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Enhancing Prospective Memory in Mild Cognitive Impairment: the Role of Enactment

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Abstract

Introduction: Prospective memory (PM) is a fundamental requirement for independent living which might be prematurely compromised in the neurodegenerative process, namely in Mild Cognitive Impairment (MCI), a typical prodromal Alzheimer's disease (AD) phase. Most encoding manipulations which typically enhance learning in healthy adults are of minimal benefit to AD patients. However, there is some indication that these can display a recall advantage when encoding is accompanied by the physical enactment of the material. The aim of this study was to explore the potential benefits of enactment at encoding and cue-action relatedness on memory for intentions in MCI patients and healthy controls using a behavioural PM experimental paradigm.
Method: We report findings examining the influence of enactment at encoding for PM performance in MCI patients and age and education matched controls using a laboratory based PM task with a factorial independent design.
Results: PM performance was consistently superior when physical enactment was used at encoding and when target-action pairs were strongly associated. Importantly, these beneficial effects were cumulative and observable across both a healthy and a cognitively impaired lifespan as well as evident in the perceived subjective difficulty to perform the task.
Conclusions: The identified beneficial effects of enacted encoding and semantic relatedness have unveiling the potential contribution of this encoding technique to optimize attentional demands through an adaptive allocation of strategic resources. We discuss our findings with respect to their potential impact on developing strategies to improve PM in AD sufferers.

Keywords: Prospective Memory; Mild cognitive Impairment; Enactment; Dementia; Rehabilitation

According to the World Health Organization there are currently 36 million people worldwide suffering from Alzheimer's disease (AD), a figure projected to nearly double by 2030 to 66 million. This neurodegenerative disorder related to the deposition of amyloid $\beta_{1\text{–}42}$ peptide and hyperphosphorylated tau protein in the brain, initially affects the hippocampus and other medial temporal lobe structures, which are brain areas commonly involved in memory processes (cf. de Mendonça, 2012; Blennow, Leon, & Zetterberg, 2006).
Therefore, it is not surprising that this degenerative brain disorder gravely hinders one of most treasured capacities of the human being - autonomy (Bárrios et al., 2013; Lechowski et al., 2004). That is why serious attention needs to be paid to the development of innovative techniques which could positively influence the personal activities of daily living not only for such patients, but also for all the population in general.
Remembering to perform intended activities (e.g. taking medication or attending an appointment) is a fundamental requirement for independent living. Such prospective memory (PM; Meacham & Leiman, 1982) is especially disrupted in AD (Thompson, Henry, Withall, Rendell, & Brodaty, 2011), presenting a severe threat to the individual's health and social relationships while increasing the burden of care (e.g. Eschen, Martin, Gasser, & Kliegel, 2009; Zogg, Woods, Sauceda, Wiebe, & Simoni, 2012).
PM deficits may appear early in the neurodegenerative process (cf. McDaniel, Shelton, Breneiser, Moynan, & Balota, 2011), namely at the stage of Mild Cognitive Impairment (MCI), which usually represents an early stage of Alzheimer's related neurodegeneration, as patients diagnosed with MCI are assumed be at a higher risk of developing AD (de Mendonça, Guerreiro, Ribeiro, Mendes, & Garcia, 2004; Petersen, et al., 2013).
The essential role of PM increases in importance in such contexts as it becomes evident that PM measures are able to capture unique variance in discriminating mild AD and healthy older adults above and beyond other traditional neuropsychological assessment tools, such as measures of retrospective memory, making a higher contribution to prediction of subsequent Alzheimer's disease than retrospective memory up to three years prior to a dementia diagnosis (Jones, Livner & Bäckman, 2006) and capturing unique variance in discriminating mild Alzheimer's disease and healthy older adults above and beyond standard measures of retrospective memory (Blanco-Campal, Coen, Lawlor, Walsh, & Burke, 2009; Duchek, Balota & Cortese, 2006).
It is commonly accepted that aging adversely affects memory function by placing an increased load on attentional processing, thus reducing the amount of processing resources available (cf. Grady & Craik, 2000). PM does not usually constitute an exception to this affirmation (Uttl, 2008). However, given that aging is presumed to be associated with deficits in attentional capacities, the multiprocess framework (McDaniel & Einstein, 2000) predicts that the magnitude of age effects on PM tasks is determined by the extent to which the task depends on automatic processing versus controlled resource-demanding processing.
By the same token an AD-related decline is usually expected in cognitively demanding PM tasks, as it is the case in the present paradigm in which six different cue-action pairs will be presented that will require the performance of six different intended actions (cf. Pereira, Ellis, & Freeman, 2012a). We propose that such tasks require the engagement of attentional resources that are compromised even with very mild AD (cf. Lee, Shelton, Scullin, & McDaniel, 2015; Balota & Faust, 2001). In fact, PM deficits have been identified in participants with amnestic MCI (Tam & Schmitter-Edgecombe, 2013) and with mild AD (Farina, Young, Tabet, & Rusted, 2013) across non-focal PM tasks, i.e. PM tasks in which participants must rely on demanding, strategic monitoring processes to support PM retrieval, given that the processes needed to detect the PM cue do not match the processes required to perform the ongoing task (McDaniel & Einstein, 2007). Notwithstanding, in recent

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studies, even focal PM tasks in which spontaneous retrieval of the PM would be highly expectable (McDaniel & Einstein, 2007) have revealed a generally lower performance for mild AD patients than for their healthy counterparts if the association between the PM cue and the intended action task is not sufficiently fomented (Lee, et al. 2015).

While much recent interest has focused on evaluating the usefulness of external memory aids (e.g. electronic organizers) for patients with memory deficits (Wilson, Emslie, Quirk, & Evans, 2001) these are of limited use for many PM tasks in which an intention must be retrieved when a particular external event occurs, i.e. event-based PM tasks (Einstein & McDaniel, 1990; e.g. give a message to John when you see him) and for which it might be impossible to predict the moment of occurrence.

The level of association or integration between a retrieval cue and its intended action might also be a key factor in determining the likelihood of successfully completing a PM task (Ellis, 1996; McDaniel, Guynn, Einstein and Breneisser, 2004), especially for non-focal cues (Scullin, McDaniel & Einstein, 2010). Moreover, faster response times have been identified for cues semantically related with the respective PM action than for those which were semantically unrelated in healthy young and older adults (Pereira, Ellis & Freeman, 2012a; Maylor, Smith, della Sala & Logie, 2002). This pattern of results reveals that a strong semantic relation between the items might support retrieval by enhancing not only accuracy but also speed. Importantly, this beneficial effect has been identified in non-demented Apolipoprotein E ε4 allele carriers (a known risk factor for developing AD; Driscoll, McDaniel & Guynn, 2005).

Most studies assessing mnemonic rehabilitation strategies in cognitive impairment have generally focussed on retrospective memory (cf. Fish, Wilson & Manly, 2010). These suggest that many of the encoding manipulations that typically enhance learning in young and healthy older adults (e.g. visual imagery, semantic organisation) are of minimal benefit to AD patients (Grandmaison & Simard, 2003). However, there is some indication that these patients can display a recall advantage when encoding is accompanied by enactment (e.g. Charlesworth, Allen, Morson, Burn, & Souchay, 2014).

Given that enactment effects on retrospective memory can be preserved in the early stages of AD, this encoding method represents a potentially important and widely applicable technique for enhancing PM performance in this patient group. In keeping with this analysis, we have recently investigated whether enactment at encoding could improve PM performance and whether the benefits of enactment for prospective remembering were dependent on the relationship between the retrieval cue and its associated action in young and older healthy adults (Pereira, Ellis & Freeman, 2012a, 2012b). Encouragingly, physical encoding and semantic relatedness made independent and, vitally, cumulative contributions to prospective remembering, identified across aging even under highly demanding attentional conditions.

However, the processes involved in PM in early cognitive impairment are today largely unknown, more so the ability to use techniques for enhancing prospective remembering for such patients. This study has addressed this issue by using a laboratory-based method to examine the potentially cumulatively beneficial effects of semantic proximity of the cue with the intended action and of enactment during encoding on subsequent prospective memory performance in MCI patients and healthy controls matched in age and education.

It is anticipated that PM performance of MCI patients will be considerably lower than that of their healthy counterparts as PM measures continue to be consistently pinpointed as particularly early and sensitive indicators of the expansion of neurodegenerative processes (cf. McDaniel, et al., 2011), a pattern which is identifiable not only across resource demanding non-focal PM tasks (cf. Tam & Schmitter-Edgecombe, 2013; Farina, et al. 2013) but also in focal PM tasks which facilitate spontaneous retrieval (Lee et al., 2015).

In fact, as PM measures seem to be sensitive to the cognitive effects of early MCI-AD, capturing unique variance in discriminating mild AD and healthy older adults above and beyond other traditional neuropsychological assessment tools, such as measures of retrospective memory (Blanco-Campal, et al., 2009; Duchek, Balota & Cortese, 2006; Jones et al., 2006) we hypothesise that MCI patients will experience greater difficulties in performing the PM task in this paradigm than healthy controls.

Notwithstanding, it is expected that PM might be considerably improved by the use of enactment at encoding and also by a strong semantic relatedness between cue-action word pairs. To be precise, a better PM performance when physical enactment is used during encoding and for sets of cue-action pairs in which the cue is semantically associated with the action to be performed are anticipated. These effects might also be cumulative (cf. Pereira, et al., 2012a, 2012b) and not only beneficial for MCI patients but evident as well in healthy participants (cf. Charlesworth, et al., 2014).

Furthermore, allocation of attentional resources between the PM and ongoing tasks may be determined by each individual at the outset of a PM task according to personal metacognitive awareness of prospective remembering abilities and adapted to the perceived difficulty and characteristics of each task (e.g. Marsh, Hicks, & Cook, 2005, 2006). To be precise the amount of attention that is devoted to both the ongoing and the PM task might be determined by metacognitive factors such as how difficult or easy the participant believes it will be to succeed at both tasks. The attention allocated to the prospective task will vary, depending on the local characteristics of the perceived demands of the task. Marsh and colleagues have explored this by manipulating the difficulty of the task and subsequently assessing the impact of such manipulation on general performance (measured in reaction times and accuracy) of both ongoing and PM tasks.

We believe it would be important to explore whether such perceived difficulty would be affected by our experimental manipulations and consequently potentially influence such attentional allocation policies. We will explore this possibility through the analysis of self-reported measures of perceived difficulty of the task identified before and after performance of the main task. It is expected that the pattern of results regarding such self-reported measures will reproduce that of the actual task performance hence potentially reflecting an adaptive allocation of strategic attentional resources (cf. Meeks, Hicks, & Marsh, 2007).

To recapitulate, it is predicted that PM performance of MCI patients will be generally lower than that of their healthy counterparts (cf. Blanco-Campal, et al., 2009). Notwithstanding, it is expected that PM might be considerably improved by the use of enactment at encoding and also by a strong semantic relatedness between cue-action word pairs. These effects are hypothesised to be independent and therefore cumulatively beneficial (cf. Pereira, et al., 2012a, 2012b) for both healthy and cognitively impaired participants (cf. Charlesworth, et al., 2014). Finally, self-reported measures of perceived difficulty of the task might also mirror the pattern of actual task performance (cf. Meeks, et al., 2007).

We argue that this pattern of results would be consistent with a multi-system account of the enactment effect (Engelkamp, 1998; Engelkamp & Jahn, 2003) where the effect of semantic relatedness would be mediated by a conceptual system and the enactment effect would be essentially dependent on a non-verbal motor system. As different processes are thought to be involved in each of these effects it is expected that they should be independent. Consequently, it is anticipated that PM performance will be advantageously influenced by the use of enactment at encoding as motoric encoding might grant supplementary item-specific information, complementary to the support of the conceptual system provided by the semantic proximity of the cue-action word pair (cf. Engelkamp & Jahn, 2003; Feyereisen, 2009) hence increasing the distinctiveness of the item and reinforcing the integration between the two components. To be precise, we predict that the two manipulations will contribute independently and cumulatively to reduce the general attentional demands of the PM task not only by increasing the distinctiveness of the item but also by reinforcing the integration between the two components (cue and intended action; cf. Pereira, et al., 2012a).

Method

Participants

One hundred and twenty eight adults volunteered to participate in this experiment, of which 64 were MCI patients aged 48-95 years (*M* = 72.97, *SD* = 8.93) having spent 2-20 years in full time education (*M* = 9.19, *SD* = 5.64) and 64 age and education matched healthy older adults aged 49-89 years (*M* = 69.72, *SD* = 9.8) having spent 3-20 years in full time education (*M* = 10.86, *SD* = 5.45). All volunteers who manifested a desire to participate in the experiment were native speakers of Portuguese. MCI participants were patients attending a Memory Clinic or a Hospital Neurology Outpatient Clinic. Healthy control participants were volunteers from the local community who were recruited opportunistically.

The study was approved by the Ethics Committee of Hospital de Santa Maria. Before any procedure, participants gave written informed consent. It was made clear that potential participants would not be excluded on the grounds of age, gender, disability, or first language.

Inclusion criteria for MCI group were based on European Consortium on Alzheimer's Disease (Portet et al., 2006). For reasons of sample homogeneity, only patients with amnestic (single domain) type of MCI (single domain aMCI - with episodic memory impairments) were recruited:

1) Cognitive complaints and cognitive decline during the last year, reported by the patient and/or family.
2) Objective memory impairment, as defined by a low score in immediate free recall of story A from logical memory (LM) subtest of Wechsler Memory Scale.
3) Maintained activities of daily living or slight impairment in instrumental activities of daily living (IADL), as defined by no more than one item of IADL changed.
4) Absence of dementia, according to DSM-V and normal Mini Mental State Examination (MMSE) scores.

Inclusion criteria for healthy controls:

1) Absence of cognitive complaints.
2) Normal score in immediate free recall of story A from LM subtest of Wechsler Memory Scale.
3) Maintained activities of daily living as defined by IADL (no item of IADL changed).
4) Absence of dementia, according to DSM-V and normal MMSE scores.

Exclusion criteria for all groups:

1) History of alcohol abuse or recurrent substance abuse or dependence.
2) Other neurological, psychiatric or medical disorders that might induce cognitive deficits.
3) Major depressive episode according to DSM-V, or severe depressive symptoms as reflected by a score in the 30 item Geriatric Depression Scale (GDS30)>20.

Design

A between subjects design was employed with three factors: Cognitive Status (MCI, Controls) x Type of Cue-Action pair (verbal, motoric) x Type of Encoding (related, unrelated). The effect of these variables was examined on five measures: PM performance (proportion of PM cues responded to correctly), performance accuracy on the ongoing word-sorting task, response latency to non-PM cue items on the ongoing task, perceived difficulty pre-task, perceived difficulty post-task.

A between-subjects design was specifically chosen to ensure the avoidance of not only practice effects but also carry over effects (cf. Greenwald, 1976; Field, 2013). To be precise, the persistent effects of the encoding manipulation involving the motoric enactment of the action to be performed have 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). Consequently, such carry over effects would be problematic to avoid even by counterbalancing or by increasing in time the separation of the sequences of administration of the experimental conditions.

Materials

MCI patients underwent a standard protocol with clinical history, neurological examination, laboratorial evaluation, and brain imaging (CT scan or MRI scan; Knopman et al., 2001), and a detailed neuropsychological evaluation with the Battery of Lisbon for Evaluation of Dementia (Garcia, 1984).

All participants were submitted to the Portuguese versions (de Mendonça & Guerreiro, 2008) of the following instruments:

Mini Mental state Examination (MMSE; Folstein, Folstein, & McHugh, 1975), MMSE is widely used for brief evaluation of the mental state and screening of dementia. It is an 11-question measure that tests five areas of cognitive function: orientation, registration, attention and calculation, recall, and language. The maximum score is 30. A score of 23 or lower is usually indicative of cognitive impairment. The MMSE takes 5-10 minutes to administer and is effective as a screening tool for cognitive impairment with older, community dwelling, hospitalized and institutionalized adults. Since its creation in 1975, the MMSE has been validated and extensively used in both clinical practice and research. The normative cut-off values for the Portuguese population adjusted to education were used. Participants should score above 22 if they had ≤ 11 years of education, or above 27 if they had > 11 years of education (Guerreiro, Silva, & Botelho, 1994).

Logical Memory (LM) is a subtest from the Wechsler Memory Scale (Wechsler, 1969), which is included in the Battery of Lisbon for the Evaluation of Dementia (Garcia, 1984). This subtest assesses narrative memory under a free recall condition. One short story was presented orally. The participants were asked to retell the story from memory immediately after hearing it using as many of the same words of the original passage as they can remember, thus encouraging word-for-word recall. Memory was considered impaired when the subjects scored on immediate free recall of story A of the test at least 1.5 standard deviation (SD) below the normative value for age and education.

Trail making test (TMT; Army Individual Test Battery, 1944) is a neuropsychological test of visual attention and task switching. Both parts of the Trail Making Test consist of 25 circles distributed over a sheet of paper. In Part A, the circles are numbered 1 – 25, and participants had to draw lines to connect the numbers in ascending order. In Part B, the circles include both numbers (1 – 13) and letters (A – L); as in Part A, participants had to draw lines to connect the circles in an ascending pattern, but with the added task of alternating between the numbers and letters. The participants were instructed to connect the circles as quickly as possible, without lifting the pen or pencil from the paper. Participants are timed as they connect the "trail." If an error was made it would be pointed out immediately and the participant would be allowed to correct it. The correction of errors is included in the completion time for the task. The Trail Making Test requires cognitive alternation reflecting executive functioning, although other cognitive abilities, such as psychomotor speed and visual scanning, are also required for the successful completion of the test (Lezak, Howieson, & Loring, 2004; Tombaugh, 2004).

Instrumental Activities of Daily Living (IADL; Lawton & Brody, 1969) is an 8-item questionnaire which assesses independent living skills. It is particularly useful for identifying how a person is functioning at the present time and for identifying improvement or deterioration over time. This instrument is intended to be used among older adults, and may be used in community, clinic, or hospital settings. However, the instrument is not useful for institutionalized older adults. There are 8 domains of function measured with the Lawton IADL scale. The IADL score reflects the number of impaired activities and ranges from 0 (no impairment) to 8 (changes in all items). Items were classified as not applicable if the activity had never been done before or if the subject stopped doing it for reasons other than cognitive difficulty. Activities of daily living were considered preserved if no item from the IADL scale suffered any change, or mildly affected if only one item from the IADL scale was altered (Pantoni et al., 2005).

Satisfaction with Life Scale (SWLS; Diener, Emmons, Larsen, & Griffin, 1985) is a short 5-item instrument designed to measure global cognitive judgments of satisfaction with one's life. The scale requires participants to respond by answering on a scale ranging from 1 (Strongly disagree) to 7 (Strongly agree) in reference to how much they agree or disagree with each statement. The scale usually requires only about one minute of a respondent's time. This scale assesses global life satisfaction reflecting subjective well-being.

Subjective Memory Complaints Scale (SMC; Schmand, Jonker, Hooijer & Lindeboom, 1996) is a 10-item questionnaire in which participants are asked to respond to questions on subjective memory complaints. The scale requires participants to answer the 10 individual items concerning difficulties in daily-life memory tasks, with total scores ranging from 0 (absence of complaints) to 21 (maximal complaints score). These items are considered representative of common memory complaints. The scale may be used with healthy, medically ill and mild to moderately cognitively impaired older adults. It has been extensively used in community, acute and long-term care settings. The validity and reliability of the tool have been supported through both clinical practice and research.

Geriatric Depression Scale (GDS; Yesavage et al., 1983) is a self-report depression assessment scale used specifically to evaluate depression in the elderly. It is a 30-item questionnaire in which participants are asked to respond by answering yes or no in reference to how they felt over the past week. The GDS may be used with healthy, medically ill and mild to moderately cognitively impaired older adults. It has been extensively used in community, acute and long-term care settings. The validity and reliability of the tool have been supported through both clinical practice and research. The 30 item version was used for this study.

PM task.
The experimental session involved a practice phase for the ongoing task, followed by instructions for the PM task, a filled delay period and the main ongoing task containing the PM cues. The ongoing task was a computer-based activity in which participants had to sort a series of nouns into one of two different categories (natural or man-made). A version with 20 nouns was prepared for a practice phase. For the main ongoing task a set of 100 nouns (94 new and 6 cue words) was created. For the PM cue-action pairings two lists of 6 noun-verb pairs were compiled: one list comprised 6 related noun-verb pairs and the other 6 unrelated pairs. For the related list noun-action words with a moderate semantic association (FAR – range = 3.2 - 4.8; Marques, 2002) were selected. The items were the Portuguese equivalent to: piano – to play; brush – to comb; purse – to save; shirt – to dress; spoon – to eat; saw – to cut. In the unrelated list the nouns from the related list were re-assembled with the verbs to create new pairs with no obvious associative relation between them: (e.g. brush – to play). The word pairs had normative medium values of familiarity (range = 1 to 1.7), imaginability (range = 5.3 to 6.6) and concreteness (range = 6 to 6.8); Marques (2004, 2005).

Assessment of Subjective Difficulty
Perceived main task difficulty was assessed through two self-report questionnaires designed to establish subjective task difficulty before ($\alpha = .8$) and after ($\alpha = .6$) main task performance. The measures were constituted by three items assessing perceived difficulty independently for ongoing task performance, PM task performance and global main task performance using a 9 point Likert scale.

Procedure
Participants were tested individually. They were informed that the session started with a practice task involving a simple computer-based activity in which they would have to allocate 20 different words into one of two different categories - natural or man-made -by pressing the appropriate key on the serial response box (left key ‘1’ for manmade and right key ‘5’ for natural). Items remained on screen until the participant produced a response.
This was followed by instructions relevant to the prospective task. Participants were presented with a set of 6 cue-action word pairs to learn. These formed the content of the prospective memory task. Half of the participants were presented with the 6 related cue-action pairs and the remainder were presented with the 6 unrelated cue-action pairs.
In the verbal encoding condition, the 6 cue-action pairs appeared on the computer screen, one at a time and participants were asked to read each one aloud three times. Participants in the enactment encoding condition were given the same information. However, in addition to reading the instructions aloud they were asked to physically perform the action on the imagined designated object (e.g. participants in the related cue-action condition would have to pretend to comb their hair, or play the piano, whereas in the unrelated cue-action condition would have to pretend to play with a brush, or to comb a piano). Contrary to the practice tasks and to the main on-going task, the encoding phase was not self-paced. Instead, it was controlled by the computer, lasting 6 seconds for each of the repetitions in a total of 18 seconds per cue-action pair.
All participants were informed that they would later be asked to perform a word-sorting task similar to the one performed during the practice phase. They were told that they would see a fixation cross in the centre of the computer screen for 3 seconds and that this would be followed by a sequence of words presented one at a time. As in the practice phase, participants were asked to decide if words belonged to the category “man-made” or “natural”, by pressing the appropriate key. They were then provided with the instructions for the prospective memory task. Specifically, they were informed that if they saw a previously presented object (cue) word, from any one of the six word-pairs that they had learned, then they should press the middle ‘3’ key on the serial response box and to say aloud the second word of that pair (i.e. the action). After this they should continue the word-sorting task by pressing the appropriate key to indicate whether the object was natural or man-made. Participants were asked to respond to the task as quickly as possible without sacrificing accuracy.
At this point participants were asked to complete a self-report measure of the perceived difficulty of the task that they were about to perform.
Following PM task instructions, participants were asked to complete the SMC and SWLS questionnaires for a period of

5 minutes. Instructions for the main word-sorting (ongoing) task were then re-presented. However, no reminder of the prospective memory task was given on this occasion. The 100 words (96 new, 6 PM cues) of the word-sorting task were then presented. Items remained on screen until the participant made a key press response. In this word set the cue words were presented in the 8th, 20th, 44th, 55th, 82nd, and 99th position to ensure that they were relatively evenly spread across the set in such a way that a participant could not easily anticipate the exact position in which the next cue would appear. On completion of the word-sorting 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 as many of the 6 cue-action word pairs as possible.
At this point participants were asked to complete a self-report measure of the perceived difficulty of the task performed.
After this participants had an opportunity to finalize the completion of the SMC and SWLS questionnaires and subsequently carried out the remaining assessment tools, specifically: MMSE, LM, IADL, TMT and GDS.

Results
All data regarding the analysis of characterization variables (cognitive ability, emotional status and demographic variables) as well as of the PM task were explored using a 2 x 2 x 2 ANOVA, with Cue-Action Relatedness (related, unrelated), Method of Encoding (verbal, enactment), and Cognitive Status (healthy controls, MCI patients) as between-subject factors, unless noted otherwise.

Table 1. Mean Age and Education (and Standard Deviation) in years and mean scores (and Standard Deviation) in neuropsychological tests, global evaluation scales, functional scales, and depressive symptoms for MCI patients and healthy controls. Significant differences among the groups were assessed with Independent Samples Mann-Whitney U- test for all the measures. *ns* = not statistically significant.

	Healthy Controls	MCI Patients	*p*-values
N	64	64	
Age (years)	69.72 (9.8)	72.97 (8.93)	*ns*
Education (years)	10.86 (5.45)	9.19 (5.64)	*ns*
MMSE	29.02 (.85)	25.84 (3.51)	<.001
LM	14.79 (3.51)	8.57 (5.27)	<.001
TMT (B-A)	67.91 (46.56)	144.32 (90.52)	<.001
SWLS	23.30 (6.53)	26.59 (6.29)	.003
SMC	8.11 (4.00)	9.13 (3.91)	*ns*
GDS	7.97 (5.23)	9.54 (4.68)	*ns*

Preliminary Analysis
A preliminary exploratory analysis of our data was conducted to ensure a uniform distribution of participants across the different experimental conditions regarding not only demographic variables but also general cognitive ability and emotional status.
This analysis revealed that there were no statistical differences among the different Cue-Action Relatedness (related, unrelated), Method of Encoding (verbal, enactment), and Cognitive Status (healthy controls, MCI patients) conditions regarding demographic variables, depressive symptomatology or subjective memory complaints; all Fs < 3.09, all $\eta_p^2 < .03$.
Notwithstanding, MCI patients presented significantly lower scores on all the neuropsychological tests and yet a generally higher life satisfaction than healthy controls. To specify performance on MMSE was significantly lower for MCI patients (M = 25.84, SD = 3.51) than for healthy controls (M = 29.02, SD = .85, $F(1, 120) = 54.13$, $p < .001$, $\eta_p^2 = .32$). A similar pattern was observed on LM with MCI patients (M = 8.57, SD = 5.27) performing significantly lower than healthy controls (M = 14.79, SD = 3.51, $F(1, 120) = 60.64$, $p < .001$, $\eta_p^2 = .36$). MCI patients were also consistently slower (M = 144.32, SD = 90.52, $F(1, 120) = 34.32$, $p < .001$, $\eta_p^2 = .25$) than healthy controls (M = 67.91, SD = 46.56) on the TMT (B-A). Interestingly, this neurocognitive pattern was accompanied by the reporting of a generally higher life satisfaction for MCI patients (M = 26.59, SD = 6.29) in contrast with healthy controls (M = 23.3, SD = 6.53, $F(1, 120) = 7.97$, $p = .006$, $\eta_p^2 = .06$) on SWLS.

Prospective memory performance
The effects of Method of Encoding and Cue-Action Relatedness on prospective memory performance of MCI patients and healthy controls were examined first. The mean proportion of cues that elicited a correct response at the appropriate moment in each Method of Encoding x Cue-Action Relatedness x Cognitive Status condition was calculated, and is displayed in Figure 1.

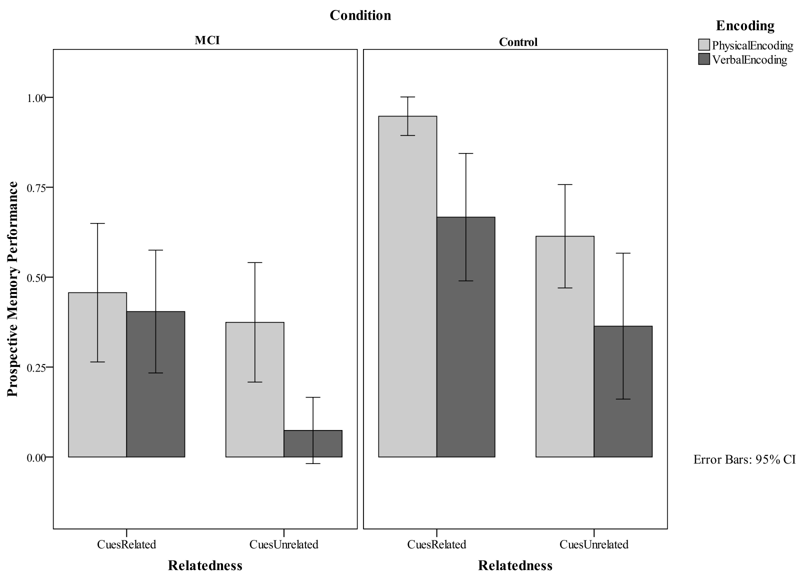

Figure 1. Mean proportion of PM cues eliciting a correct response at the appropriate moment in each Method of Encoding X Cue-Action Relatedness condition for MCI patients and healthy controls.

There was a significant main effect of Cognitive Status; $F(1, 120) = 37.66$, $p < .001$, $\eta_p^2 = .24$. As expected, prospective memory performance was significantly lower for MCI patients (M = .33, SD = .33) than for healthy controls (M = .65, SD = .35).

There was also a reliable main effect of Method of Encoding, $F(1, 120) = 17.88$, $p < .001$, $\eta_p^2 = .13$, with superior PM performance when enactment was used at encoding ($M = .60$, $SD = .35$) than when the encoding was only verbal ($M = .38$, $SD = .37$).
A main effect of Cue-Action Relatedness was also identified, $F(1, 120) = 25.24$, $p < .001$, $\eta_p^2 = .17$, with superior PM performance for cue-action pairs in which the cue was semantically associated with the action ($M = .62$, $SD = .36$) than for pairs in which the cue and action were not semantically related ($M = .36$, $SD = .35$). There were no other significant interactions between the factors; all Fs < 1.78, all $\eta_p^2 < .01$.

Prospective memory performance conditional on retrospective recall of PM task content
Participants may perform poorly in a PM task, not necessarily because of a PM failure but because of a retrospective memory failure i.e., failure to recall the content of the PM task (cf. Maylor et al., 2002; Zhou, et al., 2012). Therefore, PM data was re-analysed subsequently, using only cue-action pairs that were accurately recalled after the task. The mean proportion of intended action words produced at the appropriate moment in the PM task was calculated for each experimental condition, excluding any items that were not remembered retrospectively. The pattern was precisely identical to that observed when recall of cue-action pairs was not taken into account suggesting that the effects of semantic relatedness and enactment on PM are unlikely to be mediated by differences in retrospective memory for intention content. To specify, data revealed that the proportion of cue-action words recalled differed across Cognitive Status, $F(1, 120) = 32.01$, $p < .001$, $\eta_p^2 = .21$, with superior PM performance for healthy controls ($M = .72$, $SD = .36$) than for MCI patients ($M = .37$, $SD = .38$). Performance was also superior for item encoded through enactment ($M = .65$, $SD = .36$) than for verbally encoded ones ($M = .44$, $SD = .43$; $F(1, 120) = 10.99$, $p = .001$, $\eta_p^2 = .08$), a pattern that was also maintained for semantically related items ($M = .65$, $SD = .39$) in contrast with semantically unrelated ones ($M = .45$, $SD = .41$; $F(1, 120) = 10.82$, $p = .001$, $\eta_p^2 = .08$). There were no other significant interactions between the factors; all Fs < 1.26, all $\eta_p^2 < .01$.

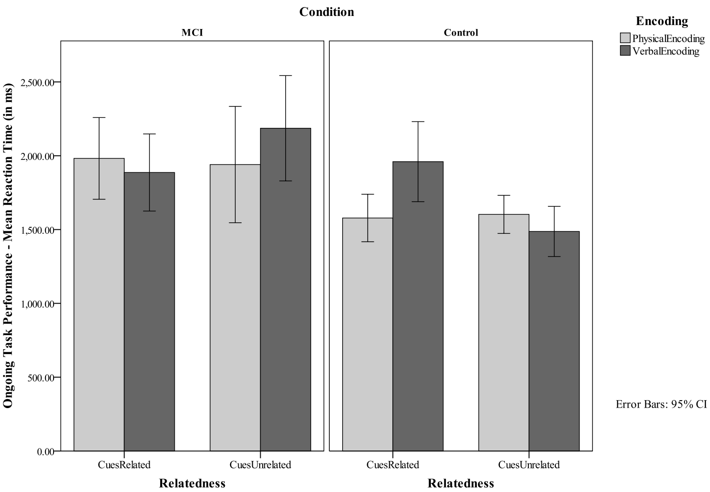

Figure 2. Mean proportion of correct responses on the ongoing task in each Method of Encoding X Cue-Action Relatedness condition for MCI patients and healthy controls.

Performance Accuracy and Reaction Times on the Ongoing Task
By examining the possible influence of encoding modality and cue-action relatedness on ongoing task performance we can gain some insight into the relative strategic demands of the PM task across conditions.

This enables us to make a preliminary investigation of the proposal that semantic relatedness and enactment at encoding might facilitate PM performance by reducing the demand for strategic processing to monitor for and respond appropriately to the cues.
Figure 2 displays the mean proportion of correct responses made on the ongoing task. There was a significant effect of Cognitive Status on accuracy of responses on the ongoing task ($F(1, 120) = 10.90$, $p = .001$, ηp2 = .08) with healthy controls ($M = .96$, $SD = .03$) consistently performing the task more accurately than MCI patients ($M = .93$, $SD = .06$).
There were no other significant main effects or interactions between the factors; all Fs < 2.22, all $\eta_p^2 < .02$.

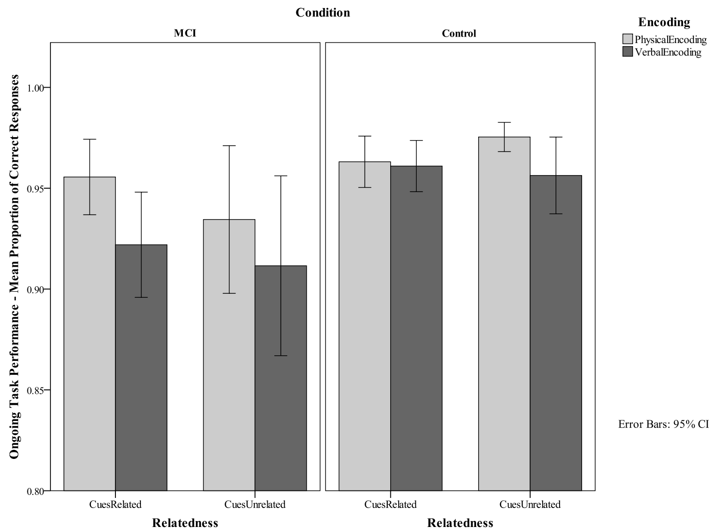

Figure 3. Mean response time in milliseconds on the ongoing task in each Method of Encoding X Cue-Action Relatedness condition for MCI patients and healthy controls.

Figure 3 displays the mean time taken to respond on ongoing task trials (excluding the time taken to react to the PM cues and the two items following a PM cue). There was a significant effect of Cognitive Status on speed of responses on the ongoing task $F(1, 120) = 14.83$, $p < .001$, $\eta_p^2 = .11$) with healthy controls ($M = 1657.00$, $SD = 392.99$) performing the task significantly faster than MCI patients ($M = 1998.70$, $SD = 609.40$). However, this main effect was mediated by a 3-way interaction between the three factors. Simple two-way interactions analysis revealed that there was a significant interaction between Method of Encoding and Relatedness for healthy controls ($F(1, 120) = 3.93$, $p = .05$) which was not emerging in MCI patients. Simple effects analyses regarding the performance of healthy controls revealed that this interaction was such that for Related Cues mean reaction time to the main task was significantly faster when enactment was used at encoding ($M = 1578.20$, $SD = 301.77$, $F(1,120) = 4.63$, $p < .05$, $\eta_p^2 = .04$) than when encoding was only verbal ($M = 1959.99$, $SD = 508.79$). There were no other significant interactions between the factors; all Fs < 2.96, all $\eta_p^2 < .03$.

Subjective Difficulty
Subjective difficulty of the task was self-reported before as well as after the main task was performed. Table 2 displays the mean perceived difficulty (and standard deviation) reported by participant before and after performing the main task in each Method of Encoding x Cue-Action Relatedness condition for MCI patients and healthy controls.

Table 2. Mean Perceived Difficulty (and Standard Deviation) reported by participant before and after performing the Main Task in each Method of Encoding x Cue-Action Relatedness condition for MCI patients and Healthy controls

	Verbal encoding		Enactment at encoding	
Perceived Difficulty	Related pairs	Unrelated pairs	Related pairs	Unrelated pairs
Pre-Task				
Healthy controls	.47 (.18)	.48 (.16)	.35 (.18)	.44 (.23)
MCI patients	.44 (.23)	.66 (.19)	.44 (.18)	.50 (.12)
Post-Task				
Healthy controls	.42 (.16)	.53 (.11)	.26 (.17)	.41 (.19)
MCI patients	.36 (.19)	.62 (.19)	.47 (.26)	.51 (.17)

Interestingly, the pattern of results regarding general PM task performance is replicated in the subjective difficulty reported by the participants prior to the performance of the actual task. In effect, the task was consistently perceived as more difficult by MCI (M = .51, SD = .20, F (1,120) = 5.31, p = .02, η_p^2 = .04) patients than by healthy controls (M = .43, SD = .19). Furthermore, enacted encoding (M = .43, SD = .19) contributed to a lower perceived difficulty (F (1,120) = 5.46, p = .02, η_p^2 = .04) than verbal encoding (M = .51, SD = .21). Finally, a high relatedness of the cue with the intended action lowered perceived task difficulty (M =.42, SD = .19, F (1,120) = 8.43, p = .004, η_p^2 = .07) when contrasting context in which the items where unrelated (M = .52, SD = .19). There were no significant interactions between any of the factors; all Fs < 3.24, all η_p^2 < .03.

Notwithstanding, this pattern of results has changed after the performance of the task, when significant effects have emerged regarding Cognitive Status, with MCI patients perceiving the task as considerably more difficult (M = .49, SD = .22, F (1,120) = 6.86, p = .01, η_p^2 = .05) than healthy participants (M = .40, SD = .18). Furthermore, the task was perceived as less difficult when participants had encoded cues through enactment (M = .41, SD = .22, F (1,120) = 4.73, p = .03, η_p^2 = .04) than when encoding was verbal (M = .48, SD = .20). However, this effect was mediated by an interaction between the two factors. Simple effects analyses revealed that, for healthy controls, the use of enactment at encoding contributed to a generally lower perceived task difficulty (M = .33, SD = .19, F (1,120) = 8.03, p = .005, η_p^2 = .06) than verbal enactment (M = .48, SD = .15). Notwithstanding this pattern was not observed in MCI patients. Nevertheless, the unmediated effect of Relatedness continued to be identified, with related cues generally contributing to a lower perceived task difficulty (M = .38, SD = .21, F (1,120) = 18.24, p < .001, η_p^2 = .13) than unrelated ones (M = .52, SD = .18). There were no other significant interactions between the factors; all Fs < 3.69, all η_p^2 < .03

Discussion

The aim of this study was to examine the influence of enactment at encoding and cue-action relatedness on memory for intentions in MCI patients and healthy controls using a laboratory based PM task.

It was hypothesised that MCI patients would experience greater difficulties in performing the PM task in this paradigm than healthy controls as PM measures seem to be able to capture unique variance in discriminating mild AD and healthy older adults above and beyond other traditional neuropsychological assessment tools, such as measures of retrospective memory (Blanco-Campal, et al., 2009; Duchek, Balota & Cortese, 2006; Jones et al., 2006). To specify, we have predicted a general decline in performance associated with cognitive impairment given that cognitively demanding PM tasks, such as the task proposed by this study (cf. Pereira, et al., 2012a) require the engagement of attentional resources that are compromised even with very mild AD (cf. Lee, et al., 2015; Balota & Faust, 2001). Our predictions were supported by our results, hence contributing to the growing body of evidence identifying PM as a particular early and sensitive indicator of the expansion of neurodegenerative processes (cf. McDaniel, et al., 2011; Lee, et al., 2015). Importantly, the results from our experiment have demonstrated that the benefits of enactment over verbal encoding, that have been observed in PM performance for healthy young and older adults (cf. Pereira, et al., 2012a, 2012b), were also identifiable in Mild Cognitive Impairment.

Moreover, results have extended previous research, regarding the crucial role of semantic proximity between the cue to be performed and the respective intended action (cf. McDaniel et al., 2004; Scullin et al., 2010) as after verbal encoding, PM performance was better for both MCI patients and healthy controls when there was a close semantic association between the retrieval cue and the intended action than when unrelated cue-action pairings were used. This study has thus provided further support for the benefits of cue-action relatedness on PM performance by revealing that PM performance of MCI patients, as well as that of healthy adults, can be sustained by this encoding technique.

Vitally, an independent and cumulative pattern of results concerning the advantageous effect of the use of enactment at encoding and of a strong semantic relatedness between items was identifiable for both MCI patients and healthy controls.

Interestingly, this pattern of results was not only identified in objective performance but also reflected in subjective perceived difficulty of the actual task. As attentional resources between the PM and ongoing tasks may be allocated by each individual before actual task performance adapted to the perceived difficulty and characteristics of each task (e.g. Marsh, Hicks, & Cook, 2005, 2006) such finding might be particularly important in the exploration of experimental manipulations that can optimize such adaptive allocation of strategic attentional resources (cf. Meeks, et al., 2007).

Future studies concerned with addressing this problematic would explore whether this subjective measure is effectively reflected on the allocation of attentional resources of healthy older adults and MCI patients when manipulating the difficulty of the task and subsequently assessing the impact of such manipulation on general performance (measured in reaction times and accuracy) of both ongoing and PM tasks.

Finally, we argue that this pattern of results seems to indicate that different systems could be playing a part in the increment identified in PM performance in contexts where enactment is used at encoding and there is a strong semantic relatedness between items. In fact, not only conceptual processes but also motor and sensorial processes might be put into play when enactment is used at encoding of a PM action. To specify, such pattern of results would be consistent with a multi-system account of the enactment effect (Engelkamp, 1998; Engelkamp & Jahn, 2003) where the effect of semantic relatedness would be mediated by a conceptual system and the enactment effect would be essentially dependent on a non-verbal motor system. As different processes are thought to be involved in each of these effects it is expected that they should be independent. Therefore, the beneficial effects of the use of enactment at encoding, identifiable for both MCI patients and healthy controls might emerge due to this motoric encoding having granted additional item-specific information about the cue-action word pair, even in contexts where the cue and the intended action were semantically related (cf. Engelkamp & Jahn, 2003; Feyereisen, 2009) which might have contributed to an enhanced salience of the item as well as to a more solid integration of the two components. Given the absence of an interaction between the two factors it is possible that the contribution of the two manipulations might indeed have been an independent one. Consequently, we propose that not only by increasing the distinctiveness of the item but also by and reinforcing the integration between the two components (cf. Pereira, et al., 2012a) the two manipulations have cumulatively contributed to reduce the considerably high attentional demands of this PM task and consequently improve PM performance. In fact, considering the identified pattern of perceived subjective difficulty of the task it is possible that a metacognitive awareness of the overall demands of the PM task may have influenced the ‘attentional allocation policy’ that participants adopted prior to task performance, through an increase in the allocation of resources to support PM performance (Marsh et al., 2005).

Notwithstanding, it is essential to explore this possibility in further depth by not only exploring the allocation of attentional resources of healthy older adults and MCI patients but also by attempting to disentangle the contribution of both factors to PM performance of healthy older adults and MCI patients. In actual fact, despite our option to use a between-subjects design which was specifically chosen to ensure the avoidance of carry over effects we cannot be sure, for example, that participants in the verbal encoding condition have not imagined performing the movement which may have activated the motoric system. Future studies should consider this avenue of research to further clarify this problematic.

Another limitation of our study concerns the fact that the literacy levels of our participants might be considered, at first glance, relatively low. However, our sample is reflective of the general literacy levels of the current Portuguese population which presents global literacy rates of only 80.5% in ages 65 and above with this percentage plummeting to 75.5 in females aged 65 and above according to the Portuguese Institute for National Statistics (Instituto Nacional de Estatística, 2014). Notwithstanding, such literacy levels should be taken into consideration when considering the implication of our results.

Final Remarks

We have demonstrated that PM performance was significantly improved for MCI patients and healthy controls when physical enactment was used during encoding in contrast with when encoding was merely verbal. Furthermore, semantically associated cue-action word pairs generally contributed to a better PM performance in contrast with sets of cue-action pairs in which the cue was semantically unrelated with the intended actions. Interestingly, an interaction between these two factors was not observed. Therefore, the multi-system account proposed by Engelkamp (1998; Engelkamp & Jahn, 2003) seems to be an effective model in explaining this pattern of results since it proposes that different independent (and hence cumulative) beneficial processes are involved in these effects.

Further studies might contribute to the clarification of the precise role of enactment at encoding in PM facilitation, not only in healthy adults but, importantly in cognitively impaired ones and hence inform the development of widely applicable rehabilitation strategies crucial for sustaining autonomy at the early stages of the neurodegenerative process by leading to the development of a practical, cost effective and widely applicable rehabilitation technique to enhance PM in mild cognitively impaired older adults.

Such a method would ideally be self-implemented after an initial instructional session based on previous findings regarding naturalistic studies with healthy adults (cf. Pereira, 2010). Patients would execute a daily identification of intended actions on a diary which they would subsequently encode through enactment, by motoric simulation of the intended action. When using this encoding strategy particular emphasis should be giving to actions which would be less associated with the context of performance as such actions would, as identified across our results, be less likely to be remembered in the absence of such manipulation.

Considering that PM may be particularly affected at an early stage in the development of Alzheimer’s Disease (Costa, et al., 2010; Lee et al., 2015), constituting a great object of concern, distress and even frustration not only for these patients but also for their carers (Eschen et al., 2009), and placing at risk individual’s social relationships and maintenance of independence (Costa, Carlesimo, & Caltagirone, 2012), the use of motoric encoding might constitute an extremely advantageous tool for PM rehabilitation in prodromal Alzheimer’s Disease with positive repercussions in the achievement of a better quality of life for healthy and cognitively impaired older adults.

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