



## Prospective memory and working memory: Asymmetrical effects during frontal lobe TMS stimulation

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### ABSTRACT

The role of working memory (WM) for the realization of an intended action (prospective memory, PM) has been debated in recent neuropsychological literature. The present study aimed to assess whether WM and PM share resources or are, alternatively, two distinct mechanisms. A verbal task was used, which manipulated the cognitive demand of both WM and PM dimensions on an event-based prospective task. Transcranial magnetic stimulation (TMS) was also employed to clarify the causal contribution of frontal areas previously related to WM, to the PM process. The prospective task required the participant to respond whenever a word appeared which had been presented before the beginning of the task. Two ongoing tasks were administered: an updating WM task (in two conditions of medium and high WM demands) and a lexical decision task (representing a low WM demand). In the first two experiments, higher PM demand affected WM only at higher loads, but the PM load effect was independent of WM, showing asymmetrical behavioural effects. In the third experiment, single pulse TMS was applied to left and right dorsolateral prefrontal cortices. When applied to the experimental sites, stimulation increased error rates of the PM task, while the effect was only marginal in the WM task. The effect was bilateral, since there was no difference between left and right stimulation sites. These findings demonstrated, from both behavioural and neurofunctional perspectives, that WM and PM processes are not based on the same memory system, but PM may require WM resources at high demand.

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### 1. Introduction

Prospective memory (PM) refers to the formation, maintenance and realization of an intention that must be delayed for a few minutes or longer; for example, remembering to take a medication under certain conditions or at a particular moment (Brandimonte, Einstein, & McDaniel, 1996). Research focusing on prospective memory underlines the importance of considering the reciprocal influence of both the ongoing activity and prospective task (e.g. Okuda et al., 1998). One issue that has recently been debated in the literature concerns the effects of the ongoing activity on the realization of the intention. That is, the ongoing activity may disturb the efficiency of PM, competing for the same resources in the WM central executive (Einstein, Smith, McDaniel, & Shaw, 1997; Kliegel, McDaniel, & Einstein, 2008; Marsh & Hicks, 1998). WM is a limited capacity cognitive system, and the central executive is assumed

to allocate resources for managing the maintenance of information while temporarily performing other activities (Baddeley, 1986, 2002). Consequently, one hypothesis is that the demands of the ongoing activity can usurp resources required by the prospective memory, resulting in interference effects arising from the main stream of action.

This hypothesis can be addressed by examining whether cue detection during an ongoing activity requires processing resources, or can be done (almost) automatically. Two alternative models have been proposed in order to explore these possibilities. According to the preparatory attention and memory processing view (PAM: Smith, 2003), the possession of an intention creates a processing demand on the ongoing activity, as because it supports cue detection and contributes to maintaining the control necessary for performing the intention (Smith & Bayen, 2005). Preparatory processing and attention control are not thought to be automatic, but to involve the allocation of cognitive resources in WM, leading to the prediction that PM processing will always affect the ongoing activity. By contrast, according to the multiprocess theory (McDaniel & Einstein, 2000), an intention can be retrieved spontaneously, under certain circumstances. Thus, prospective memory would not necessarily involve preparatory attentional and memory processes, nor

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allocation of monitoring resources from WM. In turn, this predicts that PM and WM processing should be, at least in low demand conditions, independent processes.

Additional issues emerge from the neuropsychological perspective. Both PM and WM are considered executive processes (Kliegel, Martin, McDaniel, & Einstein, 2002; Mäntylä, 2003; Okuda et al., 1998), being localized in prefrontal regions such as the bilateral rostralateral prefrontal areas, the frontopolar cortex, and the dorsolateral prefrontal cortex (DLPFC). Under the gateway theory, proposed by Burgess and collaborators (Gilbert, Spengler, Simons, Frith, & Burgess, 2006), the role of the rostralateral prefrontal regions may be related to both maintenance of intentions and attentional shift from internal thoughts to external activating stimuli; this being a crucial region for self-initiated actions (Burgess, Scott, & Frith, 2003). In addition, the DLPFC is thought to be related to the *active* maintenance of these actions and/or to inhibitory processes. The centrality of DLPFC in working memory has been supported by several studies (e.g. Passingham & Sakai, 2004), but the relationship between WM and PM is still a matter of debate in neuropsychological research.

One of the first studies investigating the relationship between WM and PM (Kidder, Park, Hertzog, & Morrell, 1997) showed that in a WM task with low demand, the PM performance was higher than in a WM task with high demand. The authors concluded that PM function was affected by the level of engagement in the WM task. Another study by Park and colleagues (Park, Hertzog, Morrell, Kidder, & Mayhorn, 1997), suggested an explanation based on a resource perspective: the more a WM task recruits the central executive, the fewer resources would be available to the prospective task. However, only a small effect on the ongoing activity was observed following interference of the WM articulatory loop (Marsh, Hancock, & Hick, 2002; McGann, Ellis, & Milne, 2002).

Using ERPs and fMRI, West and colleagues investigated PM using an N-back task (Reynolds, West, & Braver, 2009; West & Kropfing, 2005), and supported a separation of PM and WM processes. Here, the neurofunctional pattern for PM shared only slight commonality with the network subserving WM in the active maintenance of goal-relevant information for the PM task. In addition, Henry et al. (2007) summarized eleven papers which investigated PM on traumatic brain injured patients (TBI) and found a dissociation between performance of retrospective recall and intention execution. Moreover, PM task did not always affect the strategic attentional demands of the task. Carlesimo, Casadio, and Caltagirone (2004) argued that, in closed head injured patients, the impairment in PM is likely to be an “inability to keep this memory representation active” in a local buffer, which can be available when needed. Age-related effects of WM load have added further insights (Bisiacchi, Tarantino, & Ciccola, 2008; Kliegel & Jäger, 2006). In the experiment of Kliegel and Jäger (2006), in the high WM load condition, an older group of adults (above 80 years old) showed a declining trend in PM ability, while the younger groups of adults (below 80 years old) showed a slight improvement in performance. Conversely, the interaction was not present in the condition of low WM load. However, despite the relevance of the study, the WM manipulation casts doubt on unequivocal WM involvement. Their manipulation of the WM load consisted of the presence/absence of a one-digit count task during pauses in the ongoing task. Since this task is known to have little or no effect on the central executive component (Baddeley, Chincotta, & Adlam, 2001), it should not be considered a concurrent task with significant WM involvement.

These findings from behavioural and neuroscience research have not yet provided conclusive data on the interaction between WM-ongoing task and PM task.

In addition, the methodological constraints of correlational analyses (yielded by ERPs, fMRI and PET) does not allow for stringent validation of the data. In our opinion, transcranial magnetic

stimulation (TMS) could be fundamental in helping to unravel the issue by manipulating the interference to cerebral areas, and treating them as independent variables (Miniussi, Ruzzoli, & Walsh, 2010). So far, however, TMS has been used mainly to investigate WM rather than PM (Hamidi, Tononi, & Postle, 2009; Mottaghy, Gangitano, Krause, & Pascual-Leone, 2003). TMS is not the most suitable technique for stimulating frontopolar and rostralateral prefrontal cortices, the main regions involved with the prospective components according to fMRI experiments (i.e. stimulation of these regions might result in a degree of discomfort due to their proximity to the eyes). However, TMS may be used to investigate whether interference to WM elicits effects that impact upon PM, as this is a process associated with the DLPFC, a cerebral region where stimulation would be unlikely to produce discomfort. In this way, critical data could be collected to disentangle these hypotheses.

The present study aimed at assessing the interaction between an ongoing WM task and a PM task, by manipulating the cognitive demand for WM (ongoing task) and PM dimensions on an event-based prospective task. One load, close to the average WM capacity, and one lower load were selected to produce different levels of demand on the central executive WM process (updating working memory (UWM), task, Palladino, Cornoldi, De Beni, & Pazzaglia, 2001; Palladino & Jarrold, 2008). A lexical decision (LD) task was also presented, in order to obtain a control condition with low WM demand. The prospective task consisted of a delayed-recognition task, in which a varying number of words (presented before each block) had to be detected while appearing during the ongoing task.

According to the multiprocess view (McDaniel & Einstein, 2000) we should expect only a partial involvement of WM in PM function. Therefore under certain circumstances, such as a low demand ongoing condition, WM should not interfere with PM task performance. Conversely, according to PAM theory (Smith & Bayen, 2005), we should expect a constant reciprocal influence of ongoing activity on the PM task under all the conditions.

The first experiment was designed to compare the effects of two conditions on a WM task (i.e. with and without a PM task), to gain a measure of baseline performance in the WM-ongoing tasks. The second experiment concentrated more directly on the relationship between WM and PM loads, varying both tasks with high and low demand conditions. With respect to the first experiment, the modulation of both PM and WM was specifically examined in order to investigate the hypothesized reciprocal contribution of WM and PM tasks. In the third experiment, TMS stimulation was applied on the DLPFC. Given that DLPFC is known to be responsible for WM, stimulation of that area is expected to produce interference only on the levels of the WM-ongoing task. However, if an effect is found on the PM task, irrespective of the WM load, then it should be ascribed to participation of that region to the PM process.

## 2. Experiment I

### 2.1. Participants

Twenty-seven healthy volunteers, aged 21–35 years, native Italian speakers, were tested (21 females and 6 males, all right-handed). All participants had normal or corrected-to-normal visual acuity, were free of any neurological condition, and gave their informed written consent before participating. Participants were students at the local university, and received credits in return for their participation in the study.

### 2.2. Stimuli and procedure

Participants were presented with two kinds of tasks: a lexical decision task and an updating working memory task (see Fig. 1). In the lexical decision (LD) task, they were presented with a series

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