-Guided Visual Attention. Cereb. Cortex 1–15.

Rossi, S., Hallett, M., Rossini, P. M., & Pascual-Leone, A., 2009. Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. Clin. Neurophysiol. 120(12), 2008–39.

Rusted, J., Ruest, T. & Gray, M. A., 2011. Gray, Acute effects of nicotine administration during prospective memory, an event related fMRI study. Neuropsychologia 49, 2362–2368.

Scullin, M. K., McDaniel, M. A., Shelton, J. T. & Lee, J. H., 2010. Focal/nonfocal cue effects in prospective memory: monitoring difficulty or different retrieval processes? J. Exp. Psychol. Learn. Mem. Cogn. 36, 736–749.

Sestieri, C., Capotosto, P., Tosoni, A., Luca Romani, G., & Corbetta, M., 2013. Interference with episodic memory retrieval following transcranial stimulation of the inferior but not the superior parietal lobule. Neuropsychologia 51(5), 900–906.

Sestieri, C., Shulman, G. L., & Corbetta, M., 2010. Attention to memory and the environment: functional specialization and dynamic competition in human posterior parietal cortex. J. Neurosci. 30(25), 8445–56.

Thut, G., Veniero, D., Romei, V., Miniussi, C., Schyna, P., Gross, J., 2011. Rhythmic TMS causes local entrainment of natural oscillatory signatures. Curr. Biol. 21, 1176–1185.

Vilberg, K. L., & Rugg, M. D., 2008. Memory retrieval and the parietal cortex: a review of evidence from a dual-process perspective. Neuropsychologia 46(7), 1787–99.

Vilberg, K. L., & Rugg, M. D., 2009. Functional significance of retrieval-related activity in lateral parietal cortex: Evidence from fMRI and ERPs. Hum. Brain Mapp. 30(5), 1490–501.

Wagner, A.D., Shannon, B.J., Kahn, I., Buckner, R.L., 2005. Parietal lobe contributions to episodic memory retrieval. Trends. Cogn. Sci. 9, 445–453.

Figure 1. Prospective memory (PM) performance. The figure illustrates the proportion of correct responses and mean reaction times (in milliseconds, ms) in Monitoring-load and Retrospective-load PM tasks as a function of TMS condition. Error bars represent the standard error.

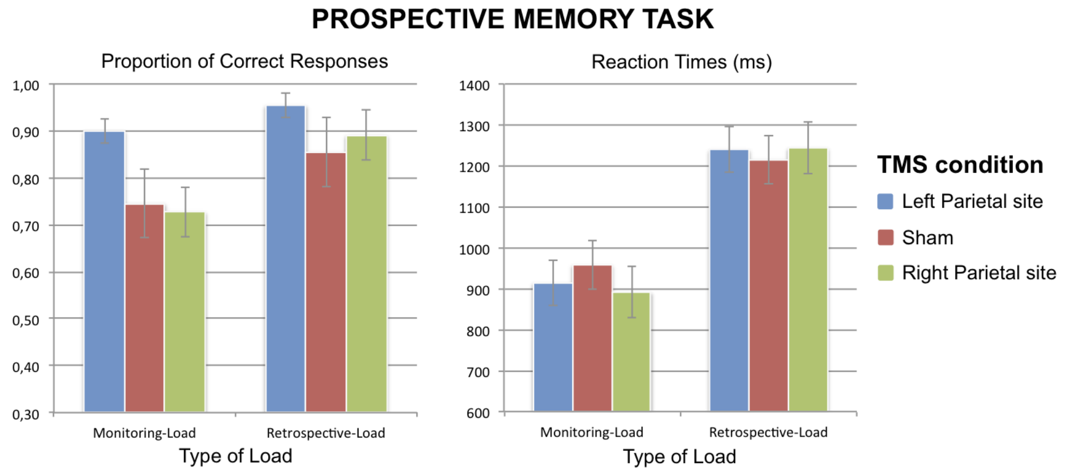
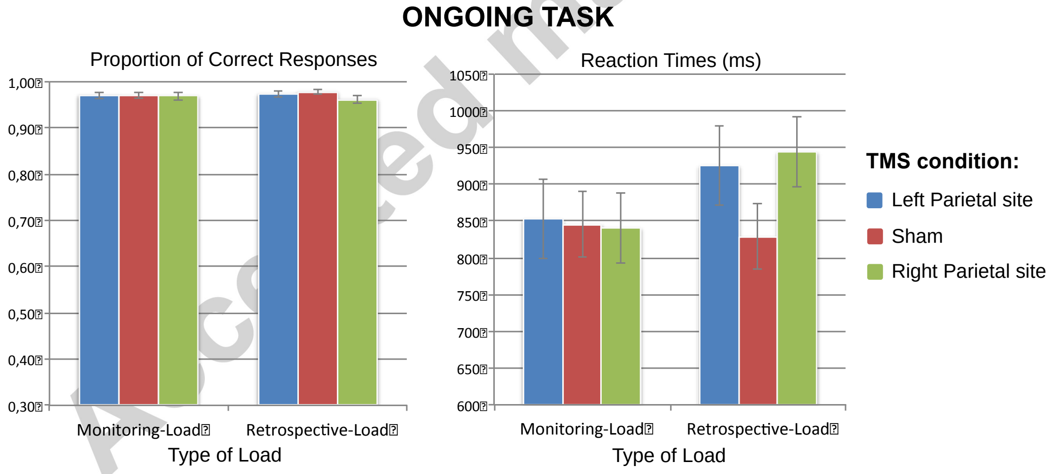


Figure 2. Performance in the ongoing task. The figure illustrates the proportion of correct responses and mean reaction times (in milliseconds, ms) in the ongoing task, separately in the Monitoring-load and Retrospective-load conditions, and as a function of TMS condition. Error bars represent the standard error.



Highlights

- Repetitive TMS of left parietal cortex facilitated prospective memory performance
- rTMS of left and right parietal cortex slowed ongoing responses in retrospective-load condition

- Superior parietal cortex biases top-down attentional resources between ongoing and PM tasks.