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Prospective memory in multiple sclerosis: The impact of cue distinctiveness and executive functioning

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ABSTRACT

Objective: Prospective memory (PM), the ability to remember to do something at the appropriate time in the future, is crucial in everyday life. One way to improve PM performance is to increase the salience of a cue announcing that it is time to act. Multiple sclerosis (MS) patients often report PM failures and there is growing evidence of PM deficits among this population. However, such deficits are poorly characterized and their relation to cognitive status remains unclear. To better understand PM deficits in MS patients, this study investigated the impact of cue salience on PM, and its relation to retrospective memory (RM) and executive deficits.
Methods: Thirty-nine (39) MS patients were compared to 18 healthy controls on a PM task modulating cue salience during an ongoing general knowledge test.
Results: MS patients performed worse than controls on the PM task, regardless of cue salience. MS patients' executive functions contributed significantly to the variance in PM performance, whereas age, education and RM did not. Interestingly, low- and high-executive patients' performance differed when the cue was not salient, but not when it was, suggesting that low-executive MS patients benefited more from cue salience.
Conclusions: These findings add to the growing evidence of PM deficits in MS and highlight the contribution of executive functions to certain aspects of PM. In low-executive MS patients, high cue salience improves PM performance by reducing the detection threshold and need for environmental monitoring.

1. Introduction

Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system (Noseworthy, Lucchinetti, Rodriguez, & Weinshenker, 2000). Its impact on cognitive functioning is well known; the prevalence of cognitive impairments ranges from 43% to 70%, in both early and late stages of the disease (Amato, Ponziani, Siracusa, & Sorbi, 2001; Chiaravalloti & DeLuca, 2008; Rao, Leo, Bernardin, & Unverzagt, 1991). Although there is great variability among patients, the most common cognitive deficits affect information processing speed, followed by episodic memory, and executive functioning (Chiaravalloti, Genova, & DeLuca, 2015; Davis, Williams, Gupta, Finch, & Randolph, 2015; Ferreira, 2010).

Cognitive deficits, especially those affecting memory and executive functions, negatively impact MS patients' daily functioning and quality of life (Benedict et al., 2005; Clavelou, Auclair, Taithe, & Gerbaud, 2009; Mitchell, Benito-Leon, Gonzalez, & Rivera-Navarro, 2005). Prospective memory – the ability to remember to carry out an intended action at the appropriate time in the future (McDaniel & Einstein, 2007) – is crucial for independent living (Twamley et al., 2008; Woods et al., 2008). MS patients frequently complain of forgetfulness related to prospective memory (PM; such as forget to take their medication or to show up to an appointment), rather than retrospective memory (RM: e.g., remembering things in the past; Sullivan, Edgley, & Dehoux, 1990). Indeed, using the Prospective and Retrospective Memory Questionnaire (PRMQ), Demers et al. (2011) showed that only domains assessing PM efficiency were significantly affected among MS patients, compared to controls. However, the investigation of PM functioning in MS has been neglected.

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Successful completion of a PM task involves remembering to perform an intended action when the right circumstances are encountered (prospective component: PC) and retrieving the appropriate action (retrospective component: RC, McDaniel & Einstein, 2007; Simons, Scholvinck, Gilbert, Frith, & Burgess, 2006). Several studies have shown that PM requires both RM – to remember the appropriate intended action – and executive functions, to implement strategies and monitor the environment in order to identify the appropriate context (cue, Einstein & McDaniel, 1990; Einstein, McDaniel, Richardson, Guynn, & Cunfer, 1995). Hence, a recent meta-analysis on the neural substrate of PM showed recruitment of regions involved in RM (temporal cortex, insula, anterior and posterior cingulate cortex), probably for the encoding and retrieving of the intention, and in executive functioning (anterior prefrontal cortex, frontoparietal networks), mainly for cue detection and intention retrieval (Cona, Scarpazza, Sartori, Moscovitch, & Bisiacchi, 2015).

Although few studies have examined the integrity of PM in MS using objective measures, there is growing evidence of PM deficits in this population (Bravin, Kinsella, Ong, & Vowels, 2000; Kardiasmenos, Clawson, Wilken, & Wallin, 2008; Miller, Basso, Candilis, Combs, & Woods, 2014; Rendell, Jensen, & Henry, 2007; Rendell et al., 2012; Thelen, Lynch, Bruce, Hancock, & Bruce, 2014; West, McNerney, & Krauss, 2007). In a series of studies using Virtual Week, a board game including various PM activities similar to those encountered in daily life, Rendell and his colleagues reported poorer performance among MS patients, compared to controls, affecting either the PC (Rendell et al., 2007) or both components of PM (PC and RC; Kardiasmenos et al., 2008). More recently, Miller et al. (2014) found that MS patients also performed worse on another PM task, the Memory for Intentions Screening Test, and their performance was inversely related to pain severity (as it increased, PM performance decreased). Furthermore, PM deficits seem to be independent of RM functioning, since MS patients with intact RM can still show impaired PM, as reported by Rendell et al. (2007) and West et al. (2007). However, little is known about the impact of executive deficits on PM functioning in MS.

Moreover, the degree to which executive functions and even RM are recruited in PM varies greatly according to the conditions in which cue detection and intention retrieval take place. Based on the multiprocess framework (McDaniel & Einstein, 2000), detection and retrieval may range from a relatively automatic process, through the involuntary capturing of attention, to strategic environmental monitoring, assured by an executive attentional system. Less executive and RM involvement is required during spontaneous detection and/or retrieval of the intention (McDaniel & Einstein, 2000). The characteristics of the event-based PM target (cue) influence the effectiveness of such processes. One such feature is the distinctiveness (or salience) of the cue relative to its context (e.g., capitalizing the target word). It is proposed that attention is involuntarily captured (and shifted from the ongoing task) by a perceptually salient cue, thereby allowing its automatic detection. The retrieval of the PM intention can also be spontaneous, if cue detection brings the intended action to mind relatively automatically.

Past studies have shown that a more salient target enhances PM performance among young (Brandimonte & Passolunghi, 1994; McDaniel & Einstein, 1993) and older adults, whose PM performance is nearly perfect under such conditions, whereas more PM failures occur when the target is non-salient (Einstein, McDaniel, Manzi, Cochran, & Baker, 2000). In order to examine cue salience on PM performance, McDaniel, Glisky, Rubin, Guynn, and Routhieaux (1999) developed a PM task, in which the participant while answering to a series of trivia questions, has to identify questions that contain a cue (PM word), that is either highlighted using bold-faced type (salient) or appears in normal font (non salient). Using this task, they showed that high-salience cues improved seniors' PM performance. Interestingly, they found that frontal functions, measured by cognitive executive tests, also had more impact on PM performance than hippocampal functioning (RM tests). Low-frontal participants performed worse than all other participants on the PM task, which supports the involvement of executive functions in PM. However, no significant interaction between frontal functioning and cue salience was found, although low-executive elders' PM performance improved when the cue was salient.

Nonetheless, to our knowledge, the impact of cue distinctiveness on MS patients' PM performance has not been investigated, especially with regard to cognitive functioning (RM and executive functions), although it would enable a better understanding of their PM deficits. Therefore, based on the results obtained with an elderly population, we adapted McDaniel et al.'s (1999) PM task to assess the impact of cue distinctiveness on PM functioning in MS patients. More specifically, the goal of this study was to investigate whether cue distinctiveness would improve patients' PM performance, through more automatic target (cue) detection. We also wanted to better understand the impact of cue salience on PM, given the executive and RM deficits in MS, using a comprehensive neuropsychological assessment.

We expected that MS patients would perform worse than controls on our PM task, irrespective of the cue's distinctiveness. We also predicted that all participants' PM performance would improve when the cue was highly salient (target word capitalized), due to more automatic target detection (PC). However, we expected that MS patients would not benefit in the same way from cue distinctiveness, depending on their cognitive functioning. More specifically, considering that cue salience seems to reduce the frontal lobes' involvement by decreasing the need for effortful strategic monitoring of the environment, we predicted that dysexecutive MS patients would perform better when the cue was salient, since it would compensate for their deficits. Furthermore, MS patients with RM deficits would benefit less from cue salience, since it has little impact on action retrieval (RC), especially if encountering the prospective target brings the intended action to mind relatively automatically.

2. Method

2.1. Participants

Thirty-nine MS patients were recruited from the multiple sclerosis clinics at Hôpital Notre-Dame (CHUM) and Hôpital du Sacré-Coeur de Montréal (HSCM). They all satisfied the 2005 Revision of the McDonald Diagnostic Criteria (Polman et al., 2005) and were diagnosed with relapsing-remitting (n = 27, time since first symptoms (*M*) = 12.33, *SD* = 9.97 years), secondary progressive (n = 5, *M* = 16.20, *SD* = 11.41 years), or primary progressive MS (n = 5, *M* = 10, *SD* = 5.48 years), or clinically isolated syndrome (n = 2, *M* = 3, *SD* = 1.41 years). Among the patients, 69% were on disease-modifying therapy, for an average of 4.14 (*SD* = 4.54) years. Other medications such as stimulants (Modafinil, Methylphenidate, Amantadine), acetylcholinesterase inhibitors, antidepressants with stimulant effects and benzodiazepines (regular use) were accepted for this group, as long as the prescribed dose had been stable for at least one month prior to the study. Patients were excluded for (a) sensory or motor deficits that might interfere with cognitive testing; (b) a history of drug abuse or a nervous system disorder other than MS; (c) a Beck Depression Inventory – Fast Screen (BDI-FS) score greater than 7, indicating possible depression (Beck, Steer, & Brown, 2000);[1] (d) a score on the Expanded Disability Status Scale

[1] Four out of 39 patients had a BDI-FS score above 7. Following a clinical diagnostic assessment, they were found not to be depressed and were included in the study.