

Improving Prospective Memory in Healthy Older Adults and Individuals with Very Mild Alzheimer's Disease

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OBJECTIVES: To test the utility of a memory-encoding strategy for improving prospective memory (PM), the ability to remember to execute future goals (e.g., remembering to take medications), which plays an important role in independent living in healthy older adults and those with very mild Alzheimer's disease (AD).

DESIGN: Participants were randomly assigned to an encoding strategy condition or a standard encoding condition.

SETTING: A longitudinal study conducted at an Alzheimer's disease research center. Testing took place at the center and in a university testing room.

PARTICIPANTS: Healthy older adults (Clinical Dementia Rating (CDR) = 0.0, n = 38) and those classified as being in the very mild stage of AD (CDR = 0.5, n = 34).

INTERVENTION: A simple strategy ("If I see Cue X, then I will perform Intention Y") was used to strengthen PM encoding and reduce the probability of forgetting to execute one's future plans.

MEASUREMENTS: PM was assessed using Virtual Week, a laboratory task that requires the simulation of common PM tasks (the types of tasks performed in everyday life), such as taking one's medication at breakfast.

RESULTS: The encoding strategy significantly reduced PM failures in healthy older adults and those with very mild AD and was effective regardless of the individual's episodic memory ability.

CONCLUSION: This encoding strategy was successful in reducing PM errors in healthy older adults and those with mild AD with a range of memory abilities. *J Am Geriatr Soc* 64:1307–1312, 2016.

Key words: Alzheimer's disease; prospective memory; memory strategy; implementation intentions

Prospective memory (PM) refers to remembering to perform an intended action in the future. There are important real-world implications associated with failures in PM, including maintaining health (e.g., forgetting to take medication) and safety (e.g., forgetting to turn off an oven). Sixty-two percent of adults attending a memory clinic reported that PM errors were one of the most important memory failures they experienced.¹ Furthermore, PM ability predicted self-reported medication adherence in older adults.² PM deficits are particularly pronounced in individuals with Alzheimer's disease (AD),^{3–5} even in its very mild or preclinical stages.^{6,7} Thus, it is critical to develop strategies for reducing PM errors in individuals with AD.⁸ The present study investigated the utility of an encoding strategy for boosting PM in healthy older adults and those with very mild AD.

Minimal research has been conducted to determine whether encoding strategies improve PM within clinical populations.^{9–11} In healthy populations, implementation intention (II) encoding has produced benefits in PM in laboratory and naturalistic settings.^{12–15} An II is a simple encoding strategy in which individuals verbalize a retrieval cue and link the cue to their plan (e.g., "When I sit down for dinner, I will take my blood pressure medication"). IIs increase the likelihood that healthy older adults will remember to perform a variety of important future intentions, in this example, remembering to monitor blood glucose levels.¹⁴

Related to the present experiment, it has been reported that II encoding improved PM for individuals with very mild AD on a simple laboratory task.⁸ Although encouraging, this initial experiment used PM tasks that were designed to be minimally challenging so that individuals with AD would perform at relatively high levels. Accordingly, it is important to investigate whether IIs improve PM over a range of more-realistic and -challenging tasks.

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The present study tested for II benefits to healthy older adults and those with very mild AD using the Virtual Week task, a highly reliable, laboratory-based PM task¹⁶ that has successfully been used in a range of clinical settings, including in individuals with mild cognitive impairment (MCI) and early dementia,¹⁷ and is sensitive to II encoding benefits.¹⁸ In Virtual Week, participants simulate the execution of intended actions in the context of a board game, with each circuit representing a virtual “day.” One strength of this task is that it creates a naturalistic context by having participants complete intentions that would plausibly be completed in daily life. Another advantage is the inclusion of a variety of PM task types (regular and irregular) and different PM cue types (time- and event-based), which are described in the Methods section. Healthy older adults typically perform regular tasks and event-based tasks at a higher level than irregular tasks and time-based tasks,^{16,19} but minimal data on this are available for individuals with very mild AD.¹⁷

METHODS

Design and Participants

The experiment was a mixed-factor design with Clinical Dementia Rating (CDR; healthy vs very mild AD) and Encoding Condition (standard vs II) as between-participant factors. PM task type (regular and irregular) and cue type (event and time) were manipulated within participants.

A notable strength of this study was the well-defined characterization of the sample. All participants were classi-

fied using the CDR scale, which consists of a 90-minute clinical interview with the individual and a close friend or relative,²⁰ conducted by clinicians at an Alzheimer’s disease research center (ADRC). A CDR rating of 0.0 reflects no dementia, and a CDR rating of 0.5 reflects the very early stages of AD. The CDR has demonstrated excellent validity and reliability (93% diagnostic accuracy).²¹ A CDR rating of 0.5 is associated with small changes in daily functioning in a variety of domains and is similar to a diagnosis of MCI; most individuals with MCI or a CDR of 0.5 progress to AD.²²

Seventy-two participants (38 with CDR 0.0, 34 with CDR 0.5) were recruited from an ADRC, where they were enrolled in a larger longitudinal study. Participants were aged 65 to 85, had normal or corrected vision, and were screened for depression and reversible dementia. Table 1 presents the demographic and neuropsychological characteristics of the sample. Mean age was higher for those with CDR 0.5 than CDR 0.0, so age was statistically controlled for in the analyses. Although assignment to encoding conditions was made using a random number generator, participants in the II condition had significantly higher Associative Memory Test scores. To ensure that this baseline difference did not affect the main outcomes, a follow-up to the primary analysis was conducted using associative memory as a covariate in an analysis of covariance (ANCOVA), and the results were unchanged.

Participants provided informed consent in accordance with the institutional review board at Washington University in St. Louis and were compensated \$10 per hour. Five participants (all CDR 0.5) were excluded from analyses

Table 1. Demographic and Neuropsychological Characteristics

Characteristic	CDR 0.0		CDR 0.5		P-Value	
	Standard Encoding	II Encoding	Standard Encoding	II Encoding	CDR Status	Encoding Condition
Female, n (%)	19 (8)	17 (10)	17 (6)	14 (4)		
Age, mean \pm SD	74.8 \pm 6.5	73.2 \pm 6.2	78.6 \pm 6.4	80.5 \pm 6.1	<.01	.89
Education, years, mean \pm SD	14.7 \pm 2.9	14.9 \pm 2.5	14.9 \pm 2.5	15.2 \pm 2.8	.72	.72
Mini-Mental State Examination score, mean \pm SD	28.8 \pm 1.3	29.1 \pm 1.2	26.5 \pm 3.2	24.9 \pm 4.0	<.01	.31
Associate Memory score, mean \pm SD	12.9 \pm 4.8	16.3 \pm 2.4	6.5 \pm 4.8	9.7 \pm 4.5	<.01	<.01
Selective Reminding Test score, mean \pm SD	47.9 \pm 0.3	47.7 \pm 0.6	45.4 \pm 3.2	44.2 \pm 6.8	<.01	.39
Forward Digit Span score, mean \pm SD	6.8 \pm 1.0	7.0 \pm 1.0	6.4 \pm 1.1	6.5 \pm 0.9	.05	.54
Backward Digit Span score, mean \pm SD	4.8 \pm 1.4	5.1 \pm 1.3	4.7 \pm 1.1	3.6 \pm 0.8	.01	.22
TMT Part A score, mean \pm SD	36.4 \pm 14.3	31.4 \pm 9.4	44.7 \pm 17.1	55.5 \pm 19.5	<.01	.45
TMT Part B score, mean \pm SD	92.7 \pm 40.9	77.2 \pm 22.2	123.9 \pm 46.3	144.0 \pm 37.7	<.01	.77
Wechsler Memory Scale Logical Memory score, mean \pm SD	13.6 \pm 3.2	14.2 \pm 4.1	7.2 \pm 4.3	7.7 \pm 5.3	<.01	.59
Letter Number Sequencing score, mean \pm SD	8.2 \pm 3.5	9.3 \pm 2.0	6.7 \pm 2.7	6.1 \pm 3.3	<.01	.74

A Clinical Dementia Rating (CDR) of 0.0 indicates cognitively normal, 0.5 indicates mild dementia.

Some participants did not have measures of Trail-Making Test (TMT) Part B (n = 1), Selective Reminding Test (n = 3), and Letter Number Sequencing (n = 5).

II = implementation intention; SD = standard deviation.

because of illness ($n = 1$), poor comprehension of instructions ($n = 1$), or failure to complete the entire experiment because of fatigue ($n = 3$).

Materials and Procedure

A computerized version of the board game Virtual Week was used to measure PM performance.^{17,19} Participants completed one practice and two experimental “virtual” days, with four PM tasks per day. Participants rolled the die to move the token around the board using a mouse click.

Each participant was tested on a computer with a touch-screen monitor in a testing room with an experimenter. After completing two laboratory memory tasks,⁸ participants were told they would play a computerized game called Virtual Week in which they would simulate daily activities and remember to perform various tasks. Participants completed a trial day in which the game was explained using detailed pop-up help messages, and the experimenter ensured that they understood the procedures. Monday and Tuesday were then completed without any assistance. At the beginning of each day, participants were asked to touch the start card on the screen to receive instructions for four different PM tasks. Both days had the same two regular PM tasks (take medication at 12 noon and at the dinner event card) and two different irregular PM tasks each day (e.g., get haircut at 2 pm, drop off dry cleaning while out shopping); half of the regular and irregular tasks had event-based cues, and the other half had time-based cues. Event-based cues were present in the title of the target event card (e.g., “dinner” was in the title of the dinner event card). The time-based tasks required participants to monitor a virtual clock located in the center of the screen that was calibrated to the position of the token on the board.^{23,24}

To perform each PM task, participants were instructed to press the “perform task” button on the screen and select the appropriate action from the drop-down menu, which consisted of a list of target and distractor actions. Participants were encouraged to perform each PM task on time (within a virtual hour for time-based tasks and before reaching the next event card for event-based tasks) but were told to perform the task even if they were late.

In the standard encoding condition, participants read the instructions out loud (e.g., “phone plumber at 4 p.m.”) for each PM task and proceeded when they were ready. Participants reviewed the instructions for each of the four PM tasks separately each day. In the II encoding condition, the parameters were identical to the standard condition except that participants were explicitly told to read a statement three times out loud for each PM task: “When I see the [PM cue], then I will press the perform task button and select the [PM task].” They were also told to imagine themselves performing that task. Each PM instruction was presented for 60 seconds to allow sufficient time to complete the II encoding.

After completing Virtual Week, participants were administered a retrospective memory questionnaire in which all of the PM tasks and cues were presented in random order on a sheet of paper. Participants were asked to match each PM task to its corresponding cue. This enabled

the assessment of the retrospective memory component of the PM task (which intention needed to be remembered). Participants were then thanked, compensated, and debriefed.

Data Analysis

The dependent measure for the primary analysis was the proportion of missed responses for each of the four categories of PM tasks: regular event based, regular time based, irregular event based, irregular time based. A mixed-factor ANCOVA was conducted with centered age as the covariate, CDR status (0.0/0.5) and encoding condition (standard/II) as between-participant factors, and PM task type (regular/irregular) and PM cue type (event/time) as within-participant factors. A similar ANCOVA was conducted with proportion correct on the retrospective memory test as the dependent measure.

The neuropsychological assessment included measures of episodic memory, such as logical memory story A—immediate, associative memory, reading span, and digit forward and backward. An episodic memory composite score was created using performance on these five measures based on their average z -scores. A hierarchical linear model was evaluated to determine the predictive utility of episodic memory for PM errors in addition to CDR status, age, education, and encoding condition. The interaction between episodic memory and encoding condition was evaluated to determine whether II encoding would be useful for individuals with varying episodic memory ability.

Analyses were conducted using SPSS version 18 (SPSS, Inc., Chicago, IL). Statistical tests were two-tailed, with an alpha level of .05. Effect sizes were estimated using partial eta squared (η^2_p).

RESULTS

Analysis of Missed PM Responses

Participants with a CDR of 0.5 committed significantly more PM errors (mean 0.73 ± 0.32) than did those with a CDR of 0.0 (0.23 ± 0.32) (ANCOVA results shown in Table 2). Participants in the II encoding condition made significantly fewer PM errors (0.35 ± 0.39) than those in the standard encoding condition (0.60 ± 0.39). (Figure 1 shows means of each CDR group.) There were no significant effects of age or PM task or cue type on the number of PM errors, although there was a significant interaction between CDR status and PM task type, such that participants with a CDR of 0.0 missed significantly fewer regular (0.16 ± 0.32) than irregular (0.30 ± 0.37) tasks, whereas participants with a CDR of 0.5 missed a similar amount of regular (0.75 ± 0.35) and irregular (0.71 ± 0.34) tasks. There were no other significant interaction effects (all $F \leq 3.14$, $P \geq .08$, $\eta^2_p \leq 0.08$).

Effect of Encoding Condition on Retrospective Memory

Retrospective memory performance (ANCOVA results shown in Table 2) was comparable across the standard (0.88 ± 0.16 for CDR 0.0; 0.58 ± 0.30 for CDR 0.5) and II (0.92 ± 0.11 for CDR 0.0; 0.62 ± 0.35 for CDR 0.5)

Table 2. Relevant Statistics for Prospective and Retrospective Memory Errors

Memory Errors	F-Value ^a	95% Confidence Interval	P-Value	Partial Eta ^{2b}
Prospective				
CDR	45.8	0.35–0.65	<.001	0.43
Encoding condition	11.1	0.10–0.40	.002	0.15
Task type	2.5	−0.11–0.01	.12	0.04
Cue	1.4	−0.08–0.02	.25	0.02
Age	1.2		.27	0.02
CDR by task type	7.8		.008	0.11
CDR by encoding condition	1.1		.30	0.02
Retrospective				
CDR	27.0	0.18–0.41	<.001	0.30
Encoding condition	0.6	−0.07–0.16	.46	0.01
Age	5.9		.02	0.09
CDR by encoding condition	0.1		.79	<0.01

The statistical tests were derived from analyses of covariance, with age as the covariate.

^aThe degrees of freedom were 1 in the numerator and 62 in the denominator for all F-values listed in the table.

^bAn index of effect size.

CDR = Clinical Dementia Rating.

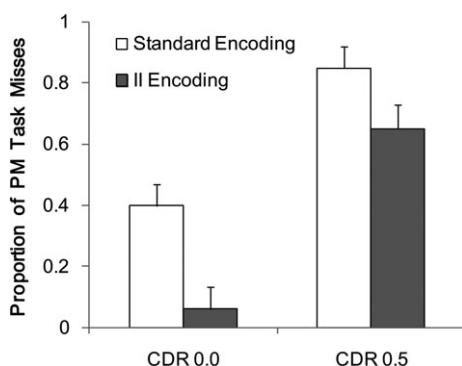


Figure 1. Mean proportion of missed prospective memory responses collapsed across regular and irregular prospective memory task types and event- and time-based cues for the implementation intention (II) and standard encoding conditions, for participants with Clinical Dementia Rating (CDR) of 0.0 and 0.5. Error bars indicate ± 1 standard error of the mean.

encoding conditions. Thus, better prospective, rather than retrospective, memory of the intentions determined the II encoding benefit. As expected, retrospective memory was worse with older age and higher CDR.

Episodic Memory Ability and Strategy Effectiveness

Episodic memory ability was a significant predictor of PM errors ($\beta = -0.25$, $p = .02$) such that individuals with bet-

ter episodic memory committed fewer PM errors. The interaction between encoding condition and episodic memory ($\beta = 0.10$, $p = .38$) did not account for significant variability in PM errors, suggesting that the encoding strategy was effective regardless of episodic memory ability.

DISCUSSION

This study investigated whether an II encoding strategy could improve PM in healthy older adults (CDR 0.0) and individuals with very mild AD (CDR 0.5). This is a critical question because PM is pertinent to maintaining independent functioning, and many people believe they cannot buffer against AD-related memory losses. The II encoding strategy was successful in restoring some PM function in a group of individuals with very mild AD (and healthy older adults). The interaction between CDR and type of PM task (regular/irregular) is notable because it speaks to the robust PM deficit observed even in the very earliest stages of AD. Participants with a CDR of 0.0 missed fewer regular tasks than irregular tasks.¹⁶ By contrast, those with a CDR of 0.5 did not differ on regular and irregular tasks. This is consistent with the idea that reflexive PM processes (e.g., spontaneous retrieval) are impaired in very mild AD but not in healthy aging.^{7,16} The disruption of more-habitual prospective remembering (e.g., remembering daily medications) could be particularly problematic for sustaining independent living in very early AD. Strengthening the encoding of PM intentions through an II strategy effectively reduced errors, regardless of the type of PM task.

It is likely that the observed benefits in the II group are due to the use of more-elaborative encoding of the PM intention. Random assignment disfavors alternative interpretations for the II effect, such as participants in II conditions being more conscientious or motivated. Additionally, the level of social interaction was held constant because participants from both groups spent the same amount of time interacting with the experimenter.

It is important to investigate the potential efficacy of behavioral interventions for individuals with AD. The most widely studied behavioral strategy for improving PM in individuals with AD is spaced retrieval,^{11,25,26} which restores some PM function in individuals with AD, although the II strategy may have several advantages over spaced retrieval (e.g., IIs are easier to use and take less time to encode a given intention). Future research is needed to compare the utility of different behavioral strategies; it is unclear whether behavioral interventions would provide benefits to cognitive performance similar to those observed in pharmacological treatments.

Limitations and Future Directions

There was potential for some training effects in this study; namely, participants completed two PM tasks before Virtual Week, and they were given similar encoding instructions in these tasks.⁸ Although training effects have been observed within PM,²⁴ such effects would not be expected to differ between experimental conditions or to be fundamentally different from natural training effects that accrue

in everyday settings in which individuals repeatedly employ the II strategy.

Another potential limitation was the use of a laboratory-based PM task, which may not reflect everyday PM behaviors. To mitigate this concern, a laboratory task, Virtual Week, that was created to simulate real-world PM was chosen, and performance on this task was found to be indicative of real-world PM in terms of activities of daily living.^{24,27,28} Furthermore, IIs have produced benefits in real-world PM tasks for healthy older adults.¹⁴ Regardless, the findings from the present study speak to the utility of IIs only in a laboratory setting, and future research is critical to determine whether IIs will lead to fewer PM errors in the everyday lives of individuals with AD. Finally, the study focused on individuals in the very early stage of dementia, and it is unclear whether observed II benefits would also accrue to individuals in later stages of AD.

CONCLUSIONS

A simple encoding strategy was effective in restoring some PM function in older adults, regardless of episodic memory ability and CDR. PM failures compromise quality of life, particularly of individuals struggling with everyday activities,²⁹ and developing simple behavioral interventions could reduce the concerns of older adults.¹ Furthermore, future research should investigate whether these interventions could reduce some of the potential burden of caregivers of individuals with AD. These results indicate the need for clinical trials to investigate the utility of strengthening the encoding of PM intentions performed at home.

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Conflict of Interest: The editor in chief has reviewed the conflict of interest checklist provided by the authors and has determined that the authors have no financial or any other kind of personal conflicts with this paper.

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