Published in final edited form as:

Aging Ment Health. 2014 August ; 18(6): 745–753. doi:10.1080/13607863.2013.875126.

Event-Based Prospective Memory Is Independently Associated with Self-Report of Medication Management in Older Adults

Steven Paul Woods^{1,2}, Michael Weinborn², Brenton R. Maxwell², Alice Gummery², Kevin Mo², Amanda R. J. Ng², and Romola S. Bucks²

¹Department of Psychiatry, University of California-San Diego, La Jolla, California

²School of Psychology, University of Western Australia, Crawley, Western Australia

Abstract

Background—Identifying potentially modifiable risk factors for medication non-adherence in older adults is important in order to enhance screening and intervention efforts designed to improve medication-taking behavior and health outcomes. The current study sought to determine the unique contribution of prospective memory (i.e., “remembering to remember”) to successful self-reported medication management in older adults.

Methods—Sixty-five older adults with current medication prescriptions completed a comprehensive research evaluation of sociodemographic, psychiatric, and neurocognitive functioning, which included the Memory for Adherence to Medication Scale (MAMS), Prospective and Retrospective Memory Questionnaire (PRMQ), and a performance-based measure of prospective memory that measured both semantically-related and semantically-unrelated cue-intention (i.e., when-what) pairings.

Results—A series of hierarchical regressions controlling for biopsychosocial, other neurocognitive, and medication-related factors showed that elevated complaints on the PM scale of the PRMQ and worse performance on an objective semantically-unrelated event-based prospective memory task were independent predictors of poorer medication adherence as measured by the MAMS.

Conclusions—Prospective memory plays an important role in self-report of successful medication management among older adults. Findings may have implications for screening for older individuals “at risk” of non-adherence, as well as the development of prospective memory-based interventions to improve medication adherence and, ultimately, long-term health outcomes in older adults.

Corresponding Author: Steven Paul Woods, Psy.D., Department of Psychiatry (8231), University of California, San Diego, 220 Dickinson St., Suite B, San Diego, California, USA 92103, spwoods@ucsd.edu, Telephone: 619-543-5004, Fax: 619-543-1235.

CONFLICT OF INTEREST

None.

DESCRIPTION OF AUTHORS' ROLES

Authors Woods, Weinborn, Maxwell, and Bucks contributed to the study design, statistical plan and analysis, data interpretation, and writing of the manuscript itself. Authors Gummery, Mo, and Ng all gathered, processed, and quality assured data for the study, as well as provided edits on the written manuscript. Authorship was determined according to APA and UWA guidelines. The present study was based, in part, on data collected by Brenton Maxwell as a part of his Doctorate in Clinical Psychology and Clinical Neuropsychology thesis. Additional data were collected and the data analyzed by Weinborn and Woods.

Keywords

Episodic memory; Adherence; Neuropsychological assessment; Geropsychology

INTRODUCTION

It has been estimated that 26–75% of older adults do not fully adhere to their prescribed medication regimens (e.g., Murray et al., 2004), and errors often involve missed doses, duplicate doses, and/or incorrect dose quantities (e.g., Park, et al., 1999). While there is evidence that older adults generally display better adherence than younger adults at a population level (e.g., Hinkin et al., 2004), older adults are nevertheless particularly vulnerable to serious mental and physical consequences of non-adherence (Park et al., 1999) that can lead to suboptimal long-term health outcomes. Accordingly, identifying potentially modifiable risk factors for non-adherence in older adults is important in order to enhance screening and intervention efforts designed to improve medication-taking behavior, and subsequently maximize the effectiveness of pharmacotherapies and reduce health-related burdens on the individual, care providers, and the healthcare system. To date, notable risk factors for medication non-adherence among older adults have included older age, lower socioeconomic status, health illiteracy, greater regimen complexity, limited use of compensatory strategies, and depression (e.g., Gellad et al., 2011).

Neurocognitive impairment is also a recognized risk factor for medication non-adherence among older adults. In fact, reciprocal effects can also be observed such that neurocognitive impairments reduce adherence, which can lead to greater neurocognitive impairment and consequently a further reduction in adherence (Albert et al., 1999). Park (1992) proposed an elegant conceptual model specific to the role of neurocognitive functions in successful medication adherence: The first step requires comprehension of the medication information on the pill bottle/pamphlet (e.g., health literacy). Working memory is required to transfer data from pill bottle labels, which then requires aspects of executive functions to organize and form a plan to take the medications as prescribed. Prospective memory is then necessary to remember to act on the previously made plan at the proper time. The cue to act on the plan could be either time-based, such as remembering to take a pill at 6:00PM, or event-based, such as taking a pill with dinner. Finally, retrospective memory is required to recall the medication dosing times and medication dosing instructions such as ‘take with food’ (Park, 1992). Although these processes are initially highly cognitively complex, medication-taking behavior can become quite habitual and routinized over time. This model has been widely adopted in the literature, with several studies showing that lower scores on measures of crystallized knowledge, working memory, executive functions and retrospective memory are at least modestly related to medication non-adherence among older adults (e.g., Park et al., 1994).

Far fewer studies, however, have specifically examined the role of prospective memory, or “remembering to remember” in the medication adherence of older adults. Prospective memory describes the complex neurocognitive process of successfully executing a future intention, and while it is comprised of a constellation of familiar cognitive constructs, such

as retrospective memory and aspects of executive functions (e.g., planning and set shifting), prospective memory is nevertheless considered to be greater than the sum of its individual cognitive parts in much the same way that executive functions may be distinguished from its component processes (e.g., attention, speed). Indeed, prospective memory is dissociable from these other aspects of neurocognition at the neurobehavioral, neurobiological, and functional levels (e.g., Gupta et al., 2010). For example, it has been shown that retrospective memory is a necessary, but not sufficient aspect of prospective memory; that is, one may accurately recall their original intention (e.g., to take a medication before going to bed) but still fail to actually complete the intended action. Prospective memory involves encoding and planning the “what” and “when” of the cue-intention pairing (e.g., taking dose of a medication before bed), monitoring one’s environment to detect the proper cue for action (e.g., bedtime), disengagement from ongoing activities (e.g., brushing one’s teeth) to recall the specific intention (e.g., name and dose of medication), and then accurately executing the intention (i.e., taking the medication as prescribed). Prospective memory is supported by the prefrontal cortex, particularly Brodmann’s area 10 (e.g., Burgess et al., 2011), as well as medial temporal structures (Gordon et al., 2011) and, accordingly, is subject to moderate decline with aging (Einstein & McDaniel, 1990). Age effects on prospective memory are particularly pronounced when the demands on self-initiated executive control processes are increased, for example time-based (i.e., the cue is based on the passage of time) and non-focal event-based (i.e., the cue is an external event that is not central to the ongoing task or focus of attention) tasks that require active monitoring resources (e.g., McDaniel & Einstein, 2007). Prospective memory is of direct relevance to real-world functioning, as several studies now show that older adults with weaker event-based prospective memory are at increased risk of everyday memory failures (e.g., Tam & Schmitter-Edgecombe, 2013) and dependence in activities of daily living (e.g., Woods et al., 2012).

Recent data in various clinical populations suggest that prospective plays a critical role in successful medication adherence. Studies in HIV infection, for example, show that deficits in the strategic aspects of prospective memory are associated with a nearly six-fold increased risk of non-adherence to antiretroviral medications (e.g., Woods et al., 2009). Non-adherence may be particularly pronounced for individuals with deficits in strategic cue monitoring over longer delays between encoding and retrieval of the intention (Poquette et al., 2013). Importantly, the relationship between prospective memory and non-adherence is independent of established risk factors, including demographics, psychiatric distress, illness severity, medication-related factors, and other aspects of neurocognitive functioning, including delayed retrospective memory and executive functions (see Zogg et al., 2012 for a review).

To date, however, we are aware of only a small number of studies to have examined prospective memory and medication adherence in older adults. In 2004, Vedhara et al. reported an association between habitual PM (i.e., a task on which the intended action is performed on a routine or systematic basis; Einstein et al., 1998) and medication adherence in older adults with Type 2 diabetes. In healthy older adults, McDonald-Miszczak et al. found that event-based prospective memory was associated with objective, but not self-report medication adherence. Most recently, Pirogovsky and colleagues (2012) showed that poorer performance on a well-validated non-focal event-based prospective memory task and

higher self-reported prospective memory complaints were moderately correlated with self-reported medication mismanagement (but not performance-based medication management capacity) in a small sample of older adults in the United States. A notable limitation of these prior studies is that the incremental value of prospective as a marker of non-adherence relative to other established predictors (e.g., retrospective memory and depressed mood) was not considered.

The primary aim of the current study was to extend this prior literature to determine the unique contribution of performance-based and self-reported prospective memory in the self-reported medication adherence of older adults relative to biopsychosocial, neurocognitive, and medication-related factors. In addition, we were interested in determining the contribution of strategic, event-based prospective memory processing in medication adherence among older adults. Our approach was rooted in McDaniel and Einstein's (2000) multi-process theory, which posits that the specific parameters of the event-based prospective memory cues may levy varying demands on ongoing cognitive resources and thereby influence performance. In this case, we focused our attention on the degree of semantic relatedness between the intention (i.e., "what") and cue (i.e., "when"). Prior research shows that semantically unrelated cue-intention pairings (e.g., remembering to take a medication that must be ingested with food before bed) place greater demands on strategic encoding and retrieval processes than do semantically linked cue-intention pairings (e.g., remembering to take that same medication after dinner), which rely more so on automatic-associative memory (e.g., McDaniel et al., 1998). We hypothesized that older adults' medication adherence would be independently reliant on prospective memory, particularly under conditions of increased strategic encoding and retrieval demands (i.e., when the cue is not semantically related to the intended action).

METHOD

Participants

Participants were 65 community-dwelling older adults recruited via flyers and word-of-mouth. Participants were between 55 and 90 years of age and had a variety of mild, chronic, neuromedical conditions common amongst older adults (e.g., hypertension, diabetes, high cholesterol) and were included in the present study if they were prescribed at least one medication with a daily dosing schedule. Participants were excluded if they scored less than 25 on the Mini Mental-State Examination (MMSE; Folstein et al., 1975) or reported a history of significant neurological (e.g., traumatic brain injury, stroke, seizure disorder, Parkinson's disease) or psychiatric (Schizophrenia, Bipolar disorder) conditions. Basic descriptive data regarding the biopsychosocial, neurocognitive, and medication-related characteristics of the sample are provided in Table 1.

The study procedures were approved by the human subjects board at the University of Western Australia, and written informed consent was obtained from all participants. Fifteen dollars was offered to defray travel expenses.

Medication-related Measures

The primary criterion of interest was self-reported memory-related problems with medication adherence. A 10-item Memory for Adherence to Medication Scale (MAMS) was constructed by adapting the seven items comprising the Cognitive subscale of the Adherence Attitude Inventory (AAI-C; Lewis & Abell, 2002), to which we added three items in order to provide a broader range of conceptual coverage and evaluate specific problems not assessed by this questionnaire. These included problems with taking medications at the right time and correct dose, as well as problems with adherence over the preceding week. Descriptive information for the individual items of the MAMS is provided in Table 2. The seven items of the AAI-C, and the newly-developed item of adherence difficulties over the last week were answered on a 7-point scale (1=problems none of the time, 7=problems all of the time), the two new questions specific to timing and dosage problems were answered on a 6-point scale (1=problems never, 6=problems always). In order to place all items on the same scale, sample-based Z-scores for each item were calculated and averaged. The standardized MAMS produced excellent reliability (Cronbach's $\alpha = .87$), with higher scores indicating poorer medication adherence. Evidence of the MAMS' construct validity was demonstrated by a significant negative relationship ($r = -.38, p = .002$) with the Medication Adherence Questionnaire (MAQ; Morisky et al., 1986), including its Unintentional Nonadherence subscale ($r = -.40, p = .001$), which is comprised of two items assessing forgetfulness and carelessness-related medication taking errors. In addition, MAMS demonstrated significant positive relationships with self-reported medication errors over the previous week ($r = .31, p = .01$), and an informant single-item report of medication adherence problems (available for 28 participants, $r = .43, p = .02$).

In addition to the above measures, participants reported their current medication regimen (most participants brought their medications to the study appointment), including number of pills taken per day for each medication, as well as any strategies used to improve their adherence (e.g., pill organizers). Participants also completed the Medication Management Ability Assessment (MMAA; Patterson et al, 2002), an objective, well-validated measure of ability to follow a series of medication instructions, role-played as if taking the required medications over the course of a day.

Prospective Memory Measures

Objective prospective memory was measured with a task adapted from the event-based portion of the Abbreviated Assessment of Intentional Memory (AAIM, Gupta et al., 2010; Woods et al, 2010). Specifically, a series of color drawings of common objects (e.g., airplane, bed) served as event-based cues for eight tasks evenly divided between semantically related (e.g., saying "sit" when presented with a picture of a dog) and unrelated (snapping their fingers when presented with a picture of a cow) cue-intention pairs. Each set of four semantically-related and unrelated prospective memory tasks was further balanced with equal (i.e., two) numbers of items with short (2 min) and long (15 min) delays as well as action versus verbal requirements for response. The four semantically-unrelated items were taken from the AAIM, and four semantically-related items were generated for the current study. Participants completed these tasks while concurrently completing an engaging ongoing task (a word search puzzle), and received 2 points if they made the correct response

after the correct cue. They received 1 point if they made a valid response after the wrong event-based cue, or an invalid or partially correct response at the correct event cue. All other responses scored 0. Scores were added together to create semantically-related (Semantically-Related PM) and semantically-unrelated (Semantically-Unrelated PM) subscales (scores range from 0–8). Three types of errors were recorded: omission (i.e., no response), task substitution (e.g., enacting a partially or completely incorrect intention), and loss of content (recognizing that a response is required, but being unable to retrieve the response) errors. Retrospective free, cued and recognition recall for the picture and/or intentions were assessed after the prospective memory component of the task was completed. Participants were first asked spontaneously to recall as many cue-intention pairs as possible, and received 1 point for every correctly recalled cue (picture) and intention regardless of whether they were recalled together accurately, for a maximum of eight points each. For any intentions not spontaneously recalled, cued recall was administered by providing the name of the object in the picture cue, and prompting for recall of the intention paired with that cue. Participants were credited for items spontaneously recalled prior to the cued recall subtest, and subsequently the maximum for the cued recall subscale was also eight. Finally, an 8-item (for intentions only) multiple-choice post-test recognition questionnaire was administered.

Self-reported prospective and retrospective memory complaints were assessed with the well-validated 16-item Prospective and Retrospective Memory Questionnaire (PRMQ; Crawford et al., 2003). This scale uses a 5-point response scale (1 = never, 5 = very often) with 8 items assessing the frequency of retrospective memory (RM scale) lapses, and 8 items assessing the frequency of prospective memory (PM scale) lapses (range = 0–40). These two scales can be further divided into self-cued or environmentally-cued memory problems (range = 0–20). Note that, the PRMQ contains only one item (#3) that uses pill taking as one of two examples of a broader question regarding short-term environmentally-cued prospective memory problems in daily life.

Other Neuropsychological Measures

General cognitive function was assessed with the Mini Mental Status Examination (MMSE; Folstein, Folstein, & McHugh, 1975). The Trailmaking Test (Reitan and Wolfson, 1985) was administered to assess set-shifting ability, the Executive Clock Drawing Task (CLOX; Royall, Corders, & Polk, 1998) assessed planning (scored as CLOX part 2 minus CLOX part 1), and the action fluency test (Woods et al., 2005) assessed verbal generativity. Sample-based z-scores were calculated for each measure and then averaged to produce an executive domain score, with positive scores indicative of better ability. Verbal working memory and attention were assessed with the Digit Span subtest of the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III; Psychological Corporation, 1997). Retrospective memory was assessed with the Delayed Story Memory and Figure Recall subtests of the Repeatable Battery for the Assessment of Neuropsychological Status-Form A (RBANS; Randolph, Tierney, Mohr, & Chase, 1998). Sample-based z-scores were calculated for these two measures and averaged to provide a retrospective delayed recall domain score with higher scores reflecting better ability. Note that, no participant fell more than 2 SD below the published normative mean on the RBANS total score.

Mood and Demographic Information

Depression was assessed with the Geriatric Depression Scale-15 item version (GDS-15; Sheikh & Yesavage, 1986) and anxiety was assessed with the Geriatric Anxiety Inventory (GAI; Pachana et al., 2007). Sample-based z-scores were calculated for each measure and then averaged to produce a single mood score, with higher scores suggesting greater levels of affective distress. The Australian version of the National Adult Reading Test (AUSNART; Hennessy & MacKenzie, 1995) was administered to estimate premorbid intelligence. Total errors on the AUSNART reading task were converted to predicted WAIS-III Verbal IQ scores using a regression equation that incorporated age, education and gender (Sullivan et al., 2000). Finally, a demographic and medical history questionnaire was administered to collect educational history, age, gender and relevant medical history (i.e., number and types of chronic medical and psychiatric conditions).

RESULTS

The results of three hypothesis-driven hierarchical linear regressions concurrently predicting the MAMS from the Semantically-Unrelated PM, Semantically-Related PM, and PRMQ PM are displayed in Table 3. After accounting for the influence of: 1) biopsychosocial factors (i.e., age, estimated cognitive reserve as measured by the AUSNART, mood, and number of neuromedical conditions); 2) other neurocognitive abilities (i.e., MMSE, RBANS delayed memory, Digit Span, executive functions z-score, and PRMQ RM); and 3) medication-related factors (i.e., dose burden, strategy use, MMAA total, and MAQ-Purposeful Nonadherence subscale), respectively, in the first step of the models. The subsequent inclusion of the 3 prospective memory variables significantly increased the amount of MAMS variance explained ($ps < .01$). In all three regressions, Semantically-Unrelated PM ($ps < .05$) and PRMQ PM ($ps < .01$) each independently accounted for significant variance in MAMS, whereas Semantically-Related PM did not ($ps > .20$). Although some of the study variables were non-normally distributed (e.g., Semantically-Related PM), a review of the regression residuals revealed no serious departures from normality.

Next, we aimed to determine the cognitive architecture of event-based prospective memory's contribution to MAMS by conducting correlations with the components (e.g., subscales and error types) of Semantically-Unrelated PM and PRMQ-PM. Given the non-normal distributions of many of the Semantically-Unrelated PM component variables (e.g., recognition), we used Spearman's rho across these analyses for consistency. As shown in Table 4, MAMS was significantly correlated in the expected directions with Semantically-Unrelated PM 2- and 15-min subscales, task substitution (i.e., intrusion) errors, and recognition post-test ($ps < .05$), as well as at a trend-level with both free- and cued-recall ($ps < .10$). MAMS was also associated with both the self- and environmentally-cued subscales of the PRMQ PM ($ps < .01$). No other notable correlations between MAMS and prospective memory variables emerged ($ps > .10$).

DISCUSSION

Ensuring adequate adherence to prescribed medication regimens among older adults is a major personal and public health challenge. The current study adds to our understanding of

this complex clinical phenomenon by demonstrating a unique role for “remembering to remember” in older adults’ ability to successfully follow their, oftentimes complex, medication regimens. Specifically, better objective event-based prospective memory performance and lower self-reported prospective memory complaints were identified as independent predictors of self-perceived medication management success in 65 older Australians. Findings are consistent with those reported by Pirogovsky and colleagues (2012), who showed that higher prospective memory complaints and lower event-based prospective memory scores were related to poorer self-reported medication management at the univariate level in a small U.S. sample of older adults. A noteworthy expansion of this prior study (as well as the studies from Vedhara et al., 2004 and McDonald Mischak et al., 2009), therefore, is that in the current investigation, prospective memory demonstrated added value in its concurrent prediction of medication management by accounting for variance above and beyond established biopsychosocial (e.g., demographics, mood) and medication-related factors (e.g., pill burden, medication management skills). Consistent with the predictions of the Park (1992) model, prospective memory’s association with medication adherence was also clearly independent of other neurocognitive functions, with which it shares some features relevant to adherence, such as delayed retrospective memory, attention and working memory, and executive functions (i.e., generativity, cognitive flexibility, and planning).

The present data also extend our understanding of the cognitive architecture of event-based prospective memory in the context of adherence. In particular, these data illustrate that the strategic (i.e., executively demanding) aspects of event-based prospective memory play a particularly important role in the medication adherence success of older adults. The sensitivity of medication adherence to alterations in strategically demanding event-based prospective memory is also in accordance with prior work showing that time-based prospective memory (Woods et al., 2009) and, particularly, long-delayed time-based prospective memory (Poquette et al., 2012), was associated with electronic monitoring of antiretroviral adherence in HIV infection. Consistent with multi-process theory (McDaniel & Einstein, 2000), the semantic-relatedness of the cue-intention (i.e., “what-when”) pairing was an important determinant of the relationship between event-based prospective memory and adherence; specifically, trials with lower levels of cue-intention semantic-relatedness (e.g., “When I show you a picture of a cow, snap your fingers”) were more strongly associated with poorer medication adherence compared to trials with higher levels of relatedness (e.g., “When I show you a picture of a dog, say ‘Sit!’”). Prior research shows that executing a future intention when the cue is unrelated to the intended action requires greater executive control (i.e., planning, cognitive flexibility) and is sensitive to the effects of aging (Cohen et al., 2001) and other conditions in which the frontal systems are affected (Woods et al., 2010). Basic research shows that minimally related cue-intention pairings are more vulnerable to increased attention allocation demands in healthy adults (McDaniel et al., 2004; Loft & Yeo, 2007). Indeed, it is now clear that overall prospective memory performance, including accuracy and reaction times, is markedly enhanced when the cue and intention are highly semantically related (e.g., McDaniel et al., 1998; Loft & Yeo, 2007), as was shown here in Table 1. When paired with the findings from the present study, these data suggest that increasing the relatedness of the cues (e.g., timing, location, supporting

materials) and intention to take one's medications as prescribed may provide support to improve adherence in older adults. Indeed, prospective memory-focused interventions to improve medication adherence in older adults are presently being developed for clinical trials (see Insel et al., 2012).

Analysis of event-based prospective memory subscales and error types also revealed important details about the cognitive architecture that supports medication adherence in older adults. The findings of increased task substitution (i.e., intrusion) errors and diminished post-test recognition, along with trend-level findings for free- and cued- post-test recall deficits suggest that encoding and online retrieval of the retrospective memory aspect of prospective memory may be of particular relevance. In other words, the process of quickly and effectively linking the semantically unrelated intention appears to have malfunctioned at initial acquisition phase and, therefore, was not available to retrieve in response to the proper cue during task performance (i.e., elevated intrusion errors) or even under more structured multi-choice recognition trials at post-test. That these effects were independent of delayed retrospective memory supports the interpretation that the findings are specific to the retrospective memory operations of prospective memory. In fact, a post-hoc analysis showed that the Semantically-Unrelated PM score was the sole predictor of MAMS ($B = -.20 [-.03, -.36], p = .02$) in a model that also included free recall and recognition ($\text{adj } R^2 = .09, p = .04$). Moreover, the Semantically-Unrelated PM score showed only very modest correlations with the PRMQ RM and RBANS memory scores (r s ranged from .20 to .29). Interestingly, a recent study from our group showed a similar profile in which the retrospective aspect of prospective memory was a unique predictor of independence in activities of daily living among a separate sample of older adults (Woods et al., 2012). Nevertheless, our use of clinical tasks does not allow us to definitively rule out the possibility that the findings simply reflect a pure failure of retrospective memory, which we noted in the Introduction is a necessary but not sufficient component of successful prospective memory. Future studies may wish to examine other manipulations of the retrospective aspect of prospective, including overall retrospective memory burden (e.g., the number of intentions to be enacted), perhaps along with strategies to improve strategic encoding that may enhance the accuracy of intention execution, such as self-generation, imagery, and spaced-retrieval (e.g., Insel et al., 2012).

A few limitations to the conclusions that may be drawn from this study deserve highlighting. One of the primary limitations of this study is its use of a novel, self-report measure of medication management (i.e., MAMS). Although there are no widely-agreed upon gold standards for adherence (Osterberg & Blaschke, 2005), it is generally held that self-report measures are subject to response bias and undue influence of mood as compared to other more objective approaches to measuring adherence. Thus, while the MAMS showed strong internal consistency and convergent validity with other indicators of medication adherence, future studies may wish to examine the association between prospective memory and adherence using other established behavioral (e.g., medication event monitoring), biological (e.g., pharmacokinetic), or manifest (e.g., pill count) approaches. Another notable limitation is the restricted range on the Semantically-Related PM scale and MAMS. Specifically, possible ceiling effects in a healthy, cognitively normal sample may have introduced

psychometric challenges that precluded the detection of significant associations with MAMS, as has been observed in prior studies using similar measures of event-based prospective memory (e.g., Woods et al., 2010). Expanding the ceiling of the Semantically-Related PM scale, perhaps by increasing the difficulty level of the cue-intention pairings, could enhance its psychometric comparability to the Semantically-Unrelated PM scale, as well as its sensitivity to non-adherence. It is also possible that this scale have better distributional properties and enhanced sensitivity in neuropsychologically impaired clinical samples (e.g., Alzheimer's disease). Another psychometric issue is the fact that both the PRMQ and MAMS are self-report measures, so the strength of their association may be inflated by shared method variance, although it deserves mention that the MAMS was not significantly associated with other self-report measures administered in this study. Psychometric limitations aside, the MAMS was nevertheless significantly associated with several clinodemographic variables in the expected direction in this study, thereby supporting its construct validity. Finally, the predictive clinical value of these findings is limited by the cross-sectional nature of the study design. Despite these limitations, findings from the current study suggest that prospective memory plays an important role in successful medication adherence among older adults and may have implications for screening for individuals "at risk" of non-adherence and the development of prospective memory-based interventions to improve medication adherence and ultimately long-term health outcomes in older adults.

Acknowledgments

This research was supported in part by National Institute of Mental Health grant R01-MH073419 to Dr. Woods. The views expressed in this article are those of the authors and do not reflect the official policy or position of the Department of the Navy, Department of Defense, nor the United States Government. Data were collected as part of Brenton Maxwell's Doctor of Psychology thesis project. The authors thank the study volunteers of the Western Australia Participant Pool for their participation.

References

- Albert SM, et al. An observed performance test of medication management ability in HIV: relation to neuropsychological status and medication adherence outcomes. *AIDS and Behavior*. 1999; 3:121–128.10.1023/A:1025483806464
- Burgess PW, Gonen-Yaacovi G, Volle E. Functional neuroimaging studies of prospective memory: What have we learnt so far? *Neuropsychologia*. 2011; 49:2246–2257.10.1016/j.neuropsychologia.2011.02.014 [PubMed: 21329712]
- Cohen AL, West R, Craik FI. Modulation of the prospective and retrospective components of memory for intentions in younger and older adults. *Aging, Neuropsychology, and Cognition*. 2001; 8:1–13.10.1076/anec.8.1.1.845
- Crawford J, Smith G, Maylor E, Della Sala S, Logie R. The Prospective and Retrospective Memory Questionnaire (PRMQ): Normative data and latent structure in a large non-clinical sample. *Memory*. 2003; 11:261–275.10.1080/09658210244000027 [PubMed: 12908675]
- Einstein GO, McDaniel MA. Normal aging and prospective memory. *Journal of Experimental Psychology: Learning, Memory, and Cognition*. 1990; 16:717.10.1037/0278-7393.16.4.717
- Einstein GO, McDaniel MA, Smith R, Shaw P. Habitual prospective memory and aging: Remembering instructions and forgetting actions. *Psychological Science*. 1998; 9:284–288.
- Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric research*. 1975; 12(3):189–198. [PubMed: 1202204]

- Gellad WF, Grenard JL, Marcum ZA. A systematic review of barriers to medication adherence in the elderly: looking beyond cost and regimen complexity. *The American Journal of Geriatric Pharmacotherapy*. 2011; 9:11–23.10.1016/j.amjopharm.2011.02.004 [PubMed: 21459305]
- Gordon BA, Shelton JT, Bugg JM, McDaniel MA, Head D. Structural correlates of prospective memory. *Neuropsychologia*. 2011; 49:3795–3800.10.1016/j.neuropsychologia.2011.09.03 [PubMed: 21982698]
- Gupta S, Woods SP, Weber E, Dawson MS, Grant I. The HIV Neurobehavioral Research Center (HNRC) Group. Is prospective memory a dissociable cognitive function in HIV infection? *Journal of Clinical and Experimental Neuropsychology*. 2010; 32:898–908.10.1080/13803391003596470 [PubMed: 20425662]
- Hennessy, Maria; MacKenzie, B. AUSNART: The development of an Australian version of the NART. In: Fourez, J.; Page, N., editors. *Treatment Issues and Long-term Outcomes: Proceedings of the 18th Annual Brain Impairment Conference*. Bowen Hill: Australian Academic Press; 1995. p. 183-188.
- Hinkin CH, et al. Medication adherence in HIV-infected adults: effect of patient age, cognitive status, and substance abuse. *AIDS (London, England)*. 2004; 18(Suppl 1):S19–s25.
- Insel KC, Einstein GO, Morrow DG, Hepworth JT. A multifaceted prospective memory intervention to improve medication adherence: Design of a randomized control trial. *Contemporary Clinical Trials*. 2012; 34:45–52.10.1016/j.cct.2012.09.005 [PubMed: 23010608]
- Lewis SJ, Abell N. Development and evaluation of the adherence attitude inventory. *Research on Social Work Practice*. 2002; 12:107–123.10.1177/104973150201200108
- Loft S, Yeo G. An investigation into the resource requirements of event-based prospective memory. *Memory & Cognition*. 2007; 35:263–274.10.3758/BF03193447 [PubMed: 17645167]
- McDaniel MA, Einstein GO. Strategic and automatic processes in prospective memory retrieval: A multiprocess framework. *Applied Cognitive Psychology*. 2000; 14:S127–S144.10.1002/acp.775
- McDaniel, MA.; Einstein, GO. *Prospective memory: An overview and synthesis of an emerging field*. Thousand Oaks, CA: Sage Publications, Inc; 2007.
- McDaniel MA, Guynn MJ, Einstein GO, Breneiser J. Cue-focused and reflexive-associative processes in prospective memory retrieval. *Journal of Experimental Psychology-Learning Memory and Cognition*. 2004; 30:605–613.10.1037/0278-7393.30.3.605
- McDaniel MA, Robinson-Riegler B, Einstein GO. Prospective remembering: Perceptually driven or conceptually-driven processes? *Memory and Cognition*. 1998; 26:121–134.10.3758/BF03211375 [PubMed: 9519702]
- McDonald-Miszczak L, Neupert SD, Gutman G. Does cognitive ability explain inaccuracy in older adults' self-reported medication adherence? *Journal of Applied Gerontology*. 2009; 28:560–581.
- Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Medical care*. 1986; 24:67–74. [PubMed: 3945130]
- Murray MD, et al. A conceptual framework to study medication adherence in older adults. *The American journal of geriatric pharmacotherapy*. 2004; 2:36–43.10.1016/S1543-5946(04)90005-0 [PubMed: 15555477]
- Osterberg L, Blaschke T. Drug Therapy: Adherence to medication. *The New England Journal of Medicine*. 2005; 353:487–97. [PubMed: 16079372]
- Pachana NA, Byrne GJ, Siddle H, Koloski N, Harley E, Arnold E. Development and validation of the Geriatric Anxiety Inventory. *Int Psychogeriatr*. 2007; 19(1):103–114. [PubMed: 16805925]
- Park, DC. Applied cognitive aging research. In: Craik, FIM.; Salthous, TA., editors. *Handbook of cognition and aging*. Hillsdale, NJ: Lawrence Erlbaum Associates; 1992. p. 449-493.
- Park DC, et al. Medication adherence in rheumatoid arthritis patients: Older is wiser. *Journal-American Geriatrics Society*. 1999; 47:172–183.
- Park DC, Willis SL, Morrow D, Diehl M. Cognitive function and medication usage in older adults. *Journal of Applied Gerontology*. 1994; 13:39–57.10.1177/073346489401300104
- Patterson TL, Lacro J, McKibbin CL, Moscona S, Hughs T, Jeste DV. Medication management ability assessment: results from a performance-based measure in older outpatients with schizophrenia. *Journal of Clinical Psychopharmacology*. 2002; 22:11–19. [PubMed: 11799337]

- Pirogovsky E, Woods SP, Vincent Filoteo J, Gilbert PE. Prospective Memory Deficits are Associated with Poorer Everyday Functioning in Parkinson's Disease. *Journal of the International Neuropsychological Society*. 2012; 18:986.10.1017/S1355617712000781 [PubMed: 22846463]
- Poquette AJ, et al. Prospective memory and antiretroviral medication non-adherence in HIV: An analysis of ongoing task delay length using the Memory for Intentions Screening Test. *Journal of the International Neuropsychological Society*. 2013; 19:155–61.10.1017/S1355617712001051 [PubMed: 23095304]
- Psychological Corporation. WAIS-III and WMS-III technical manual. San Antonio, TX: Psychological Corporation; 1997.
- Randolph C, Tierney MC, Mohr E, Chase TN. The repeatable battery for the assessment of neuropsychological status (RBANS): preliminary clinical validity. *Journal of Clinical and Experimental Neuropsychology*. 1998; 20(3):310–319. [PubMed: 9845158]
- Reitan, RM.; Wolfson, D. The Halstead-Reitan Neuropsychological Test Battery: Theory and clinical interpretation. Tucson, AZ: Neuropsychology Press; 1985.
- Royall DR, Cordes JA, Polk M. CLOX: an executive clock drawing task. *Journal of Neurology, Neurosurgery & Psychiatry*. 1998; 64(5):588–594.
- Sheikh, JI.; Yesavage, JA. Geriatric Depression Scale (GDS). Recent evidence and development of a shorter version. In: Brink, TL., editor. *Clinical Gerontology: A Guide to Assessment and Intervention*. New York: The Haworth Press, Inc; 1986. p. 165-173.
- Sullivan, R.; Senior, G.; Hennessy, M. Australian age–education and premorbid cognitive/intellectual estimates for the WAIS-III. Paper presented at the 6th Annual Conference of the APS College of Clinical Neuropsychologists; Hunter Valley, Australia. 2000 Oct.
- Tam JW, Schmitter-Edgecombe M. Event-based prospective memory and everyday forgetting in healthy older adults and individuals with mild cognitive impairment. *Journal of Clinical and Experimental Neuropsychology*. 2013 in press. 10.1080/13803395.2013.770823
- Vedhara K, Wadsworth E, Norman P, Searle A, Mitchell J, Macrae N, O'Mahony M, Kemple T, Memel D. Habitual prospective memory in elderly patients with Type 2 diabetes: Implications for medication adherence. *Psychology, Health, and Medicine*. 2004; 9:17–26.
- Woods SP, Dawson MS, Weber E, Grant I. The HIV Neurobehavioral Research Center (HNRC) Group. The semantic relatedness of cue–intention pairings influences event-based prospective memory failures in older adults with HIV infection. *Journal of Clinical and Experimental Neuropsychology*. 2010; 32:398–407.10.1080/13803390903130737 [PubMed: 19763997]
- Woods SP, Scott JC, Sires DA, Grant I, Heaton RK, Tröster AI. The HNRC Group. Action (verb) fluency: Test-retest reliability, normative standards, and construct validity. *Journal of the International Neuropsychological Society*. 2005; 11:408–415. [PubMed: 16209421]
- Woods SP, et al. Timing is everything: Antiretroviral non-adherence is associated with impairment in time-based prospective memory. *Journal of the International Neuropsychological Society*. 2009; 15:42–52.10.1017/S1355617708090012 [PubMed: 19128527]
- Woods SP, Weinborn M, Velnoweth A, Rooney A, Bucks RS. Memory for intentions is uniquely associated with instrumental activities of daily living in healthy older adults. *Journal of the International Neuropsychological Society*. 2012; 18:134–138.10.1017/S1355617711001263 [PubMed: 22032776]
- Zogg J, Woods SP, Saucedo JA, Weibe JM, Simone JS. The role of prospective memory in medication adherence: A critical review of an emerging literature. *Journal of Behavioral Medicine*. 2012; 35:47–62. [PubMed: 21487722]

Table 1

General descriptive data for the study sample of 65 older adults

Variable	Mean (SD)	Range
Biopsychosocial Variables		
Age (years)	71.8 (7.4)	56–89
Education (years)	13.6 (3.1)	2–20
Gender (% Male)	35%	
AusNART predicted VIQ	110.0 (5.3)	93–120
Geriatric Depression Scale (short form)	1.7 (2.2)	0–10
Geriatric Anxiety Inventory	2.1 (3.1)	0–15
Number of chronic neuromedical conditions	2.9 (1.4)	1–7
Medication-Related Variables		
Medication Regimen (number of pills/day)	4.1 (2.6)	1–12
Strategy Use (percent who use)	53.8%	
Medication Management Ability Assessment (MMAA)	30.4 (2.9)	19–33
Medication Adherence Questionnaire-4 (MAQ-4)	3.7 (0.5)	2–4
Neurocognitive Variables		
Mini Mental Status Examination Score	28.6 (1.2)	25–30
RBANS Delayed Story Memory Raw Score	8.4 (2.2)	3–12
RBANS Delayed Figure Recall Raw Score	12.5 (3.8)	0–20
Trailmaking Test B (sec)	88.1 (44)	38–297
CLOX Executive Clock Drawing Task (executive index)	1.4 (1.8)	–2 – 7
Action Fluency	17.5 (4.5)	9–29
WAIS-III Digit Span (age-corrected scaled score)	11.5 (2.8)	6–19
PM-Semantically Related PM	7.3 (0.8)	4–8
PM-Semantically Unrelated PM	5.8 (1.2)	2–8
PM-SUR-Omission Errors	0.1 (0.3)	0–2
PM-SUR-Task Substitution Errors	1.4 (0.9)	0–4
PM-SUR Loss of Content Errors	0.6 (0.7)	0–2
PM-SUR Free Recall of Intention	1.7 (1.0)	0–4
PM-SUR Cued Recall of Intention	1.8 (1.0)	0–4
PM-SUR Recognition	3.7 (0.5)	2–4
PM-Ongoing Word Search Task	17.1 (4.7)	11–32
Prospective and Retrospective Memory Questionnaire		
Prospective Memory	20.2 (5.6)	0–40
Environmentally-Cued	9.9 (2.9)	0–20
Self-Cued	10.3 (3.0)	0–20
Retrospective Memory	17.8 (4.7)	0–30

Note: Values reported are means (SD) and ranges except as noted. AusNART=Australia National Adult Reading Test and Demographics-Predicted WAIS-III Verbal IQ Score, PM=Prospective memory measure, RBANS = Repeatable Battery for the Assessment of Neuropsychological Status, SUR = Semantically-Unrelated WAIS-III = Wechsler Adult Intelligence Scale–third edition.

Table 2

Descriptive data for the Memory for Adherence to Medication Scale (MAMS) in the study sample of 65 older adults

Item	Mean (SD)	Range
1. How much difficulty do you typically have taking the medications at the time prescribed (that is, within 30 minutes of the correct time)?	2.3 (1.1)	1–6
2. How much difficulty do you have taking your medications in exactly the correct amount/dose prescribed (that is, too many or too few pills)?	1.2 (0.5)	1–3
3. Overall, how much difficulty did you have in the PAST WEEK with taking your medication?	1.2 (0.8)	1–5
4. In the afternoon, I have a hard time remembering if I took my early dose of medication.	1.4 (0.9)	1–6
5. I have forgotten whether I took my medication, even while I am in the middle of doing it.	1.1 (0.7)	1–6
6. I often have trouble remembering to get refills for my medication on time.	1.4 (0.9)	1–6
7. I forget to talk to my medical provider about side effects of my medication.	1.4 (1.0)	1–6
8. Even though I want to take my medication, I just forget to take it.	1.5 (1.2)	1–7
9. I lose track of time, and I have to take my medication late or not at all.	1.7 (1.3)	1–7
10. I have a hard time remembering to take my medication with me when I leave home.	1.5 (1.1)	1–6

Note. Higher scores reflect greater levels of medication related difficulties.

Table 3

Hierarchical regressions predicting the Memory for Adherence to Medication Scale (MAMS) from prospective memory, controlling for biopsychosocial, neurocognitive and medication-related factors in 65 older adults.

Predictors	B	B 95% CI	β	R ²	Adj. R ²	R ²
1) Biopsychosocial Factors						
Step 1:				.01	-.06	
Age	.00	-.03, .02	-.04			
AusNART Predicted VIQ	-.01	-.04, .03	-.07			
Mood	.03	-.17, .23	.05			
Number Medical Conditions	.01	-.11, .14	.03			
Step 2:				.30	.21**	.28**
PM-Semantically-Related	.05	-.15, .26	.07			
PM-Semantically-Unrelated	-.15	-.30, -.01	-.28*			
PRMQ-Prospective Memory	.05	.02, .09	.41**			
2) Neurocognitive Factors						
Step 1:				.12	.04	
MMSE Total Score	-.06	-.20, .09	-.10			
RBANS-Delayed Memory	.01	-.23, .25	.01			
Executive Domain Z Score	.05	-.14, .25	.08			
WAIS-III Digit Span	-.01	-.07, .05	-.04			
PRMQ-Retrospective Memory	.05	.01, .09	.33**			
Step 2:				.32	.22**	.20**
PM-Semantically-Related	.05	-.16, .26	.06			
PM-Semantically-Unrelated	-.17	-.32, -.02	-.33*			
PRMQ-Prospective Memory	.06	.02, .11	.47**			
3) Medication-related Factors						
Step 1:				.12	.06	
Number of Pills/Day	-.02	-.08, .05	-.07			
MAQ-Purposeful Nonadherence	-.16	-.34, .01	-.23#			
MMAA	.01	-.04, .07	.06			

Predictors	B	B 95% CI	β	R ²	Adj. R ²	R ²
Medication Strategy Use (y/n)	.37	.04, .70	.28*			
Step 2:				.35	.27**	.23**
PM-Semantically-Related	.05	-.15, .24	.06			
PM-Semantically-Unrelated	-.14	-.28, -.01	-.26*			
PRMQ-Prospective Memory	.05	.02, .08	.39**			

$p < .10$,
* $p < .05$,
** $p < .01$

Note: AusNART=Australia National Adult Reading Test and Demographics-Predicted WAIS-III Verbal IQ Score, Mood is the averaged sample-based Z score for the Geriatric Depression Scale and Geriatric Anxiety Inventory, PM=Prospective memory measure (semantically related and unrelated subscales reported), PRMQ = Prospective and Retrospective Memory Questionnaire (Prospective and Retrospective subscales reported), MMSE=Mini Mental State Examination, RBANS = Repeatable Battery for the Assessment of Neuropsychological Status (Sample based averaged Z Score for the Delayed Story and Figure Recall subtests, Executive Domain Z Score is the averaged Z Score for Trailmaking Test B, CLOX (executive dysfunction index), and Action Fluency, WAIS-III = Wechsler Adult Intelligence Scale-third edition, MAQ=Medication Adherence Questionnaire (Purposeful Nonadherence subscale), MMAA=Medication Management Ability Assessment.

Table 4

Correlations between the Memory for Adherence to Medications Scale (MAMS) and prospective memory (PM) components among 65 older adults

PM Measure	Spearman's Rho	p-value
Performance-Based PM		
Ongoing Task (word search)	.03	.839
Semantically-Related (SR)	-.09	.478
Semantically Unrelated (SUR)	-.37	.002
SUR 2-min	-.26	.039
SUR 15-min	-.32	.010
SUR Error Types		
Omissions	-.05	.707
Task Substitutions	.27	.029
Loss of Content	.19	.140
SUR Free Recall Intention	-.23	.063
SUR Cued Recall Intention	-.22	.080
SUR Recognition	-.27	.030
Self-Reported PM		
PRMQ PM Total	.38	.002
Self-Cued	.42	.001
Environmentally-Cued	.30	.016

Note. MAMS = Memory for Adherence to Medications Scale. PM = prospective memory. PRMQ = Prospective and Retrospective Memory Questionnaire. SR = semantically-related. SUR = semantically unrelated.