Sustaining Prospective Memory Functioning in Amnestic Mild Cognitive Impairment: a Lifespan Approach to the Critical Role of Encoding

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Abstract

Objective: Prospective memory (PM), the ability to remember to perform future activities, is a fundamental requirement for independent living. PM tasks pervade throughout our daily lives and PM failures represent one of the most prominent memory concerns across the entire lifespan. This study aimed to address this issue by exploring the potential benefits of specific encoding strategies on memory for intentions across healthy adulthood and in the early stages of cognitive impairment.

Method: PM performance was explored through an experimental paradigm in 96 participants: 32 amnestic mild cognitively impaired patients aged 64-87 years (M=76.06, SD=5.88), 32 healthy older adults aged 62-84 years (M=76.06, SD=6.03) and 32 younger adults 18-22 years (M=19.75, SD=1.16). The potential benefit of the use of enactment (i.e. physically simulating the intended action) at encoding to support an autonomous performance despite neuronal degeneration was assessed.

Results: PM was consistently identified as a sensitive and specific indicator of cognitive impairment. Importantly, enacted encoding was consistently beneficial for PM performance of all the participants, but especially so in the case of healthy and cognitively impaired older adults. These positive results have unveiled the potential of this encoding technique to optimize attentional demands through an adaptive allocation of strategic resources across, both, a healthy and cognitively impaired sample. Theoretical implications of this work are discussed as well as the considerable translational potential to improve social well-being.

Conclusions: A better understanding of the strategies that can enhance PM offers the potential for cost effective and widely applicable tools which may support independent living across the adult lifespan.

Keywords: Prospective Memory; Mild Cognitive Impairment; Enactment; Dementia; Rehabilitation
first time, an all-encompassing adult lifespan approach to this effect which will be essential to genuinely understand the cognitive mechanisms involved in the rise and fall of PM. The main aim of this study is to understand the ageing pathway of PM in terms of underlying processes. To this end, we will (1) focus on the unexplored evolution of PM from young adulthood through to healthy and cognitively compromised older adulthood, and (2) identify the impact of a specific encoding strategy on PM performance that might support the RM function. Specifically, we will explore the impact of reducing RM and executive control demands through enactment (i.e., physically simulating the performance of the intended action) on PM performance. Enactment might constitute an easily implementable and widely applicable encoding method to enhance PM performance across healthy and cognitively compromised adulthood (cf. Pereira, et al., 2015). In fact, we have previously explored the influence of enactment at encoding for PM performance in amnestic patients and age and education matched healthy controls. Here, PM performance was consistently superior when physical enactment was used at encoding; for both healthy and cognitively impaired participants (Pereira, et al., 2015). In terms of underlying mechanisms, enactment encoding is assumed to facilitate PM performance by increasing the level of association between the PM cue and the intended action which may decrease the need for memory and executive control resources by rather automatically prompting retrieval of the intended action and switching from the ongoing to the PM task (Ellis, 1996; McDaniel, Guynn, Einstein & Brenneiser, 2004). Similarly, there is evidence that a strong semantic relation between the retrieval cue and the intended action might reduce the executive demands of the task by supporting retrieval in healthy young and older adults (Maylor, Smith, della Sala & Logie, 2002) as well as for participants in the early stages of cognitive impairment (Driscoll, McDaniel & Guynn, 2005). Interestingly, physical encoding and semantic relatedness seem to contribute independently and cumulatively to prospective remembering; an effect that has been identified across aging in healthy (Pereira, et al., 2012a, 2012b) and cognitively compromised adults (Pereira, et al., 2015). The use of enactment at encoding is predicted to improve PM performance by considerably reducing RM and executive control demands. Specifically, motoric encoding is anticipated to support PM performance by engaging additional sensorial processes (e.g. tactile, proprioceptive) which might contribute to enhanced encoding and enhanced salience of PM cue (Pereira, et al., 2012a, 2015). Furthermore, it is anticipated that the effects of enactment at encoding in combination with the effects of semantic relatedness between cue-action word pairs will be cumulatively advantageous; both in healthy adults (cf. Pereira, et al. 2012b) and those in the early stages of cognitive impairment (cf. Pereira, et al. 2015). This hypothesis would be congruent with a multi-system account of the enactment effect (cf. Engelpkamp & Jahn, 2003) in which enactment is assumed to rely on a non-verbal motor system, whereas semantic relatedness would rely on an independent conceptual system instead. The combined effect of the two manipulations would consequently increase the salience of the cue and reinforce the integration of the two components (cf. Feyereisen, 2009).

With respect to the effect of age, it is anticipated that a decline in PM performance from young to old adulthood will emerge (Zimmermann & Meier, 2006). This decline is anticipated to be even more marked for cognitively compromised older adults (Thompson, et al., 2017). The encoding strategy proposed is expected to facilitate PM performance across adulthood (Pereira, et al., 2012a), being particularly beneficial in later life given the well-documented decline in RM and executive functions in older age, especially in the context of neuronal degeneration (Pereira, et al., 2015).

In short, a decline in PM performance is anticipated from young adulthood to healthy and cognitively compromised older adulthood. The effects of enactment at encoding and of a proximal semantic relatedness between cue-action word pairs are expected to independently mitigate this effect and are predicted to be cumulatively advantageous across healthy and cognitively compromised aging.

Method

Participants

Ninety-six adults participated in this study, aged 18-87 years (M = 57.52, SD = 2.79) and having spent 7-16 years in full time education (M = 14.19, SD = .22). Thirty-two volunteers were amnestic patients aged 64-87 years (M = 76.75, SD = 5.88) having spent 7-16 years in full time education (M = 14.38, SD = 2.54); 32 age- and education-matched healthy older adults aged 62-84 years (M = 76.06, SD = 6.03) having spent 7-16 years in full time education (M = 13.56, SD = 2.61) and 32 younger adults aged 18-22 years (M = 19.75, SD = 1.16) having spent 14-16 years in full time education (M = 14.62, SD = .79).

Sample size was based on an a priori power analysis using GPOWER ( Faul, Erdfelder, Buchner, & Lang, 2009). The effect size f was established using previous research ( Pereira, 2015) and determined from means (defined as f = ηm/ση) to be large (f > .5; Cohen, 1969, p. 348). The a priori power analysis was conducted with an alpha level of .05, power at .95, and was performed considering a size effect of 5. To find a statistically significant effect in the model 90 participants would be necessary. To accommodate for any eventual dropouts, a sample size of 96 was set as the goal.

The study was approved by the Research Ethics Committee of the University of Chichester and by the South Central – Hampshire B Research Ethics Committee - HRA REC Ref: 13/SC/0531. Healthy participants were volunteers from the local community recruited in Chichester, and surrounding areas through word of mouth whereas patients were recruited through the Memory Assessment Service, Sussex Partnership NHS Foundation Trust.

Inclusion criteria for amnestic patients (aMCI group): The inclusion criteria for the aMCI group were based on Recommendations from the National Institute on Aging-Alzheimer’s Association workgroups on diagnostic guidelines for Alzheimer’s disease (Albert et al., 2011). Only single domain amnestic MCI patients (characterized by a neuropsychologist at the Memory Assessment Service as a single domain aMCI - with episodic memory impairments after a comprehensive neuropsychological assessment) were recruited. Specifically, they needed to fulfil the following criteria:

1) Report by patient and/or family of subjective cognitive decline and cognitive complaints during the last year.
2) Objective retrospective narrative memory impairment, as assessed by the logical memory (LM) subtest of the Wechsler Memory Scale – IV (WMS-IV; Wechsler, 2009).
3) Preserved or minor impairment in activities of daily living, as defined by no more than one item changed in the Bristol Activities of Daily Living (BADL; Buck, Ashworth, Wilcock, & Siegfried, 1996) based on self-report.
4) Absence of major neurocognitive disorder, according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-V; American Psychiatric Association, 2013) and scores on the Mini Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975).

Inclusion criteria for healthy participants:
1) Absence of self-reported subjective cognitive decline and cognitive complaints.
2) Absence of objective retrospective narrative memory impairment, as assessed by the LM subtest of the WMS-IV.
3) Preserved activities of daily living as defined by no item changed in BADL.
4) Absence of dementia, according to the DSM-V and scores on the MMSE.

Exclusion criteria for all groups:
1) Self-reported history of alcohol abuse, substance abuse or dependence.
2) Self-reported psychiatric, neurological, or medical disorders likely to entail cognitive deficits.
3) Self-reported major depressive episode (DSM-V; American Psychiatric Association, 2013), or severe depressive symptomatology assessed by the depression symptomatology subsection of the Hospital Anxiety and Depression Scale (HADS; Snath, 2003; Zigmond & Snath, 1983)
Design
A mixed-factorial design was employed with within-subjects factor Cue-Action Relatedness Method (related, unrelated) and two between-subject factors Group (younger adults, older adults, aMCI patients) and Encoding (verbal, enactment).

This design was specifically chosen to defuse potential carry over effects (cf. Greenwald, 1976) concerning the enactment encoding manipulation which has been identified as producing an impact on performance of healthy adults in naturalistic settings up to a week after the encoding has occurred (cf. Pereira, 2010).

Materials
All participants underwent a protocol which involved a self-reported account of relevant demographic information, lifestyle and clinical history, as well as the completion of the following instruments:

Addenbrooke's Cognitive Examination-Revised (ACE-R; Mioshi, Dawson, Mitchell, Arnold, & Hodges, 2006) is a brief cognitive test widely used to assess cognitive function and to screen for dementia. The maximum score (MS) is 100; with higher scores indicating better cognitive functioning. It assesses five cognitive domains, namely attention/orientation (MS: 18), memory (MS: 26), verbal fluency (MS: 14), language (MS: 26) and visuospatial abilities (MS: 16). Since its creation in 2006, the ACE-R has been validated and extensively used in both clinical research and practice. The ACE-R takes 15–20 minutes to administer and is effective as a screening tool for cognitive impairment with community dwelling, hospitalized and institutionalized adults. A cut-off below 88 provides a 94% sensitivity and 89% specificity for dementia. The normative cut-off values proposed by the original authors were used.

Mini Mental State Examination (MMSE; Folstein et al., 1975) is a brief cognitive tool traditionally used to screen for cognitive impairment and dementia. The normative cut-off values proposed by the National Institute for Health and Clinical Excellence (NICE; National Collaborating Centre for Mental Health, 2007) were used. Participants should score 26 or above to be considered within the normal range.

Logical Memory (LM) is a subtest of the WMS-IV (Wechsler, 2009) assessing retrospective narrative memory through the free recall of a short story. Memory impairment was determined when participants presented a performance of ≤ 1.5 standard deviation (SD) below the normative scores for respective age and education.

Trail making test (TMT; Army Individual Test Battery, 1944) is a cognitive assessment of task switching and visual attention which taps into executive functions as well as other cognitive functions, such as visual scanning and even psychomotor speed (Lezak, Howieson, Bigler, & Tranel, 2012; Tombaugh, 2004). In this study, the TMT quotient (Part B/ Part A) was calculated.

Bristol Activities of Daily Living (BADL; Bucks et al., 1996) represents a 20-item questionnaire which assesses the capacity to live autonomously, assessing current function as well as deterioration or improvement over time. Severity judgements on each activity of daily living range from independence (score 0 – no help required) to dependence (score 3 – unable even with supervision), rated on a four-point scale. This produces a total score range of 0–60. Activities of daily living are considered preserved if no item from the BADL scale suffered any change

Participants were randomly assigned to one of four different cue categories. The four categories were: animal, flower, vegetable and fruit. The respective four encoding verbs were: to pet, to smell, to cook and to eat. The following are examples of PM cues pertaining each respective category: dog, cat, horse, dolphin; daisy, rose, violet, poppy; carrot, turnip, cabbage, onion; orange, watermelon, strawberry; banana). The PM cue and action word pairs were matched for strength of association (PSG ≤ 0.1; Nelson, McEvoy, & Schreiber, 2004).

Procedure
Participants were individually tested. Sixteen participants in each group (aMCI patients, older adults and younger adults) were sequentially randomly allocated to the verbal encoding condition and the other 16 to the enactment encoding condition. All participants started the session by providing a self-reported account of relevant demographic information, lifestyle and clinical history.

Then the session would proceed with a practice of the one-back word task where participants would have to press the left key ‘1’ on a serial response box if the word presented matched the word presented on the previous trial and the right key ‘5’ if it did not. This was followed by instructions to the PM task. Participants were told that next time, in addition to the previous task, if they noticed that any of the words belonged to a specific category (animal, flower, vegetable or fruit), they would have to press the middle key ‘3’ on the serial response box instead or responding to the ongoing task. Participants were asked to respond to the task as quickly as possible without sacrificing accuracy.

Participants in the verbal encoding condition were then asked to read aloud the cue-target combination (i.e. repeating three times the sentence ‘to pet an animal!’ ‘to smell a flower’, ‘to cook a vegetable’ or ‘to eat a fruit’). The instructions were presented on the screen and the experimenter read through them with the participants. Participants were also required to demonstrate understanding of each sentence by pressing a particular key before proceeding. Any queries were answered by the experimenter before administration. All administration was designed to match the enactment at encoding condition as closely as possible, ensuring that any effects observed are attributable to this manipulation.

Participants in the enactment encoding condition were given the same information however, in addition to the instructions aloud they were asked to physically perform the action on the imagined designated object (e.g. participants in the enactment of daily-life memory tasks, representative of typical memory complaints. The level of internal consistency of the scale was good (α = .78; Cronbach, 1951).

PM task – a computer based PM task which included a practice phase concerning the ongoing component of the PM task which was subsequently followed by the main PM task and then by a filled delay interval which preceded the main ongoing task in which the PM cues were embedded. The ongoing task consisted of a one-back word task. The option to use a this ongoing task was informed by a previous exploratory study conducted at our lab in which most impaired older adults and in fact, even some of the healthy older adults presented great difficulty in performing more complex n-back tasks. We were conscious that a one-back task could lead to ceiling effects in PM (or ongoing task) performance for younger adults and that, in that case, this could have influenced the results. However, we are confident that performance was not at ceiling for these measures given that younger adults presented a wide range in performance on both the ongoing task (range: .75 to 1) and the main PM task (range: .5 to 1).

A baseline block was created, comprising 20 stimuli, and a main ongoing task block with 225 stimuli (6 PM cue words, 219 ongoing task stimuli; 69 n-back targets and 150 non-targets). The overall frequency of PM targets was 2.6%.

Each trial consisted of 500ms of a fixation cross, followed by presentation of the stimulus for a maximum of 2000ms. There was an inter-trial interval of 250ms. All trials were self-paced (with an upper limit of 2000ms) to prevent rehearsal of the given instructions (cf. Burgess, Scott, & Frith, 2003). The number of ongoing task trials between each PM target was the same for all participants, and followed a fixed order. Specifically, the intervals were arranged as follows (50, 33, 17, 25, 41, 57). Words were drawn from the MRC Psycholinguistic Database (Wilson, 1988), and were matched for written frequency, familiarity, imageability and concreteness.

Subjective Memory Complaints Scale (SMC; National Collaborating Centre for Mental Health, 2007) was used. Participants should score 26 or above to be considered within the normal range.

Psychological Questionnaire (PQ; Mioshi, Dawson, Mitchell, Arnold, & Hodges, 2006) used to screen for depression in older adults (HADS; Zigmond & Snaith, 1983). The PQ represents a self-report assessment scale, developed to detect states of depression and anxiety. Prior to completing the scale patients are asked to “complete it in order to reflect how they have been feeling during the past week” (Zigmond & Snaith, 1983). After implementation, the level of internal consistency of the scale in what concerns the items that constitute the construct of anxiety was high (α = .82; Cronbach, 1951). The level of internal consistency of the depression scale was good (α = .78; Cronbach, 1951).

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encoding condition would have to pretend to pet an animal, or to smell a flower).

As a filled delay participants were asked to complete the SMC and HADS questionnaires for a period of 5 minutes. Participants were reminded about the instructions for the main task (ongoing) task. However, no reminder of the PM task was given on this occasion.

On completion of the PM task, participants were asked if they remembered the instructions that had been given to them by describing what they had been asked to do and recalling the task instructions.

After this, participants had an opportunity to finalize the completion of the SMC and HADS questionnaires and subsequently carried out the remaining assessment tools, specifically: ACE-R, MMSE, LM, TMT and BADL.

Results

Mixed-design Factorial 3-way ANOVAs with Cue-Action Relatedness (related, unrelated) as a within subjects factor and Encoding (verbal, enactment) and Group (younger adults, older adults, aMCI patients) as between-subject factors are reported for our main analysis exploring PM performance as well as performance accuracy and reaction time on the ongoing task as the main outcome measures. All the post-hoc analyses were conducted using a Bonferroni adjustment whereby the critical p value (α) was divided by the number of comparisons being made.

Prospective memory performance

The effects of Method of Encoding and Cue-Action Relatedness on PM performance of aMCI patients, older adults and younger adults were examined first.

There was a significant main effect of Group; F(2,90)=196.13, p<.001, ηp²=.81. Post-hoc tests revealed that PM performance was significantly lower for aMCI patients (M=7, SD=16) than for older adults (M=32, SD=26, 95%CI[-21 to -.07]) or younger adults (M=7, SD=12, 95%CI[-65 to -.5]); healthy older adults also performed poorer than younger adults (95%CI[-.5 to -.36]).

There was also a critical main effect of Method of Encoding, F(1,90)=49.74, p<.001, ηp²=.36, with superior PM performance when enactment was used at encoding (M=58, SD=27) than when the encoding was only verbal (M=41, SD=28).

Importantly, these effects were moderated by an interaction between Group and Method of Encoding, F(2,90)=5.99, p=.004, ηp²=.12. Simple effects analyses revealed that this interaction was such that physical encoding consistently supported a higher performance than verbal encoding especially for aMCI patients (MDifference=-14, 95%CI[-05 to .22]). F(1,90)=19.98, p<.002, ηp²=.10 and even more so for older adults (MDifference=-20, 95%CI[-21 to .38], F(1,90)=46.79, p<.001, ηp²=.33); despite still being evident for younger adults (MDifference=-49, 95%CI[-.10 to .18], F(1,90)=4.83, p=.03, ηp²=.05).

Furthermore, a main effect of Cue-Action Relatedness was identified, F(1,90)=10.82, p<.001, ηp²=.05, with superior PM performance for items in which the cue was semantically as well as the action (M=58, SD=32) than for items in which the cue and action were not semantically related (M=40, SD=29). This effect was moderated by an interaction between Group and Cue-Action Relatedness, F(2,90)=5.99, p=.006, ηp²=.11. Simple effects analyses revealed that this interaction was such that strongly related cues led to a higher performance than unrelated ones. This was especially true for aMCI patients (MDifference=14, 95%CI[.08 to .19]. F(1,90)=20.78, p<.001, ηp²=.19) and older adults (MDifference=15, 95%CI[.09 to .21]. F(1,90)=24.1, p<.001, ηp²=.21); despite still being evident for younger adults (MDifference=-26, 95%CI[-20 to .32]. F(1,90)=16.78, p<.001, ηp²=.46) There were no other significant interactions; all F<4.1, all ηp²<.05.

Results are displayed in Figure 1.

Figure 1. Mean proportion of PM cues eliciting a correct response at the appropriate moment in each Method of Encoding X Cue-Action Relatedness condition for aMCI patients, older adults and younger adults

Performance Accuracy and Reaction Times on the Ongoing Task

The potential effect of encoding modality and cue-action relatedness on ongoing task performance (accuracy and speed) was explored.

Figure 2 displays the mean proportion of correct responses on the ongoing task in each Method of Encoding X Cue-Action Relatedness condition for aMCI patients, older adults and younger adults.

Figure 2. Mean proportion of correct responses on the ongoing task in each Method of Encoding X Cue-Action Relatedness condition for aMCI patients, older adults and younger adults

Importantly, these effects were moderated by an interaction between Group and Method of Encoding, F(2,90)=5.99, p=.004, ηp²=.12. Simple effects analyses revealed that this interaction emerged because despite the beneficial effects of physical encoding being evident for both younger adults (MDifference=-09, 95%CI[.01 to .18], F(1,90)=4.83, p=.03, ηp²=.05) as well as for aMCI patients (MDifference=14, 95%CI[0.05 to .22], F(1,90)=10.09, p<.002, ηp²=.10) it was for older adults that this encoding strategy was particularly beneficial (MDifference=-29, 95%CI[.21 to .38], F(1,90)=46.79, p<.001, ηp²=.34).

Furthermore, a main effect of Cue-Action Relatedness was identified, F(1,90)=1219.77, p<.001, ηp²=.93, with superior ongoing task accuracy when the PM cue was semantically associated with the action (M=93, SD=01) than for items in which the cue and action were not semantically related (M=78, SD=01).

There were no other significant main effects or interactions between the factors; all F<.24, all ηp²<.01.
In this study, we examined the encoding of prospective memory (PM) actions and their retrieval in amnestic mild cognitive impairment (aMCI) patients. Our findings were consistent with previous research on the role of encoding in PM performance, suggesting that enactment encoding is a beneficial strategy for PM tasks in healthy individuals and those with aMCI.

**Figure 3.** Mean response time in milliseconds on the ongoing task for the aMCI patient group, older adults, and younger adults.

**Discussion**

The main goal of this study was to examine the encoding of prospective memory tasks in aMCI patients and to compare their performance with that of healthy older adults and younger adults. Our findings suggest that enactment encoding is a beneficial strategy for PM tasks in healthy individuals and those with aMCI. This strategy appears to support the retrieval of the intended action, thereby improving PM performance in these groups.

**Conclusion**

In conclusion, our study provides new insights into the use of enactment encoding as a beneficial strategy for PM tasks in healthy older adults and aMCI patients. This strategy seems to support the retrieval of the intended action, thereby improving PM performance in these groups. Further research is needed to investigate the generalizability of these findings to other groups and to explore the mechanisms underlying the benefits of enactment encoding in PM tasks.
characteristics of an experimental scenario such as this one. To be precise, one of the limitations of the present study concern the fact that this experiment, as will all the experiments involving the direct intervention of an experimenter, is a social context wherein the experimenter is required to explain the instructions to the participants in greater detail. As such, participants and in particular, those in the enactment condition might be lead to feel an increment in social expectations to perform well on the PM task. This consideration might be particularly important in what concerns the performance of older adults and especially that of those at the early stages of cognitive impairment who are already at greater risk of being affected by stereotype threat, given the comparative nature of the present study which assessed and aimed to tease apart differences between participants of different age groups (cf. Barber, Mather & Gatz, 2015; Chasteen et al., 2005).

**Final remarks**

Consistent with the literature, we have identified a marked and systematic decline in PM performance from young adulthood to healthy and cognitively compromised older adulthood. Encouragingly, the effects of enactment at encoding and of semantic relatedness between cue-action word pairs seem to reduce the detrimental dimension of this effect across all three groups, thus, constituting an evident cumulative advantage across healthy and cognitively compromised aging.

It is now crucial for future studies to explore and extend the findings of this study by attempting to disentangle the multifaceted benefits of this encoding strategy to improve PM performance. For example, to explore the extent to which enactment might lower the RM versus the executive functioning load of PM tasks and how groups with different levels of cognitive compromise might differ in their benefit from this encoding strategy. Such studies may inform the development of easily implementable rehabilitation techniques that might contribute to promote independence at the early stages of the neurodegenerative process.

**References**


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