Journal of the International Neuropsychological Society (2013), **19**, 1109–1118.
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doi:10.1017/S1355617713001045

Prospective Memory in Parkinson's Disease: A Meta-analysis

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(RECEIVED April 2, 2013; FINAL REVISION August 20, 2013; ACCEPTED August 20, 2013; FIRST PUBLISHED ONLINE September 18, 2013)

Abstract

Prospective memory (PM) refers to the ability to remember to carry out an intended action in the future and it is pervasive in our daily living. A failure to execute an intended action (e.g., take medication) at the appropriate juncture in future (e.g., after dinner) can negatively affect our daily functioning and at times, may have devastating effects (e.g., forgetting to turn off the gas stove before leaving the house). Patients with Parkinson's disease (PD) exhibit widespread cognitive deficits including deficits in PM. The present study provides a meta-analytic review of PM in PD. Results across nine studies indicated time and event-based PM to be similarly impaired in PD, with time-based PM compromised to a slightly larger extent (Hedges' $g = -0.71$) as compared to event-based PM (Hedges' $g = -0.55$). The impairment in PM is more likely due to failure in self-initiated retrieval of intention to be executed, rather than forgetting the content of the intention itself. Furthermore, factors such as intervening task complexity and the mediating role of other executive functions have also been proposed to be responsible for impaired PM in PD. (*JINS*, 2013, *19*, 1109–1118)

Keywords: Meta-analysis, Prospective memory, Parkinson's disease, Delayed intention, Prospective remembering, Remembering to remember

INTRODUCTION

Prospective memory (PM) can be defined as remembering to perform an intended action at an appropriate time or at the occurrence of a certain event in the future (Scullin, McDaniel, Shelton, & Lee, 2010). It involves multiple cognitive processes related to retrospective memory or RM (e.g., forming associations between cues and intentions, remembering the content of the intention: Kliegel, Phillips, Lemke, & Kopp, 2005) and executive functions (e.g., dividing attention, monitoring the environment for the cue, interruption of the ongoing task, and retrieval and execution of the intention: McFarland & Glisky, 2009).

PM is commonly divided into time-based (TBPM) and event-based (EBPM) types (McDaniel & Einstein, 2000). While TBPM involves remembering to perform an intended action at a specified time (e.g., remembering to phone a friend in half an hour), EBPM involves remembering to perform the action at the occurrence of a certain external event (e.g., remembering to buy bread when passing by a grocery store). Unlike EBPM where the cue to execute the intention is explicit, TBPM requires more cognitive effort as it places considerable demands on self-initiated monitoring and retrieval mechanisms and is therefore, assumed to be susceptible to poor performance due to lack of explicit external cues (Smith, Souchay, & Moulin, 2011).

The neurobiological underpinnings of PM have been a recurrent topic of investigation in cognitive neuroscience. Neuroimaging studies assessing maintenance of intentions over a delay during engagement in the ongoing task have revealed activations in the rostral prefrontal cortex (PFC) and lateral PFC areas for both EBPM and TBPM (Burgess, Gonen-Yaacovi, & Volle, 2011; Burgess, Scott, & Frith, 2003; Okuda et al., 2007). Successful PM intention retrieval and execution therefore, seem to hinge on the coherence of the frontal systems.

As most of our daily activities revolve around carrying out actions at the right moment, dramatic implications of PM failure under certain conditions (e.g., failure in remembering to take medication) have instigated exponential research toward PM functioning, especially in a variety of neuropsychological populations. Data comparing clinical populations to healthy controls have therefore, surmised PM performance to be impaired in older adults (Einstein, McDaniel, Manzi, Cochran, & Baker, 2000; Henry, MacLeod, Phillips, & Crawford, 2004),

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https://doi.org/10.1017/S1355617713001045 Published online by Cambridge University Press

patients with Mild Cognitive Impairment and dementia (van den Berg, Kant, & Postma, 2012), Schizophrenia (Kumar, Nizamie, & Jahan, 2005, 2008; Wang et al., 2009) and closed head injury (Schmitter-Edgecombe & Wright, 2004; Shum, Levin, & Chan, 2011), with TBPM almost always compromised to a greater extent than EBPM.

Etiology of Parkinson's Disease and Subsequent Neuropsychological Findings

The neuropathological markers of Parkinson's disease (PD) include degeneration of dopaminergic cells in the basal ganglia (Yarnall, Archibald, & Burn, 2012) with utmost severity noted in the striatum (Owen, 2004). Notably in PD, neuronal loss of dopaminergic neurons in the substantia nigra and surrounding areas reduce dopaminergic connections to the adjacent striatum, in turn impoverishing efferent connections to the frontal lobes (Owen, 2004). This dopamine depletion in the fronto-striatal circuitry causes bradykinesia, tremors, rigidity, and postural instability, all of which are the cardinal motor-related clinical features of PD (Yarnall et al., 2012) as well as patterns of cognitive impairment resembling those of patients with frontal lobe damage (Cools, 2006; Foster, McDaniel, Repovš, & Hershey, 2009). Given damaged fronto-striatal routes, studies assessing cognitive functions in PD patients consistently report deficits in planning (Kliegel et al., 2005; Lewis et al., 2003; Owen, Doyon, Dagher, Sadikot, & Evans, 1998), set shifting and inhibition (Dujardin, Defebvre, Grunberg, Becquet, & Destée, 2001; Muslimovic, Post, Speelman, & Schmand, 2005; Werheid, Koch, Reichert, & Brass, 2007), working memory and attention (Lewis et al., 2003, Muslimovic et al., 2005), and PM (Katai, Maruyama, Hashimoto, & Ikeda, 2003; Kliegel, Altgassen, Hering, & Rose, 2011), including other cognitive deficits such as bradyphrenia, perseveration, and visuo-spatial deficits (Bradley, Welch, & Dick, 1989; Sinforiani, Banchieri, Zucchella, Pacchetti, & Sandrini, 2004).

With regard to RM, studies have noted PD patients to show impairments in this domain as well (Lezak, 1995; Higginson et al., 2003). Evidence indicates that PD patients seem to perform better on recognition (Flowers, Pearce, & Pearce, 1984; however, see Whittington, Podd, & Kan, 2000; Whittington, Podd, & Stewart-Williams, 2006; Davidson, Anaki, Saint-Cyr, Chow, & Moscovitch, 2006) and cued recall tasks (Higginson et al., 2003; Marinus et al., 2003) than free recall tasks (Altgassen, Zollig, Kopp, MacKinlay, & Kliegel, 2007; Drag, Bieliauskas, Kaszniak, Bohnen, & Glisky, 2009; Dujardin et al., 2001; Green et al., 2002; Higginson et al., 2003; Lezak, 1995; Muslimovic et al., 2005). These results suggest that PD patients may find less difficulty in retaining information in memory (as they are able to recognize learnt items using cues: Higginson et al., 2003), than in retrieving information as seen in free recall performance (suggesting an executive deficit; see Bondi, Kaszniak, Bayles, & Vance, 1993). Altogether, these RM deficits have been suggested to be 'secondary' to conspicuous executive impairment seen in patients with PD (Davidson et al., 2006).

Prospective Memory in Parkinson's Disease

As noted above, studies assessing PM in PD generally agree that PD patients find difficulty in retrieving the intention *per se* (Kliegel et al., 2005) despite accurately remembering contents of both simple and complex intentions (Altgassen et al., 2007). For example, Kliegel et al. (2005) found PD patients to be selectively impaired in forming detailed intentions and initiating them, though able to retain them in memory. Since both intention formation and initiation stages are representative of executive functions like planning and inhibition, failure in these steps suggests poor executive functioning in these patients (Kliegel et al., 2011). It is not surprising that detrimental PM performance has also been ascribed to disrupted executive functions such as working memory (Altgassen et al., 2007; Kliegel et al., 2011; Raskin et al., 2011), planning (Kliegel et al., 2005), and self-initiated retrieval (Katai et al., 2003), all of which are primarily mediated by the frontal lobe.

To better understand PM functioning in PD patients, we attempted to conduct a meta-analysis of studies assessing PM in PD. Furthermore, given the diversity in tasks used to assess various executive functions and RM in these studies, we did not attempt a meta-analysis of results for these cognitive functions. We, however, extracted findings on RM and executive functions from individual studies and discussed them in relation to PM in PD.

METHOD

Literature Search

A computer-based search between 1990 and 2013, involving PubMed, Science Direct, EBSCOhost, Web of Science, and Google Scholar for keywords: "prospective memory" or "remembering to remember" or "delayed intention" or "prospective remembering," in combination with "Parkinson's disease," in complete or shortened versions (with and without quotation marks) was conducted. Additionally, we scanned journals that publish on cognition in neurodegenerative diseases, using the keywords 'memory' and 'neurodegeneration,' to ensure inclusion of articles that may not have explicitly reported 'prospective memory' in their title or abstract. Reference lists of all retrieved articles were further scanned for potential eligibility. For inclusion in the quantitative analysis, few criteria were exercised: (1) the study had to be a journal article, original in nature, in full text, and not a review; (2) EBPM and/or TBPM had to be assessed using an experimental paradigm or a naturalistic setting optionally in conjunction to, but not solely using questionnaires; (3) If not reported directly, the study had to report enough statistics (mean, standard deviation, standardized difference) to calculate effect sizes. We attempted to contact the authors in case of insufficient statistical data.

Where numerous variables were manipulated, performance on conditions closely resembling methodologies of other studies and/or traditional measures of PM were chosen

https://doi.org/10.1017/S1355617713001045 Published online by Cambridge University Press

to maintain uniformity. Studies that reported only F values had to be excluded from our statistical analysis, since we were unable to generate means and standard deviations to elicit comparison with other studies. This included two studies, namely by Costa, Peppe, Brusa et al. (2008) and Foster, Rose, McDaniel, and Rendell (2013). Similarly, unlike other studies involving response to the PM cue at multiple instances, the PM task by Kliegel et al. (2005) was a single instance intention task (participants either initiated the response or did not) hence we did not include their χ^2 value into our analysis. It should also be noted that Smith et al. (2011) who intended to primarily investigate meta-memory along with PM, reported percentage scores of performance on both PM tasks. However, they also reported an alternative TBPM score consisting of mean number of key presses (response to the PM cue); therefore, we included this particular statistic, and excluded their EBPM measure from our analysis. Altgassen et al. (2007) manipulated task importance between the PM and the ongoing task, therefore we included performance on the PM task where the focus was on the PM cue. Foster et al. (2009) altered focality of cues on the PM and the ongoing task as well as tested patients on and off medication, therefore, as advised by one of the authors (M. McDaniel, personal communication, February 26, 2013), we averaged performance across focal and non-focal conditions for the PM task and chose performance on the "on" medication condition. Where the Memory for Intentions Screening Test (MIST; Raskin, 2009 - which consists of four TBPM and four EBPM tests to be completed in 30 min) was used, only summary scores for TB and EBPM tasks were used.

Results were computed using R Studio v2.13.1 (R Development Core Team, 2011) and its "meta" package (Schwarzer, 2010). For computing effect sizes, Hedges' g was chosen as it corrects Cohen's d for a small sample size (McGrath & Meyer, 2006). Negative effect sizes indicate better performance in controls. Performance on TBPM and EBPM were assessed separately and data were analyzed using a mixed-model analysis of which we chose the outcome of a fixed-effects model (as suggested by Field & Gillett, 2010). Heterogeneity statistics reported are in concordance with recommendations of Higgins, Thompson, Deeks, and Altman (2003).

RESULTS

The literature search yielded 12 studies. Nine satisfied our inclusion criteria for quantitative analysis, of which four exclusively tested EBPM, and five tested both EBPM and TBPM.

Time-Based and Event-Based Prospective Memory Performance

An overall calculation of effect size for PM (TB and EBPM) across all included studies indicated an effect size of -0.61 (-0.76 to -0.46; $Z = -8.07$; $p < .001$). TBPM was assessed in five studies with an overall effect size of -0.71 (-0.96 to -0.46; $Z = -5.56$; $p < .001$) (see Figure 1). EBPM was assessed in eight studies with an overall effect size of -0.55 (-0.73 to -0.36; $Z = -5.86$; $p < .001$) (see Figure 2). The effect sizes on both TB and EBPM tasks indicate medium difference ($d = 0.50$) in performance between groups as per Cohen's nomenclature (Cohen, 1988). Tests of heterogeneity revealed that the Q-statistic was not significant for studies evaluating TBPM [$Q = 5.05$; $p = .28$; $I^2 = 20.8\%$ (0% to 66.4%)] or EBPM in PD [$Q = 7.81$, $p = .34$; $I^2 = 10.4\%$ (0% to 70.9%)], not greater than expected by sampling error (Higgins & Thompson, 2002; Higgins et al., 2003). On comparing effect sizes for EBPM and TBPM, heterogeneity values did not achieve significance [$Q = 13.91$, $p = .30$; $I^2 = 13.7\%$ (0% to 52.9%)] suggesting that there was no difference in the impairment between these

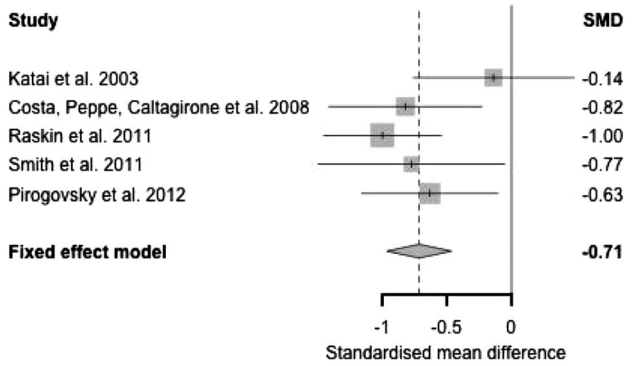


Fig. 1. Comparison of time-based prospective memory (TBPM) performance between patients and controls. SMD indicates Hedges' g effect size metric. Negative effect sizes indicate better performance in controls. The size of the square indicates weight given to each study, and the horizontal lines indicate 95% confidence intervals for the SMD. The diamond indicates the pooled effect size for the above studies.

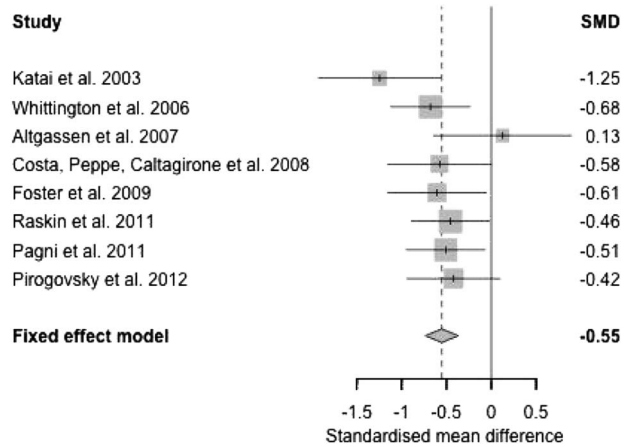


Fig. 2. Comparison of EBPM performance between patients and controls. SMD indicates Hedges' g effect size metric. Negative effect sizes indicate better performance in controls. The size of the square indicates weight given to each study, and the horizontal lines indicate 95% confidence intervals for the SMD. The diamond indicates the pooled effect size for the above studies.

https://doi.org/10.1017/S1355617713001045 Published online by Cambridge University Press

two measures. Publication bias using fail-safe *N* (Rosenthal, 1979) indicated that 10 and 19 unpublished studies for TBPM and EBPM, respectively, were necessary to render statistically non-significant results. We, therefore, acknowledge publication bias, since it is plausible for this small number of unpublished results to exist.

Correlations between PM and Performance on Other Neuropsychological Tests

Findings concerned with RM (both retrospective component of the PM task and traditional measures of RM) from the considered studies were consolidated (Table 2). Four studies (Table 3) provided correlation values for PM performance and various tests of executive functions and memory in PD patients. No meta-analysis was conducted for these scores. The correlation values were small to moderate in size between overall PM (TB and EBPM) and executive functions (range = −0.43 to 0.52; median $r = 0.12$), PM and RM (range = −0.27 to 0.62; median $r = 0.16$), and PM and overall performance on neuropsychological tests (RM and executive functions) (range = −0.43 to 0.62, median $r = 0.14$). Approximately 47% and 15% of the correlations between PM and executive functions, and PM and RM respectively were significant.

DISCUSSION

The present study involved a meta-analytic review of PM in patients with PD to understand the magnitude of impairment in these patients. A quick glance at the results reveals PM to be impaired (to a medium effect) in patients as compared to controls. As per heterogeneity statistics and Cohen's *d* cutoffs, the current results failed to document a significant difference between TBPM and EBPM, suggesting both measures to be impaired to a similar extent. The current results are in concordance with a few findings in the past that have failed to find a significant discrepancy between performance on TBPM and EBPM tasks in clinical populations (Costa, Peppe, Caltagirone, & Carlesimo, 2008; van den Berg et al., 2012). Nevertheless, the current findings should be approached with caution. As noted elsewhere, evidence, even across clinical populations, has suggested TBPM to be more cognitively demanding than EBPM (Smith et al., 2011) and this can be noted in studies investigating PM in PD (Table 1). In the present meta-analysis, a closer look at the results indicates TBPM to be compromised to a marginally greater extent than EBPM. However, similarity in the effect size bracket for both measures may be due to the following reasons. First, the number of studies evaluating both measures is unequal, additionally supported by publication bias documented. Therefore, there is possibility for TBPM to be "under-represented" in the current study. Second, there are differences in the sample size of studies that may have contributed to differential results. For instance, we see that of the five studies that found impaired TBPM in PD patients, the study with the largest sample size (33% of the total sample for studies included for the meta-analysis, which report TBPM in PD) (Raskin et al., 2011) demonstrated the largest effect (Table 1). Surprisingly, this was not noted in EBPM; the two largest effects were noted in studies with a combined sample size of only 21% of the total sample for studies measuring EBPM in PD. Moreover, the smallest effect sizes (<0.30) in TBPM and EBPM were noted in studies by Katai et al. (2003) and Altgassen et al. (2007), respectively, that typically recruited lesser than 40 participants. Therefore, such differences in sample sizes could also have contributed to comparable effect sizes for EBPM and TBPM in PD. It is worth mentioning that the effect size in the EBPM measure of Katai et al. (2003) was the largest of its kind, possibly due to the relative ease of their TBPM over their EBPM measure. Similar variables that may have additionally contributed to distinct results are discussed below.

It is suggested that different task paradigms will elicit results exhibiting differential impairment (Kliegel et al., 2011). Unfortunately, while attempting to attain better experimental control, most laboratory-based experiments may accidentally weaken participants' ability to perform normally on PM tasks. For instance, as Kliegel et al. (2011) note, in day-to-day life instead of remembering to take medication at a particular time, one may link the activity to an event such as post-dinner. In such natural settings, people use cues from the environment to remember for the future (see Kvavilashvili & Fisher, 2007). Similarly, variation in PM task demand may also lead to variable performance. For example, Katai et al. (2003) found EBPM to be impaired to a greater extent in patients, when their TBPM task and RM task were seemingly easy and could have resulted in ceiling effects. As Kliegel et al. (2011) note, the cues used by Katai et al. (2003) were embedded in their EBPM task, whereas the cues used to initiate the EBPM action by Costa, Peppe, Caltagirone, et al. (2008) were conspicuous (a timer ring), possibly prompting different retrieval strategies. It is thus necessary to consider such differences in methodologies.

Similarly, it is essential to investigate variables like motivation and task importance that regularly assist people in efficiently meeting prospective memory demands in naturalistic environments. Early support comes from findings by Kvavilashvili (1987, 1998), who found tasks receiving more attention to benefit from enhanced performance. In the current context, Altgassen et al. (2007) deliberated on task importance and found patients to perform on par with controls, when instructed to weigh importance to successful planning and execution of the PM task over the ongoing task. This suggests that simply downgrading the importance of the ongoing task (McDaniel & Einstein, 2000) or enhancing cue-monitoring strategies (Raskin et al., 2011) may enhance performance on PM tasks in PD patients. In combination with reminders (Cook, Marsh, & Hicks, 2005) and similar methods (Fish, Wilson, & Manly, 2010), adequate training to use such strategies may benefit patients with PD in improving execution of delayed intentions (McDaniel & Einstein, 2000; Kliegel et al., 2011).

https://doi.org/10.1017/S1355617713001045 Published online by Cambridge University Press

https://doi.org/10.1017/S1355617713001045 Published online by Cambridge University Press

Table 1. Summary of studies included in the meta-analysis

Study (year)	*n*		Mean age (SD)		Education (years)		PD disease duration	Ongoing task	PM[c] type	PM task description	*g*[f]
	PD[a]	HC[b]	PD	HC	PD	HC					
Katai et al. (2003)	20	20	64.6(5.2)	63.1(5.6)	10.0(2.1)	11.2(2.0)	5.5(3.0)	Number and word selection task		Respond	
									EBPM[d]	- to two target words	−1.25
									TBPM[e]	- at a certain time	−0.14
†Kliegel et al. (2005)	16	16	61.1(6.9)	62.6(9.1)	11.0(2.4)	11.4(1.7)	4.8(3.0)	Executive and memory tasks	EBPM	Fill in date of birth on completion of ongoing task	0.63§
Whittington et al. (2006)	41	41	69.5(6.0)	69.8(5.3)	—	—	8.6(6.3)	Memory tasks	EBPM	Collect belonging and ask question at end of session	−0.68
Altgassen et al. (2007)	13	13	60.2(7.4)	62.0(8.6)	10.8(2.5)	11.5(1.7)	4.8(3.0)	Two-back working memory task	EBPM	Respond to target letters	0.13
†Costa, Peppe, Brusa et al. (2008)	20	15	60.3(9.5)	61.1(7.0)	10.0(3.2)	9.7(3.6)	6.1(6.1)	Action triplets	TBPM	Carry out actions within specified time limit	0.39
Costa, Peppe, Caltagirone et al. 2008	23	25	63.5(10.0)	65.0(7.7)	9.9(4.3)	10.7(4.3)	7.6(8.5)	Action triplets	EBPM	Carry out actions when timer rings	−0.58
									TBPM	Carry out actions within specified time limit	−0.82
Foster et al. (2009)	24	30	59.0(7.8)	60.0(7.8)	14.9(2.3)	15.3(3.2)	4.5(2.6)	Word categorization	EBPM	Respond to target words+PRMQ[g]	−0.61
Raskin et al. (2011)	54	34	61.9(7.6)	61.0(2.6)	14.7(2.1)	14.5(2.1)	—	Word search puzzles	EBPM	MIST[h] battery	−0.46
									TBPM		−1.00
Smith et al. (2011)	16	16	72.5(5.8)	74.1(3.7)	—	—	8.0(4.8)	String of words presented		Respond	
									EBPM†	- to target words	—
									TBPM	- at a certain time + PRMQ	−0.77
Pagni et al. (2011)	41	40	67.2(5.6)	67.5(4.6)	9.3(4.2)	10.6(4.5)	1.2(0.9)	Word categorization	EBPM	Respond to target words	−0.51
Pirogovsky et al. (2012)	33	26	71.2(1.4)	69.8(1.3)	16.6(0.4)	16.4(0.5)	11.1(1.1)	Word search puzzles	EBPM	MIST battery+PRMQ	−0.42
									TBPM		−0.63
†Foster et al. (2013)	24	28	67.0(5.9)	69.2(5.9)	15.3(2.8)	16.5(2.8)	5.7(4.3)	—	EBPM	Computerized Virtual Week[i]	−0.14◇

Note. † = excluded from quantitative analysis; § = calculated from chi-square value; ◇ = eta-squared value [a] = Parkinson's Disease; [b] = Healthy Controls; [c] = Prospective memory; [d] = Event-based Prospective Memory; [e] = Time-based Prospective Memory; [f] = Hedges' *g* (effect size metric; negative value indicates better performance in controls); [g] = Prospective and Retrospective Memory Questionnaire (Crawford et al. 2003); [h] = Memory for Intentions Screening Test (Raskin, 2009) is a 30 minute 8-trial test in which the participant engages in a word search puzzle as the ongoing task, responds to certain cues and initiates actions at specified time periods; [i] = Desktop computer game involving intermittent response to PM cue amidst ongoing activities (Rendell & Henry, 2009).

Table 2. Summary of findings on retrospective memory in studies assessing prospective memory in Parkinson's disease

	Retrospective component of PM task (recall of task instructions) in PD patients		Performance-based RM measure in PD patients	
Study	TBPM	EBPM	Recall	Recognition
Katai et al. (2003)	n.s.	n.s.	Impaired on total no. of words and immediate recall on RAVLT**	—
Kliegel et al. (2005)	—	n.s.	n.s. on digit span	—
Whittington et al. (2006)	—	—	Impaired on recall task of KOLT**	Poor non-verbal recognition on NRMT† and VRMT†
Costa, Peppe, Brusa et al. (2008)	n.s.	—	—	—
Costa, Peppe, Caltagirone et al. (2008)	Impaired**	Impaired**	—	—
Foster et al. (2009)	—	n.s.	—	—
Raskin et al. (2011)	Poor performance on recognition on MIST	Poor performance on recognition on MIST	n.s. on delayed prose recall‡; impaired** on immediate prose recall ◇ and digit span	n.s. on Logical Memory II‡
Smith et al. (2011)	Impaired*	n.s.	—	—
Pagni et al. (2011)	—	n.s.	Impaired on RAVLT immediate**, delayed recall**, and ROCF copy**	—
Foster et al. (2013)	—	Impaired	—	—

Note. PM = prospective memory; TBPM = Time-based prospective memory; EBPM = Event-based prospective memory; RM = retrospective memory; PD = Parkinson's disease; RAVLT = Rey Auditory Verbal Learning Test; KOLT = Kendrick Object Learning Task; NRMT = Nonverbal Recognition Memory Task; VRMT = Verbal Recognition Memory Task; MIST = Memory for Intentions Screening Test; ROCF = Rey-Osterrieth Complex Figure.
† = n.s in early-PD group, but significant ($p < 0.05$ for NRMT hard level; $p < 0.01$ for VRMT) impairment in advanced-PD group; ‡ = WMS III Logical Memory II; ◇ = WMS III Logical Memory I
*$p < 0.05$; **$p < 0.01$; n.s. = not significant.

Relationship with RM

Deficits in episodic memory in PD patients may go undetected if the sole measure used to test RM is the recall of the RM component of the PM task (i.e., recall of PM cue/task instructions). This excessively simple measure may not impose as much cognitive load as a traditional task of RM, and may easily elicit ceiling effects. For instance, in the current study, we can note seven reports (Table 2) of comparable memory for recall of task instructions for the RM component of the PM task between patients and controls. However, studies focused on investigating the status of RM in PD have repeatedly reported impairments in episodic memory in these patients (Green et al., 2002; Higginson et al., 2003; Marinus et al., 2003; Muslimovic et al., 2005). In line with these reports, the same studies that did not find any impairment in the RM component of the PM task in PD patients, indicate these patients to show deficits in immediate and delayed recall and recognition on traditional measures of RM (Table 2), which interestingly also seem to be associated with their performance on PM tasks (Table 3). However, it is important to note that impaired recall of information in PD patients may be "secondary" to impaired executive functioning (especially working memory: Bondi et al., 1993; Cooper, Sagar, & Sullivan, 1993; Davidson et al., 2006; Higginson et al., 2003) that has been noted in these patients (Green et al., 2002). Moreover, the nature of these executive deficits may involve either poor working memory (Higginson et al., 2003), difficulty in engaging specific semantic strategies to retrieve episodic information (Dujardin et al., 2001), or difficulty in self-initiated retrieval of information, all of which reflect in PM and RM performance, and are compliant with fronto-striatal deficits noted in PD.

PM and Other Executive Functions in PD

Since most lab-based PM engagements involve dual tasking, they impose requirements of competent working memory and cognitive flexibility on participants. Moreover, in TBPM, absence of an explicit association between cue and action requires efficient working memory to continuously switch between the ongoing task and monitoring time to execution of intention. In such cases, increasing the strategic demand and attentional monitoring on the PM task (from focal to nonfocal: as in Katai et al., 2003 and Foster et al., 2009, 2013) would not only require additional working memory resources, but would affect performance in PD patients who have frontal impairments, even with presence of an external cue.

Of the studies considered in the meta-analysis, four reported correlations between PM performance and various tests of executive functioning (Table 3). In line with previous findings (Davidson et al., 2006; Higginson et al., 2003), PM performance correlated significantly with set shifting, verbal fluency, inhibition, and planning tasks. More importantly, results across five studies (Altgassen et al., 2007, Costa, Peppe, Brusa, et al., 2008; Costa, Peppe, Caltagirone, et al., 2008;

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Table 3. Summary of correlations between PM and other neuropsychological tests as reported in considered studies

		Correlation with PM score in PD patients	
Test	Study	TBPM	EBPM
Executive functions			
MCST categories achieved	Costa, Peppe, Caltagirone et al. (2008)	0.44*	0.11
MCST perseverative errors	Costa, Peppe, Caltagirone et al. (2008)	−0.43*	−0.09
MCST non-perseverative errors	Costa, Peppe, Caltagirone et al. (2008)	−0.31	0.01
Phonological verbal fluency	Costa, Peppe, Caltagirone et al. (2008)	0.08	0.13
Verbal fluency	Raskin et al. (2011)†	0.38**	0.35**
Stroop Neuropsychological Test	Raskin et al. (2011)†	0.52**	0.50**
Trail Making test	Raskin et al. (2011)†	−0.15	−0.13
Trail Making A & B	Pagni et al. (2011)	—	sig but not specified
D-KEFS Tower test	Raskin et al. (2011)†	0.26	0.29*
Memory			
Digit span forward	Costa, Peppe, Caltagirone et al. (2008)	0.62**	0.18
Digit span forward	Pagni et al. (2011)		n.s.
Digit span backward	Costa, Peppe, Caltagirone et al. (2008)	0.45*	−0.11
Digit span backward	Pagni et al. (2011)	—	n.s.
Digit span total	Raskin et al. (2011)†	0.20	0.19
Corsi block tapping test (forward)	Costa, Peppe, Caltagirone et al. (2008)	0.16	−0.03
Corsi block tapping test (backward)	Costa, Peppe, Caltagirone et al. (2008)	0.38	0.42
Prose recall (immediate)	Costa, Peppe, Caltagirone et al. (2008)	0.36	0.11
Prose recall (immediate)◇	Raskin et al. (2011)†	0.21	0.39**
Prose recall (delayed)	Costa, Peppe, Caltagirone et al. (2008)	0.16	0.06
Prose recall (delayed)‡	Raskin et al. (2011)†	0.38**	0.45**
RAVLT immediate	Costa, Peppe, Caltagirone et al. (2008)	−0.21	0.11
RAVLT immediate	Pagni et al. (2011)	—	n.s.
RAVLT delayed	Katai et al. (2003)	0.57*	n.s.
RAVLT delayed	Costa, Peppe, Caltagirone et al. (2008)	−0.27	−0.10
RAVLT delayed	Pagni et al. (2011)	—	n.s.
ROCF copy	Pagni et al. (2011)	—	sig but not specified
ROCF immediate	Costa, Peppe, Caltagirone et al. (2008)	0.07	−0.16
ROCF immediate	Pagni et al. (2011)	—	n.s.
ROCF delayed	Costa, Peppe, Caltagirone et al. (2008)	0.16	−0.10
ROCF delayed	Pagni et al. (2011)	—	n.s.

Note. Correlations reported are unadjusted Spearman's (rank) or Pearson's values extracted from studies.
◇ = Wechsler Memory Scale-III Logical Memory I; ‡ = Wechsler Memory Scale-III Logical Memory II.
† = correlations reported by Raskin et al. (2011) derived from TBPM/EBPM subscales of the MIST; PM = Prospective memory; PD = Parkinson's disease; TBPM = Time-based prospective memory; EBPM = Event-based prospective memory; MCST = Modified Card Sorting Test; D-KEFS = Delis-Kaplan Executive Function System; RAVLT = Rey Auditory Verbal Learning Test; ROCF = Rey-Osterrieth Complex Figure Test.
*$p < 0.05$; **$p < 0.01$; n.s. = not significant.

Foster et al., 2009; Kliegel et al., 2005) indicated impaired working memory in PD patients and found it to explain a significant percentage (47% on nonfocal PM task: Foster et al., 2009; 52%: Kliegel et al., 2005) of the variance of PM. These findings are consistent with evidence for reduced working memory capacity (Bondi et al., 1993; Lewis et al., 2003; Weintraub et al., 2005) as well as impaired cognitive functions involving cognitive flexibility (i.e., planning, inhibiting, manipulating, all of which are also required in working memory: Zgaljardic et al., 2006) in PD patients that mediate PM performance. To add, these deficits in cognitive flexibility may arise from depleted dopamine levels in the PD brain (Cools, 2006) and therefore, would likely hamper performance on tasks that involve time-estimation and flexibility of cognitive representation (Owen, 2004; Cools, 2006), both of which are essential in executing the PM cue. More evidence for deficits in working memory in PD patients come from reduced activity noted in the dorsolateral prefrontal cortex (responsible for planning, set shifting, working memory, and verbal fluency: Weintraub et al., 2005; Zgaljardic et al., 2006) and the anterior cingulate cortex (involved in response inhibition: Zgaljardic et al., 2006), both of which are also required in successful PM execution (Burgess et al., 2011) and are affected in PD (Higginson et al., 2003; Owen, Sahakian, & Robbins, 1998; Owen, 2004).

Everyday Functioning and PM in PD

It is important to realize that in our daily lives, PM challenges would not require us to press a button or tap the table whenever we see a certain word. Everyday demands would for the most part, necessitate using cues in the environment to

https://doi.org/10.1017/S1355617713001045 Published online by Cambridge University Press

bring the intention to mind. For instance, on assessing TBPM by having healthy adults call the experimenter after a 1-week delay, Kvavilashvili and Fisher (2007) found intentions to be "either triggered by incidental cues or periodically pop into one's mind without any apparent reason" (p. 118). Contrary to previous findings, self-initiated retrieval was reported in less than 10% of their sample, suggesting usage of more automatic attentional processes and external cues to operate in execution of TB intentions as well. PM deficits are, therefore, best witnessed and understood in such naturalistic settings in the presence of considerable environmental support, where factors like motivation have been noted to play a role (Kvavilashvili & Fisher, 2007).

Functional decline in daily life due to impaired PM in PD patients has rarely been investigated. Only one of 12 available studies measured performance in PM tasks and its direct association to everyday functioning in PD patients. Pirogovsky, Woods, Filoteo, and Gilbert (2012) administered the MIST (Raskin, 2009) and the PRMQ (Crawford, Smith, Maylor, Della Sala, & Logie, 2003) in addition to self-report measures of medication management efficacy, quality of life, activities of daily living and performance related measures of medication management and finance management. Only time-based MIST scores correlated significantly with medication management (both performance and self-report scores) and finance management. This association is of crucial significance to PM literature in that impaired TBPM has extended effects with regards to overseeing daily medication intake and financial activities. Admittedly, the inability to consistently monitor time to next dosage of medication would result in delayed or missed doses, which would be unfavorable to amelioration of cognitive deficits in the disease. However, since only one study has explored this concept, it is necessary to find consistent evidence for the same.

In summary, the current meta-analysis found PM to be impaired in PD patients, with TB and EBPM impaired to a similar extent. Also, PD patients seem to show deficits in RM as well as other executive functions such as working memory, which are essential in successful execution of the PM task. However, the relatively small number of studies in the present meta-analysis and lack of uniform measures of PM hinders generalization of results.

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