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Modulation of a fronto-parietal network in event-based prospective memory: An rTMS study

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A B S T R A C T

Event-based prospective memory (PM) is a multi-component process that requires remembering the delayed execution of an intended action in response to a pre-specified PM cue, while being actively engaged in an ongoing task. Some neuroimaging studies have suggested that both prefrontal and parietal areas are involved in the maintenance and realization of delayed intentions. In the present study, transcranial magnetic stimulation (TMS) was used to investigate the causal involvement of frontal and parietal areas in different stages of the PM process (in particular, target checking and intention retrieval), and to determine the specific contribution of these regions to PM performance.

Our results demonstrate that repetitive TMS (rTMS) interferes with prospective memory performance when applied at 150–350 ms to the right dorsolateral prefrontal cortex (DLPFC), and at 400–600 ms when applied to the left posterior parietal cortex (PPC).

The present study provides clear evidence that the right DLPFC plays a crucial role in early components of the PM process (target checking), while the left PPC seems to be mainly involved in later processes, such as the retrieval of the intended action.

1. Introduction

Over the last few decades, great progress has been made in our knowledge of the neural substrates involved in prospective memory (PM), which is the ability to remember to execute an intended action at a pre-determined time in the future (Brandimonte, Einstein, & McDaniel, 1996; Kliegel, McDaniel, & Einstein, 2008), while engaged in a different ongoing activity. PM is widely considered as a multi-component process (McDaniel & Einstein, 2000), which includes the formation, maintaining, updating, and retrieval of an intention. One critical component of PM is the strategic monitoring for the prospective cue (McDaniel & Einstein, 2000; see also Smith & Bayen, 2004), nevertheless the specific processes that monitoring comprises are still unclear. Guynn (2003, 2008) claimed that essentially there are two independent resource-demanding processes in strategic monitoring: a retrieval mode and a target checking mechanism. The retrieval mode is a continuous monitoring process that consists of maintaining the representation of prospective task active in memory; whereas target checking was hypothesized to be a more transient process that involves checking for the presence/absence of PM cues in the environment. According to this model, in event-based PM tasks such as, for example, remembering to fill the car with fuel, it is fundamental to keep the intention active in memory, as well as to check the presence of a PM cue (e.g., a gas station along the street). In addition to monitoring for the presence of a PM cue, the correct execution of a PM task also requires correctly retrieval of the intention to execute the PM action (i.e., to stop at the gas station) when the PM cue is detected. In the present study we intended to focus on the neural basis of these two PM components, namely: target checking and intention retrieval.

At present, neuroimaging and electrophysiological techniques have only rarely focused on these aspects. Among others, work by Reynolds, West, and Braver (2009) and by Kalpouzos, Eriksson, Sjolie, Molin, and Nyberg (2010) seem particularly relevant for identifying the neural correlates of strategic monitoring as well as intention retrieval. Reynolds et al. (2009) identified two distinct neural circuits supporting PM processes. The first is a sustained network, including the bilateral regions of anterior prefrontal cortex (aPFC), which seems to be involved in maintaining an intention

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active in memory (i.e., retrieval mode; for a review, see: Burgess, Gonen-Yaacovi, & Volle, 2011). The second one is a transient component activated when a PM cue is encountered, which includes a region along the middle temporal cortex, and has also been associated with processes related to the detection of a PM cue. However, this study did not identify any cortical network related to target checking. Cue detection and target checking are two qualitatively different processes, since cue detection initiates when a PM cue appears and is recognised, while target checking occurs with every new event, in order to evaluate whether it represents a PM cue or not. In respect of the neural correlates of intention retrieval, Kalpouzos et al. (2010) proposed a neurocognitive model of PM (i.e., PROspective MEmory Dynamic, PROMEDY), in which the parietal regions play a crucial role in mnemonic components of PM. Specifically, they state that the left angular gyrus "would mainly be involved during intention maintenance after target detection, allowing maintenance of episodic information in relation to the target until the action can be performed" (p. 7). Therefore, this area appears to be activated, consequently to target detection when the intention must be retrieved for executing the planned action.

In addition to neuroimaging data, the contribution of electrophysiological research may consist of elucidating the time course of the neural correlates of PM components in an event-based PM task (Leynes, Marsh, Hicks, Allen, & Mayhorn, 2003; West, 2007; West & Ross-Munroe, 2002; West, Wymbs, Jakubek, & Herndon, 2003). At the moment, two major event-related potentials (ERPs) components have been identified: (1) a parieto-occipital N300 associated with a frontal positivity, mainly related to cue detection process; and (2) a late parietal positivity, that appears to reflect later processes of intention retrieval and task-set remapping. The N300, typically observed between 150 and 400 ms after stimulus onset over occipito-parietal regions (Bisiacchi, Schiff, Ciccola, & Kliegel, 2009; Dockree, Kelly, Robertson, Reilly, & Foxe, 2005; West & Krompinger, 2005), is associated with a frontal positivity, which is greater along the midline in this time window. The N300/frontal positivity complex is greater for PM hits (i.e., for PM cues followed by a prospective response) than for PM misses (i.e., PM cues without any prospective response) and ongoing trials (West, 2007; West & Ross-Munroe, 2002). West and collaborators pointed out that this component may be an index of PM cue detection (West & Krompinger, 2005). In particular, the N300/frontal positivity complex seems to reflect the allocation of resources needed for strategic monitoring, since it decreases in amplitude as working memory demands of the ongoing activity increase (West, Bowry, & Krompinger, 2006). In this first component, the coupling between medial–frontal and posterior associative perceptual areas suggests the presence of top-down PM directed control over environmental information.

The second component, namely parietal positivity, is typically observed in the time window between 400 and 1000 ms after stimulus onset, and is broadly distributed over the parietal regions of the scalp. The parietal positivity, greater in PM trials compared to ongoing trials, has been associated with the retrieval of an intended action from long-term memory (retrospective component of prospective memory), as well as with task set coordination and post-retrieval monitoring processes (West & Krompinger, 2005). Indeed, parietal positivity may be associated to other ERP components such as the parietal old-new effect and the prospective positivity effect (e.g., West & Krompinger, 2005; West, 2007; West, 2011, for a review). The parietal old-new effect is a positive component appearing between 400 and 800 ms after stimulus onset, and is greater in amplitude over the left than the right regions (Paller & Kutas, 1992; Rugg & Nagy, 1989). It distinguishes old items from new items and it is associated with general memory processes (Rugg et al., 1998). On the other hand, the prospective positivity represents a sustained positivity over parietal regions between 500 and 1200 ms after stimulus onset, and reflects switching between PM and ongoing activity (Bisiacchi et al., 2009; West, 2007; West & Krompinger, 2005; West et al., 2007). More specifically, in a recent electrophysiological study, Bisiacchi et al. (2009) recorded ERPs comparing two different PM task settings: dual-task vs. task-switch. In this study, the authors observed a greater parietal positivity during the task-switch compared with the dual-task setting, particularly in the left hemisphere, confirming that the parietal positivity is likely to be related to those processes involved in task-set remapping and coordination. In summary, during event-based PM, electrophysiological studies suggest a specific time-course for frontal and parietal areas involvement in processes such as target checking (i.e., the occipito-parietal N300/frontal positivity), intention retrieval and task set remapping (i.e., the parietal positivity).

One limitation of both electrophysiological and neuroimaging studies is their reliance on the use of a correlational approach. This approach assumes that that these measures of brain functioning reflect cognitive processing related to the observed behaviour. Indeed, the observed activations are not sufficient to assert a causal relationship. In contrast, Transcranial Magnetic Stimulation (TMS) allows direct determination of whether a specific stimulated area is causally involved in a certain task (de Graaf & Sack, 2011; Miniussi, Ruzzoli, & Walsh, 2010; Sandrini, Umilta, & Rusconi, 2011). Therefore, the present work focused on the role of the fronto-parietal network in transient components of PM, as related to target checking and intention retrieval by using repetitive TMS (rTMS). This technique is adopted to determine whether neural activity in areas of the fronto-parietal network is causally related to PM processes. Specifically, we focused on the role of the dorsolateral prefrontal cortex (DLPFC) and posterior parietal cortex (PPC), because there is evidence for the involvement of these regions of the brain: the former is expected to respond with monitoring the presence/absence of relevant PM events in the environment, while the latter with retrieving the intended action from memory at the proper moment.

To date, only one study has investigated PM using TMS stimulation; Basso, Ferrari, and Palladino (2010) showed that single-pulse stimulation was associated with significantly worse PM performance when applied to either the left or right DLPFC, particularly under conditions requiring high working memory (WM) demands. The involvement of the DLPFC in PM is a consistent result through many electrophysiological and neuroimaging studies (see for example, Reynolds et al., 2009; West & Krompinger, 2005; West et al., 2006). However, most of the tasks used in these studies require significant WM resources, and this fact may be a source of confound, because it is difficult to disentangle effects due to WM and PM demands. We decided to employ the same behavioural paradigm adopted by Bisiacchi et al. (2009) in a recent study of electrophysiological correlates of PM, since it successfully demonstrated the minimalization of unwanted WM effects, and allows direct comparison between electrophysiological data and TMS results. Moreover, this paradigm allows distinguishing between target checking and cue detection, since the former process is performed for each item, while the latter is performed only when a target is included in the item.

Repetitive TMS (rTMS) was applied to the DLPFC and PPC using one of two stimulation intervals: (1) early stimulation (between 150 and 350 ms after stimulus onset); and (2) late stimulation (between 400 and 600 ms). Detrimental effects on PM performance during early stimulation of frontal sites (150–350 ms) may be related to target checking and cue detection, while an effect on PM during late stimulation of parietal sites (400–600 ms) may be ascribed to later processes such as intentions retrieval.

In addition, because the PM cue is embedded in the ongoing trials, we expect that frontal and parietal stimulation will also affect performance of the ongoing task, depending on the characteristics of the ongoing trial itself. In particular, TMS should affect PM