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Remember to Buy Milk on the Way Home! A Meta-analytic Review of Prospective Memory in Mild Cognitive Impairment and Dementia

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Abstract

Prospective memory (PM) is the ability to remember to execute delayed intentions. Previous studies indicate that PM is impaired in persons with mild cognitive impairment (MCI) and dementia, but the extent, nature, and cognitive correlates are unclear. A meta-analytic review was, therefore, performed (literature search 1990 to July 2011) on case-control studies on PM in dementia (10 studies, 336 patients, 505 controls) and MCI (7 studies, 225 patients, 253 controls). Differences between event-based and time-based PM and between measures of prospective and retrospective memory were examined, as well as correlations with other cognitive functions. Results showed that patients with dementia or MCI exhibit large deficits in PM (Hedges' d −1.62 [95% confidence interval −1.98 to −1.27; $p < .0001$] for dementia; −1.24 [−1.51 to −0.995; $p < .0001$] for MCI; difference dementia *vs.* MCI: $Q_M = 1.94$, $p = .16$). Impairments were comparable in size for event-based and time-based PM ($p > .05$), as well as for prospective and retrospective memory ($p > .05$). PM showed modest correlations with measures of retrospective memory (median $r = 0.27$) and executive functioning (median $r = 0.30$). PM appears a valid construct in neuropsychological assessment in patients with dementia or MCI, but more insight is needed in the optimal characteristics of PM tasks to be used in clinical practice. (*JINS*, 2012, *18*, 706–716)

Keywords: Aging, Memory, Executive functioning, Meta-analysis, Alzheimer's disease, Validity

INTRODUCTION

Prospective memory (PM) is defined as remembering to carry out intended actions at an appropriate time in the future (McDaniel & Einstein, 2011). It requires multiple cognitive operations, including forming and organizing an intention, remembering the intention over a delay period, monitoring when and how to execute the intention, performing the intention, and remembering that is has been carried out (Glisky, 1996). Successful functioning of PM is crucial to independent living in the community (Cockburn & Smith, 1988; Sinnott, 1989). Two distinct components concur in the performance of a typical PM task: (1) a *prospective component* which refers to remembering the intention to perform an action at the appropriate moment without an explicit external prompt and (2) a *retrospective component* in which the specific action to be performed is recalled once the prospective intention to act has been retrieved (Einstein & McDaniel, 1990, 1996). A critical difference with retrospective memory (RM), that is, the recollection of past events, is that PM is believed to be more dependent on internal control mechanisms (Craik, 1983, 1986). Whereas in RM tasks subjects are prompted by the examiner to initiate retrieval of a certain item, in PM tasks there is no external agent requesting memory search when the target event occurs (McDaniel & Einstein, 2000). PM, therefore, involves both episodic memory and executive abilities, and thus may rely on multiple neurocognitive systems, most prominently the prefrontal and medial temporal lobe systems (Burgess, Quayle, & Frith, 2001; West, 2005).

A distinction has been made between time-based and event-based PM (Einstein & McDaniel, 1990). Event-based PM involves remembering to perform an intended action when a specific event occurs (e.g., remembering to mail a letter when passing a mailbox). Time-based prospective memory involves remembering to perform an intended action at a specified time (e.g., remembering to ring the doctor in the

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afternoon). It is thought that time-based PM is even more reliant on internal, self-initiated control mechanisms than event-based PM because it is not prompted by an external cue (e.g., the mailbox) (d'Ydewalle, Bouckaert, & Brunfaut, 2001). It may, therefore, be particularly sensitive to age-related decline (Maylor, 1995; for a review, see Henry, MacLeod, Philips, & Crawford, 2004; Uttl, 2008).

Interest in the PM construct began in the 1990s in the field of cognitive psychology and only recently became a relevant topic in the field of clinical neuropsychology. As a consequence, PM has been studied most extensively in healthy persons in laboratory settings (e.g., d'Ydewalle, Luwel, & Brunfaut, 1999). This is surprising since PM complaints are common in clinical neuropsychology (Smith, Della Sala, Logie, & Maylor, 2000) and anecdotal evidence suggests that older persons initially consult their doctors because of their (relatives') PM rather than RM problems (Camp, Foss, Stevens, & O'Hanlon, 1996). Moreover, adequate PM performance is critical to quality of life (Burgess, 2000) and to several daily activities, such as medication adherence and keeping appointments (Einstein, Holland, McDaniel, & Guynn, 1992). One reason for the lack of clinical studies could be difficulty in applying the experimental methods in clinical settings and/or translating these methods into everyday functioning.

Deficits in memory and executive functioning, which are involved in PM, are characteristic features of (Alzheimer's) dementia (Arnaíz & Almkvist, 2003; Backman, Jones, Berger, Laukka, & Small, 2005) and its prodromal stage: mild cognitive impairment (MCI; Arnaíz & Almkvist, 2003; Baddeley, Baddeley, Bucks, & Wilcock, 2001; Hodges, 2000; Petersen, 2004). Both dementia and MCI are, to varying degrees, associated with functional and structural decline of the medial temporal and prefrontal areas in the brain (Bell-McGinty et al., 2005; Feldman & Jacova, 2005; Masdeu, Zubieta, & Arbizu, 2005; Scheltens, 2009). Since these cognitive functions and the affected brain structures are central to PM, prominent PM deficits are to be expected in dementia and MCI. Some authors have documented that PM tasks have a higher discriminative power in detecting MCI and dementia than traditional RM measures (Blanco-Campal, Coen, Lawlor, Walsh, & Burke, 2009; Huppert & Beardsall, 1993), thereby suggesting that a deficit in PM might be an early marker of cognitive decline. Surprisingly, evaluation of cognitive deficits in these conditions within the PM framework is still limited. Moreover, in the scarce literature of PM performance in dementia and MCI, several inconsistent findings emerge. For example, some results indicated that patients with dementia showed greater impairment on time-based PM measures as compared with event-based PM measures (Costa et al., 2010), as is found in normal aging (Henry et al., 2004). This effect was, however, not found invariably (Maylor, Smith, Della Sala, & Logie, 2002). Alternatively, it has been suggested that any differential effect on event-based and time-based measures is merely due to differences in task characteristics (Maylor et al., 2002), such as the extent to which a task depends on automatic *versus* controlled (effortful) processing, rather than the difference in type of cue for action (a particular time or event, respectively). Similarly, while some studies showed greater deficits in PM performance as compared with RM performance in dementia or MCI (Blanco-Campal et al., 2009; Costa et al., 2010), others show no such effect or even reverse effects (Thompson, Henry, Rendell, Withall, & Brodaty, 2010).

The primary aim of the present meta-analysis was to quantify the nature and extent of PM deficits in MCI and dementia. First, this provides a reliable estimate of the size of PM problems in these conditions, based on the present literature. Second, the proposed differences between time-based and event-based PM performance, between prospective and retrospective memory performance and the cognitive correlates of PM performance in MCI and dementia will also be examined in this meta-analysis to provide further insight in the construct validity, as well as the value of PM measures in clinical evaluation of cognitive deficits in these conditions.

METHODS

Identification of Studies

The aim of this meta-analysis was to include all published studies that provide an estimate of prospective memory performance in patients with MCI or dementia. Studies were selected by means of a MedLine literature search (1990 to July 1, 2011) using the keywords ("prospective memory" or "prospective remembering" or "delayed intention") in combination with ("dementia" or "Alzheimer's disease" or "mild cognitive impairment") in full or truncated versions. Titles and abstracts were scanned and potentially eligible papers were collected in full-text. Additional studies were identified by examining the list of references of these studies. Several inclusion criteria were applied to perform a quantitative analysis: (1) the study was an original article; (2) prospective memory performance was assessed in both patients and a control group that was matched for demographic variables such as age, gender, and level of education; (3) test scores were presented for the patients and the control group (mean and standard deviation), or the exact p values, t values, or F values were given. In case of insufficient statistical data, an attempt was made to contact the authors. E.vdB. judged eligible papers according to the inclusion criteria.

Data Synthesis and Analysis

Effect sizes were calculated for the difference in test scores between patients and control participants. This was done for MCI and dementia separately. The effect size estimate used was Hedges' d, that is, the standardized difference between the groups (Hedges & Olkin, 1985). Hedges' d was used instead of the more commonly reported Cohen's d or Hedges' g since it is corrected for a bias due to small sample size (Hedges & Olkin, 1985). The direction of the effect size was negative if the performance of the patient group was worse than the control group. For variables with a non-normal distribution, nonparametric variance estimates were calculated.

In the meta-analysis, an overall d value was calculated, expressing the magnitude of associations across studies,

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weighted for sample size (Hedges & Olkin, 1985). Stouffer's *Z* provided an indication of the significance of the difference in task performance between the patients and the control group. A 95% confidence interval was calculated based on the standard error. In addition, the overall effect size was used in a random effects model to determine the total heterogeneity of the effect sizes (Q_T) and tested against the χ^2 distribution (with n-1 degrees of freedom; Hedges, 1981). A significant Q_T means that the variance of the effect sizes is greater than to be expected from sampling errors and suggests that other explanatory variables should be investigated.

The difference between the overall effect size for MCI *versus* dementia, for event-based prospective memory (EBPM) *versus* time-based prospective memory (TBPM) and for PM *versus* RM was examined with the Q-statistic for heterogeneity. This procedure is analogous to analysis of variance, where one is interested in determining whether or not there is a difference among group means. It is performed by partitioning the total heterogeneity Q_T in Q_M, which is the variation in effect sizes explained by the model, and Q_E which is the residual error variance not explained by the model. Q_M is thus a description of the difference among group cumulative effect sizes and a significant Q_M suggests a difference between the overall effect sizes for the groups (Hedges & Olkin, 1985).

The fail-safe number was computed to explore the robustness of the results to the possibility of publication bias. The fail-safe number of studies N_R provides an estimation of how many non-significant or missing studies would be needed to render the observed meta-analytical results non-significant (Rosenthal's method: $\alpha < 0.05$). All analyses were performed with MetaWin version 2.0 (Rosenberg, Adams, & Gurevitch, 2000).

Data for event-based and time-based prospective memory as well as summary/total scores representing both types of PM were separately included in the analysis. However, when multiple measures of the *same* cognitive construct were provided (e.g., ≥ 2 EBPM-measures in a single study; Blanco-Campal et al., 2009; Kazui et al., 2005; Huppert & Beardsall, 1993), the effect sizes were averaged to give each construct measured in each study the same weight in the analysis. Duchek, Balota, and Cortese (2006) provided data on two different control groups; for this study the effect sizes were averaged. Schmitter-Edgecombe, Woo, and Greeley (2009) provided data on two different MCI-groups; for this study the effect sizes were also averaged. One study presented data on activity-based PM, which is defined as a kind of PM in which the target event is represented by finishing an ongoing activity (Schmitter-Edgecombe et al., 2009). Because data on activity-based was limited and it is in many ways similar to EBPM (Kvavilashivili & Ellis, 1996), this measure was incorporated as EBPM in the present meta-analysis (see also Brewer et al., 2011). When reported, measures of RM were also extracted from the included studies. Separate analyses were performed for RM measures that were *unrelated* to the PM task and RM measures that were *part of* the PM task.

This meta-analysis was performed in 4 consecutive steps. First, overall effect sizes for dementia *versus* controls and MCI *versus* controls were calculated and compared between dementia and MCI. Second, overall effect sizes for time-based and event-based PM were calculated and compared within and between both patient groups. Third, overall effect sizes for prospective and retrospective memory measures were calculated and compared within and between both patient groups. Finally, correlational data were summarized from studies that examined the association between PM measures and other neuropsychological measures.

RESULTS

The literature search yielded 35 hits, 15 of which considered one or more measures of prospective memory in patients with MCI or dementia (excluded studies: 4 reviews; 9 did not include a control group, investigated other patients groups [e.g., Down's syndrome, Parkinson] or only healthy persons; 3 investigated the effect of an intervention to improve prospective memory; 4 examined subjective complaints or used a questionnaire as a measure of prospective memory). After examination of the reference lists one more eligible study was added (Huppert, Johnson, & Nickson, 2000). Three studies were subsequently excluded because of insufficient statistical data provided (Huppert et al., 2000; Livner, Laukka, Karlsson, & Bäckman, 2009) or lack of formal testing of prospective memory (Anderson & Schmitter-Edgecombe, 2010), leaving 13 studies in the present analysis. Tables 1 and 2 display the characteristics of the included studies for dementia and MCI separately. Two studies provided data on both dementia and MCI (Thompson et al., 2010; Troyer & Murphy, 2007) and were thus included in both tables.

Seven of the 13 included studies used laboratory-based PM tasks (Blanco-Campal et al., 2009; Duchek et al., 2006; Karantzoulis, Troyer, & Rich, 2009; Kinsella, Ong, Storey, Wallace, & Hester, 2007; Maylor et al., 2002; Schmitter-Edgecombe et al., 2009; Troyer & Murphy, 2007). These tasks typically involve an ongoing cognitive exercise (e.g., making puzzles, reading sentences or watching a film) during which a specific event occurred (a target stimulus or expiration or a certain time-period), after which a specified action should be performed (e.g., name target animal, ask for a colored pen). The other 6 studies used PM tasks that resembled more naturalistic situations that could occur in normal daily living. For example, the prospective subtasks of the Rivermead Behavioral Memory Test (i.e., ask for a belonging, remind examiner that he or she has an appointment and remembering to deliver a message after walking a route; Wilson, Cockburn, and Baddeley (1985) were administered in several studies (Huppert & Beardsall, 1993; Kazui et al., 2005; Mori & Sugimura, 2007). EBPM tasks were administered more frequently than TBPM tasks.

Prospective Memory Performance in Patients With Dementia or MCI

For dementia, a total of 336 patients and 505 control participants from 10 studies were included in the meta-analysis (Table 1).

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

	n		age		Gender (% male)		Education (years)		MMSE					
Study (year)	D	C	D	C	D	C	D	C	D	C	Dementia diagnosis	PM type	PM task description	*d*
Thompson et al. (2010)	39	53	79.8 ± 6.2	77.8 ± 4.7	51	42	12.0 ± 4.5	11.3 ± 3.3	25.3 ± 4.3	28.7 ± 1.4	DSM–IV	PM	"Virtal Week", perform 4 tasks per day over 2 days	−1.46
												EBPM	- when event occurs	−0.60
												TBPM	- at a specific time	−1.19
Martins et al. (2008)	20	20	75.6 ± 7.8	74.1 ± 6.8	45	45	5.6 ± 4.5	5.8 ± 4.4	22.6 ± 1.9	29.0 ± 1.3	NINCDS/ ADRDA, DSM–IV	PM	RBMT + target animal, remind examiner in 5 min.	−2.35
Mori et al. (2007)	52	50	81.2 ± 5.3	80.0 ± 5.0	0	0	9.1 ± 1.9	8.9 ± 1.8	17.6 ± 4.1	27.2 ± 2.2	Not specified	EBMP	RBMT total PM score	−1.05
Kinsella et al. (2007)	14	14	79.1 ± 6.2	75.7 ± 4.2	36	36	11.0 ± 3.5	11.6 ± 3.0	23.3 ± 3.0	28.9 ± 1.5	NINCDS/ ADRDA	EBPM	Substitute target word in text-reading task	−1.99
Troyer et al. (2007)	45	42	78.4 ± 5.6	75.1 ± 6.4	58	41	12.5 ± 2.4	13.8 ± 3.3	25.5 ± 2.2	28.7 ± 1.2	NINCDS/ ADRDA		During cognitive testing:	
												EBPM	Use colored pen in task requiring writing	−1.72
												TBPM	Report time every 30 min.	−1.86
Duchek et al. (2006)	27	20	78.0 ± 7.5	72.5 ± 3.4	–	–	14.2 ± 3.2	14.5 ± 2.7	–	–	NINCDS/ ADRDA	EBPM	Respond to target word in	−2.22
		13		86.8 ± 4.8		–		15.0 ± 4.0		–			general knowledge test	−1.10
Jones et al. (2006)	46	188	84.0 ± 4.9	84.0 ± 5.2	–	–	8.2 ± 2.4	8.9 ± 2.8	24.4 ± 2.8	27.1 ± 2.2	DSM–III–R	EBPM	Remind test leader to make phone call (+cue)	−0.60
Kazui et al. (2005)	48	48	67.7 ± 8.5	66.7 ± 9.4	37.5	37.5	11.4 ± 2.2	11.5 ± 2.5	21.9 ± 2.3	28.2 ± 1.8	NINCDS/ ADRDA	EBPM	RBMT	
													Belonging	−4.18
													Appointment	−1.71
													Message (immediate)	−1.57
													Message (delay)	−1.6
Maylor et al. (2002)	24	30	68.5 ± 8.0	67.3 ± 4.2	–	–	10.1 ± 2.1	12.3 ± 3.6	22.1 ± 3.6	–	Spinnler (1988)		Watch film	
												EBPM	Name animal target	−0.28
												TBPM	Indicate 3 minutes	−1.95
Huppert et al. (1993)	12 min. AD	27	87.3 (77–92)	81.1 (76–86)	42	37	14.5 age left school	14.5 age left school	19.8 (12–25)	24.8 (22–30)	MMSE, CAMCOG	EBPM	RBMT	
													Belonging	−2.20
													Appointment	−2.07
													Message (immediate)	−2.14
													Message (delay)	−1.89
	9 mod. AD	27	80.6 (70.86)	81.1 (76–86)	33	37	14.1 age left school	14.5 age left school	15.3 (7–23)	24.8 (22–30)	MMSE, CAMCOG	EBPM	RBMT	
													Belonging	−2.49
													Appointment	−3.27
													Message (immediate)	−2.17
													Message (delay)	−2.22

D = dementia; C = control group; MMSE = Mini Mental State Examination; EBPM = Event-based prospective memory; TBPM = Time-based prospective memory; PM = prospective memory summary score; RMBT = Rivermead Behavioral Memory Test; CAMCOG = cognitive part of the Cambridge examination for mental disorders of the elderly; NINCDS-ADRDA = National Institute of Neurological and Communicative Disorders and Stroke – Alzheimer's Disease and Related Disorders Association; DSM-III-R/DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, revised 3rd edition/4th edition.

All but two studies on persons with dementia specifically included patients with Alzheimer's disease (AD). Thompson et al. (2010) and Huppert & Beardsall (1993) did not explicitly specify the dementia type. The overall weighted effect size for patients *versus* controls was −1.62 (95% confidence interval −1.98 to −1.27; $Z = 20.32$; $p < .0001$). For MCI, a total of 225 patients and 253 control participants from seven studies were included in the meta-analysis (Table 2). All MCI studies included patients with amnestic type MCI. Schmitter-Edgecombe et al. (2009) and Costa et al. (2010) also included non-amnestic MCI and dysexecutive MCI, respectively. The overall weighted effect size for patients *versus* controls was −1.24 (−1.51 to −0.995; $Z = 16.92$; $p < .0001$).

According to the nomenclature of Cohen (1988), these effect sizes indicate a large difference ($d > 0.80$) between the patients and the control participants for both dementia and MCI. The test for heterogeneity was not significant (dementia studies $Q_T = 10.58$; $p = .57$, MCI studies $Q_T = 10.68$; $p = .38$), suggesting that the variance among the effect sizes was not greater than expected by sampling error.

The fail-safe number of studies was 320.3 for the dementia results and 313.3 for the MCI results, indicating that at least 320 and 313 unpublished null-findings were needed to render the effects on prospective memory statistically non-significant. It is unlikely that such a large number of unpublished studies with null effects relative to published studies exist.

Despite a trend toward a larger effect size for dementia ($d = -1.62$) compared with MCI ($d = -1.24$), the confidence intervals of both estimates show considerable overlap, and the Q-statistic (using study type as a categorical moderator) indeed showed that the effects were homogeneous ($Q_M = 1.94$; $p = .16$), indicating no statistically significant difference between the overall effect sizes for dementia and MCI.

Event-Based and Time-Based Prospective Memory

For dementia, EBPM was assessed in nine studies with an overall effect size of −1.48 (−1.90 to −1.06; $Z = 17.87$; $p < .0001$). TBPM was assessed in three studies with an overall effect size of −1.42 (−1.95 to −0.60; $Z = 8.53$, $p < .0001$). For MCI, EBPM was assessed in seven studies with an overall effect size of −1.13 (−1.48 to −0.82; $Z = 15.80$; $p < .0001$). TBPM was assessed in four studies with an overall effect size of −1.34 (−1.85 to −1.14; $Z = 9.03$; $p < .0001$). Again, these effect sizes indicate a large difference between patients and control participants for both dementia and MCI. Despite a trend toward larger effect sizes for the TBPM measures in the MCI studies (see Table 2), the effect sizes for EBPM and TBPM were homogeneous, thereby indicating no statistically significant difference between EBPM and TBPM measures, neither when the dementia and MCI studies were taken together ($Q_M = 0.05$; $p = .83$), nor in the dementia ($Q_M = 0.02$; $p = .88$) and MCI studies ($Q_M = 0.64$; $p = .42$) separately, possibly due to the relatively small number of TBPM measures available.

Relation Between Measures of Prospective and Retrospective Memory

As PM is considered to be related to RM, and PM tasks generally have both a retrospective and a prospective component, the relation between PM and RM was investigated in two ways. First, 11 studies reported results of separate measures of retrospective memory in their study samples. The items that were to be recalled or recognized in the RM tasks were unrelated to the PM task. Table 3 shows the effect sizes for both the PM and the RM measures that were extracted from those studies. For dementia *versus* controls, this resulted in an overall effect size of −1.66 (95% CI −2.08 to −1.23) for the measures of prospective memory and −1.76 (−2.14 to −1.39) for the measures of retrospective memory. The difference between these two overall effect sizes was not statistically significant ($Q_M = 0.11$; $p = .74$). For MCI *versus* controls the overall effect sizes for prospective and retrospective memory were also similar [prospective −1.41 (−1.72 to −1.11); retrospective −1.10 (−1.27 to −0.85), $Q_M = 1.69$; $p = .19$]. In two studies (Karantzoulis et al., 2009; Troyer & Murphy, 2007), the retrospective measures were used in the diagnosis of MCI and dementia, possibly resulting in a bias toward worse performance on the retrospective memory measures. However, exclusion of these studies did not notably alter the results (data not shown). Also, when taking dementia and MCI studies together, the difference between the overall effect sizes for PM and RM was not statistically significant ($Q_M = 0.05$; $p = .83$).

Second, six studies presented a separate analysis on the prospective and retrospective component *within* their measure of prospective memory (Dementia: Jones, Livner, & Bäckman, 2006; Huppert & Beardsall, 1993; Maylor et al., 2002; Thompson et al., 2010; MCI: Costa et al., 2010; Karantzoulis et al., 2009; Thompson et al., 2010). Effect sizes could be calculated from four of these studies to examine the difference between patients and controls in the prospective and retrospective components (Costa et al., 2010; Karantzoulis et al., 2009; Maylor et al., 2002; Thompson et al., 2010). These effect sizes were either calculated from the difference between the retrospective component and total PM performance (Maylor et al., 2002; Thompson et al., 2010) or from the difference between the prospective and retrospective components within the task (Costa et al., 2010; Karantzoulis et al., 2009). The overall effect size (dementia and MCI studies taken together) was −1.51 (−2.09 to −0.99) for the prospective component and −1.38 (−2.05 to −0.82) for the retrospective component (difference: $Q_M = 0.07$; $p = .79$). Of the two studies that could not be included in the effect size calculation, one showed no difference between the prospective and retrospective component in patients with dementia (Jones et al., 2006); the other showed a significant difference between persons with dementia and controls in the prospective component even when adjusting for the retrospective component in analysis of covariance (Huppert & Beardsall, 1993).

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Table 2. Summary of studies included in the meta-analysis: MCI

	n		age		Gender (% male)		Education (years)		MMSE					
Study (year)	MCI	C	MCI	C	MCI	C	MCI	C	MCI	C	MCI diagnosis	PM type	PM task description	*d*
Costa et al. (2010)	20	20	72.2 ± 5.9	71.5 ± 6.1	40	55	10.3 ± 3.7	10.5 ± 4.8	26.0 ± 1.4	28.2 ± 1.4	Petersen (2004)	EBPM	Six triplets of actions	−1.21
												TBPM	Six triplets of actions	−2.24
Thompson et al. (2010)	48	53	78.6 ± 4.9	77.8 ± 4.7	54	42	12.2 ± 3.9	11.3 ± 3.3	28.0 ± 1.6	28.7 ± 1.4	Petersen (2007)	PM	"Virtal Week," perform 4 tasks per day over 2 days	−0.77
												EBPM	- when event occurs	−1.20
												TBPM	- at a specific time	−0.70
Schmitter-Edgecombe et al. (2009)	27 aMCI	42	71.3 (52–91)	72.5 (50–92)	48	40	16.1 (12–20)	16.1 (11–20)	26.9 (24–30)	28.7 (26–30)	Petersen (2001)	EBPM[+]	During cognitive testing: Ask examiner for pill bottle after every task	−1.63
	15 naMCI		72.2 (48–95)		27		15.9 (12–20)		27.4 (24–30)					−1.10
Blanco-Campal et al. (2009)	19	21	71.15 ± 5.6	72.5 ± 5.6	47	29	3: > 13y 16: ≤ 13y	8: > 13y 13: ≤ 13y	25.7 ± 2.0	29.4 ± 0.7	Portet (2006)	EBPM	"Silly sentences"	
													Non-specific target	−2.53
													Specific target	−1.27
Karantzoulis et al. (2009)	27	27	75.7 ± 7.6	73.0 ± 5.9	44	26	13.0 ± 3.5	14.2 ± 3.1	–	–	Petersen (2004)	PM	MIST during word puzzle	−1.48
												EBPM	e.g. "rewind a tape"	−0.70
												TBPM	e.g. "take break after 2 m"	−1.21
Troyer et al. (2007)	45	42	75.8 ± 6.7	75.1 ± 6.4	53	41	13.6 ± 3.3	13.8 ± 3.3	27.8 ± 1.4	28.7 ± 1.2	Petersen (2004)		During cognitive testing:	
												EBPM	Use colored pen in task requiring writing	−0.67
												TBPM	Report time every 30 min.	−1.08
Kazui et al. (2005)	24	48	66.9 ± 9.4	66.7 ± 9.4	37.5	37.5	11.5 ± 2.6	11.5 ± 2.5	26.7 ± 1.9	28.2 ± 1.8	Petersen (1995)	EBPM	RBMT	
													Belonging	−2.26
													Appointment	−2.56
													Message (immediate)	−0.27
													Message (delay)	−1.84

MCI = mild cognitive impairment; C = control group; MMSE = Mini Mental State Examination; EBPM = event-based prospective memory; TBPM = Time-based prospective memory; PM = prospective memory summary score; RMBT = Rivermead Behavioral Memory Test; aMCI = amnestic MCI; naMCI = nonamnestic MCI; MIST = memory for intentions screening test; [+]activity-based task = a kind of EBPM in which the target event is represented by finishing an ongoing activity.

Table 3. Prospective and retrospective memory performance

	Prospective memory		Retrospective memory			
	Effect size *d*	variance	Effect size *d*	variance	Difference	
Dementia vs. control						
Kazui et al. (2005)	−2.23	0.07	−2.04	0.06		
Maylor et al. (2002)	−1.09	0.19	−1.46	0.10		
Mori et al. (2007)	−1.05	0.04	−2.42	0.07		
Duchek et al. (2006)	−1.65	0.13	−1.22	0.13		
Jones et al. (2006)	−0.60	0.03	−0.92	0.03		
Troyer et al. (2007)*	−1.79	0.09	−1.96	0.11		
Martins et al. (2008)	−2.35	0.17	−2.52	0.18		
Huppert et al. (2003)						
– minimal dementia	−2.07	0.18	−1.17	0.14		
– moderate dementia	−2.48	0.24	−2.39	0.24		
Overall effect size	−1.66	0.13	−1.76	0.12	$Q_M = 0.11$	$p = .74$
MCI vs. control						
Blanco-Campal et al. (2009)	−1.88	0.15	−1.19	0.12		
Kazui et al. (2005)	−1.72	0.09	−1.31	0.08		
Troyer et al. (2007)	−0.88	0.05	−1.14	0.06		
Schmitter-Edgecombe et al. (2009)	−1.38	0.09	−0.64	0.08		
Karantzoulis et al. (2009)*	−1.48	0.09	−1.26	0.09		
Overall effect size	−1.41	0.09	−1.10	0.09	$Q_M = 1.69$	$p = .19$

*RM measures used in diagnostic process.

Correlations Between PM Performance and Other Neuropsychological Tests

Four studies on dementia and seven studies on MCI provided correlation analyses between measures of prospective memory and other neuropsychological test measures (Table 4). Due to considerable variability in chosen measures and analyses a formal meta-analysis was not performed, but a descriptive analysis of these data is presented below. Measures of memory and executive functioning were primarily used in the correlation analyses. A small number of studies also provided data on working memory, attention, processing speed, and perception. Overall, the correlation coefficients were small to moderate in size, ranging from −0.22 to 0.72 (median $r = 0.27$; interquartile range, 0.12 to 0.43), a third of which reached statistical significance. The correlations appeared stronger within the patient groups than within the controls. All eight studies explicitly hypothesized significant correlations with retrospective memory and executive functioning, thereby supporting convergent validity of the PM construct. In six of eight of these studies, this hypothesis was (partly) confirmed (median $r = 0.27$ for memory, median $r = 0.30$ for executive functioning).

DISCUSSION

The present study involved a meta-analytic review of prospective memory in patients with dementia or mild cognitive impairment (MCI), to explore the extent, nature and cognitive correlates of PM in these patients. The results of the meta-analysis, which incorporated 13 studies in total, showed large deficits in PM in both patient groups (Hedges' d −1.62 for dementia, −1.24 for MCI), compared with control participants. There was no statistically significant difference in effect sizes between MCI and dementia. To further characterize the nature of these deficits, several contrasts that were proposed in the current literature were tested statistically. These secondary analyses revealed no significant differences between time-based prospective memory (TBPM) and event-based prospective memory (EBPM) (d −1.42 *vs.* −1.48 for dementia and −1.34 *vs.* −1.13 for MCI), or between prospective and retrospective memory (components) (d −1.66 *vs.* −1.76). Correlation analysis showed significant associations between PM performance and measures of RM and executive functioning. Weak correlations were also observed for working memory and attention, but as these cognitive domains were scarcely examined, strong conclusions about the specificity of these relations cannot be drawn.

Interest in the PM concept in patients with AD or MCI is increasing. This is not surprising since the cognitive functions and brain areas that are typically affected in these conditions (Arnaíz & Almkvist, 2003; Backman et al., 2005; Baddeley et al., 2001; Bell-McGinty et al., 2005; Feldman & Jacova, 2005; Hodges, 2000; Masdeu et al., 2005; Scheltens, 2009) are also involved in PM performance. The finding that the effect sizes in MCI were large and, more importantly, similar in size to those found in dementia corroborates earlier suggestions that PM is already affected in the early stages of the disease (Huppert & Beardsal, 1993). For some other conjectures in the current PM literature, no clear support was found in the present meta-analysis. Some authors propose that PM tasks add additional discriminative power in the detection

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Table 4. Correlations between prospective memory and other neuropsychological tests

Test	Study	Correlation with prospective memory		
		Control group	MCI patients	Dementia patients
Memory				
Word list immediate recall	Costa et al. (2010)		0.38**	
Word list delayed recall	Costa et al. (2010)		ns	
Short story immediate recall	Costa et al. (2010)		ns	
Short story delayed recall	Costa et al. (2010)		ns	
RAVLT total trial 1-5	Schmitter-Edgecombe et al. (2009)	ns	>0.45**	
RAVLT immediate delay	Schmitter-Edgecombe et al. (2009)	ns	>0.45**	
RAVLT long delay	Schmitter-Edgecombe et al. (2009)	ns	>0.45**	
RAVLT total trial 1–5	Martins et al. (2008)			not specified
Recall of 6 object	Huppert et al. (1993)	0.08; 0.18; −0.06; −0.1[d]		0.19; 0.28; 0; 0.36[d]
Free recall of words	Huppert et al. (1993)	0.07; 0.16; 0.13; 0.04[d]		0.61**; 0.58**; 0.34; 0.17[d]
Route – immediate recall	Huppert et al. (1993)	0.22; 0.22; 0.4; 0.29[d]		0.36; 0.51*; 0.39; 0.17[d]
Route – delayed recall	Huppert et al. (1993)	0.11; 0.34; −0.03; 0.44*[d]		0.61**; 0.24; 0.29; 0.42[d]
Recall of name	Huppert et al. (1993)	−0.16; 0.27; −0.22; 0.46*[d]		0.24; 0.17; 0.16; −0.08[d]
HVLT immediate recall	Troyer et al. (2007)[b]		0.48**	0.48**
BVMT immediate recall	Troyer et al. (2007)[b]		0.34**	0.34**
Working memory				
Visual span	Thompson et al. (2010)[b]		0.49**	0.49**
Letter-Number Sequencing (WAIS-III)	Schmitter-Edgecombe et al. (2009)	ns	ns	
Digit Span backward (WAIS-III)	Martins et al. (2008)			−0.02
Executive functioning				
MCST (categories)	Costa et al. (2010)		0.33*	
MCST (perseverative errors)	Costa et al. (2010)		ns	
Word fluency	Costa et al. (2010)		ns	
Trailmaking Test – Part B[a]	Duchek et al. (2006)	Group 1: −0.72** Group 2: 0.004		
Trailmaking Test – Part B[a]	Troyer et al. (2007)[b]		−0.47**	−0.47**
Trailmaking Test – Part B[a]	Martins et al. (2008)			0.09
Trailmaking Test – Part B[a]	Schmitter-Edgecombe et al. (2009)	ns	−0.51**	
D-KEFS design fluency	Schmitter-Edgecombe et al. (2009)	ns	0.43**	
D-KEFS letter fluency	Schmitter-Edgecombe et al. (2009)	ns	ns	
Composite score[c]	Karantzoulis et al. (2009)	0.30	0.21	
Tower of London	Thompson et al. (2010)[b]		0.27**	0.27**
Attention				
Digit Span forward (WAIS-III)	Martins et al. (2008)			−0.10
Processing speed				
SDMT	Schmitter-Edgecombe et al. (2009)	ns	ns	
Trailmaking Test – Part A[a]	Martins et al. (2008)			−0.23
Perception				
Visual perception	Martins et al. (2008)			−0.07

Note. Data are unadjusted Pearson or Spearman (rank) correlation coefficient extracted from the studies. No meta-analysis was performed.
MCST = Modified Card Sorting Test; HVLT = Hopkins Verbal Learning Test; BVMT = Brief Visuospatial Memory Test; RAVLT = Rey Auditory Verbal Learning Test; WAIS-III = Wechsler Adult Intelligence Scale 3rd Edition; SDMT = Symbol Digit Modalities Test; ns = not significant.
[a] Higher score reflects worse performance.
[b] Troyer et al. and Thompson et al. present correlation coefficients for MCI and dementia combined, these are presented in both columns.
[c] Composite score for executive functioning consisting of MCST, word fluency, WAIS-III Arithmetic, Wechsler Memory Scale-Mental Control, WAIS-III Digit Span backward.
[d] Huppert et al. presented correlation coefficients for RMBT appointment, belonging, and immediate & delayed recall of a message.
*$p < .05$, **$p < .01$, ***$p < .001$

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of dementia, above and beyond known psychometric tests for RM (Duchek et al., 2006; Huppert & Beardsall, 1993). This suggestion was not corroborated by the present meta-analysis, which showed that the difference in PM and RM performance between patients and controls was rather similar in size. Whereas this might be somewhat surprising, the large effects of dementia and MCI on PM that were demonstrated in the present meta-analysis strongly suggest that PM measures should be part of neuropsychological assessment in clinical practice. As yet, it remains to be evaluated what characterizes a valid and reliable measure of PM in clinical populations. Many PM tasks that can be used in clinical populations have a restricted range of scores that can be obtained (one either remembers to remind the experimenter, or one does not), which may cause limited statistical sensitivity (for a review of methodological issues, see Costa et al., 2010). In addition, studies in healthy participants show effects of the nature and importance of the ongoing task on PM performance (e.g., d'Ydewalle et al., 1999), which is particularly relevant since in clinical practice, PM tasks are typically part of a larger neuropsychological test battery. The effect sizes of the six studies in the present meta-analysis that used naturalistic PM measurement tended to be slightly smaller than those found in studies that used laboratory-based measures, but whether this reflects a true difference or rather results from differences in task characteristics remains to be evaluated.

Several authors proposed a larger effect of (pathological) aging on time-based measures as compared with event-based measures of PM, because the former places a greater burden on internal control mechanisms (Henry et al., 2004). A trend toward a greater effect size for TBPM than for EBPM was indeed observed for MCI, but the difference between the effect sizes did not reach statistical significance for either MCI or dementia. The absence of statistical significance could be, at least in part, due to the relatively limited number of studies that examined TBPM. However, alternative explanations should be considered as well. For one, the observed results raise important questions about the true difference in nature of event-based and time-based PM. Should these concepts be viewed as theoretically different, or is it better to explain reported differences in PM performance in terms of differences in task characteristics? In their multiprocess framework, McDaniel, Einstein, Guynn, and Breneiser (2004) propose that PM performance may rely on both strategic monitoring and automatic retrieval processes. Based on this premise one may argue that both time- and event-based tasks can vary in the amount of self-initiated activity required or environmental support available. As such, certain EBPM tasks may be more demanding than some TBPM tasks and the reported differences in performance between PM tasks may thus be determined by the extent to which the task depends on automatic *versus* controlled (effortful) processing, rather than by a difference in type of cue for action (a particular time or event, respectively). This hierarchical viewpoint could provide a more valid explanation for differences in PM performance than the simple distinction between TBPM and EBPM. It should be noted that in the review by Henry et al. (2004), on which many authors have based the hypothesized difference between TBPM and EBPM, a significant difference was indeed *only* observed between conditions with high demand TBPM and low demand EBPM. The results of the present meta-analysis that indicate that patients with MCI and dementia are equally impaired in time-based and event-based PM, seems to be most in line with a difference in terms of task demands. A recent meta-analytic review in patients with schizophrenia did reveal a greater impairment in TBPM than in EBPM (Wang et al., 2009), but it should be noted that the overall effect sizes, particularly those for EBPM, were considerably smaller, probably reflecting a greater overall memory deficit in patients with MCI or dementia compared with patients with schizophrenia. More specifically, the impaired PM performance observed in MCI or dementia may, at least in part, be explained by the presence of a RM deficit in these patients. Indeed, a recent study by Costa et al. (2011), in which executive load was manipulated experimentally, showed that reduced performance on the PM tasks was at least partially underlain by their inability to remember the target words. Thompson et al. (2010) illustrate this possible effect of disease severity by arguing that the difference between TBPM and EBPM is present in patients with MCI, but is no longer visible once patients progress toward dementia. Recent experimental studies increasingly consider the dimensions of focality and regularity in PM (e.g., Rose, Rendell, McDaniel, Aberle, & Kliegel, 2010), but these concepts were not commonly examined in the patient studies included in the present meta-analysis. Therefore, these dimensions were not considered here.

As an indication of construct validity, correlations with tests measuring memory, executive functioning and other cognitive domains were examined. The observed significant correlations between PM and measures of RM and executive functioning indicate adequate convergent validity of the PM construct. However, correlations with other cognitive functions, such as fluid intelligence and perceptual speed, are similar in size (Salthouse, Berish, & Siedlecki, 2004), which is inconsistent with discriminant validity of the PM construct, at least in dementia and MCI. Also, secondary analysis indicated no significant difference between the effect size for the MMSE score and the PM measures (−1,68 [−2,11 to −1,26] *vs.* −1,48 [−1,90 to −1,06]; $Q_M = 0.53$; $p = .47$ from five studies for MCI, seven for dementia), although one should keep in mind that MMSE was not included as an outcome measure in any of the studies. Since the present review included only case-control studies in which samples of patients were compared with healthy persons matched for age, gender and educational level, the effect of these demographics on PM was not specifically examined. One would expect that demographics, age in particular, are related to PM performance as is also indicated in a previous review (Henry et al., 2004). Detailed analysis of the impact of gender and level of education would further increase insight in the PM construct.

Strengths of the present study include the use of a meta-analytical approach that provides a weighted estimated

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of the magnitude of the effects. A limitation concerns the heterogeneity of the included studies with regard to sample size and characteristics of the PM tasks. Also, some of the secondary analyses included a relatively small number of studies. Finally, the vast majority of included studies was performed in patients with Alzheimer's disease. Whether these finding can be extrapolated to other types of dementia remains to be evaluated.

In sum, the present meta-analysis shows a large deficit in PM in patients with dementia or MCI compared with healthy controls. PM performance was also associated with measures of RM and executive functioning. These impairments were comparable in size for TBPM and EBPM as well as for PM and RM in general. PM appears a valid construct in neuropsychological assessment in patients with dementia or MCI, but more insight is needed in the optimal characteristics of PM tasks to be used in clinical practice.

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