

**An Examination of Prospective Memory in Multiple Sclerosis: A Theoretical
Approach Using Objective and Subjective Measures**

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Abstract

An Examination of Prospective Memory in Multiple Sclerosis: A Theoretical Approach Using Objective and Subjective Measures

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Objective: Prospective Memory (PM) is the ability to complete a task at some specific point in the future without constant rehearsal. PM is noteworthy for the impact it may have on everyday functioning in patient populations, but it is difficult to assess using objective neuropsychological tests, and thus self-report has commonly been used as a measure of PM function. One problem with this method of assessment is the lack of a theoretical basis for current measures, especially in light of the many recent advances toward a theory of PM. Individuals with Multiple Sclerosis (MS) are often high-functioning, but 50-72% suffer from some form of cognitive impairment, especially in cognitive domains thought to be essential to PM. The goals of the current study were to a) use a theoretically-based approach to examining PM in the MS population, using objective and subjective measures of PM; and b) assess the usefulness of a novel measure of subjective PM problems (the Prospective Memory Complaints Questionnaire (PMCQ)) in the MS population.

Participants: Twenty-seven individuals with MS and twenty healthy controls, matched on distributions of gender, age, and education level.

Methods: Participants underwent a series of 3 measures, which included 1) a novel self-report questionnaire (the PMCQ) assessing PM difficulties administered in an interview format; 2) a standardized, objective measure of PM (the MIST); and 3) a theoretically-based experimental PM task (the Complex Prospective Memory (CPM) task).

Demographic variables, depression level, fatigue, quality of life, and level of MS symptom severity were also collected.

Results: No significant between-group differences were found in performance on any of the objective and subjective measures of PM in the MS vs. HC groups. Within-groups analyses indicated that distinct factors in each group predicted objective PM (MIST) performance, and factors related to the utility of both the CPM task and the PMCQ (and the underlying theoretical model of each) were identified.

Discussion: Overall, the current study demonstrated discrepant predictors of PM performance in MS and HCs, despite nonsignificant overall differences in performance when controlling for significant psychosocial and symptom severity factors. While much further research is needed to isolate the factors impacting PM performance in the MS population, the usefulness of a theoretical model of PM was demonstrated, as was the utility of examining PM using both performance-based and self-report measures.

1. INTRODUCTION

1.1 Specific Aims

The overarching goal of this research project was to examine impairments in Prospective Memory (PM) and inform a more comprehensive depiction of functional impairment in individuals with Multiple Sclerosis (MS). It is hoped that this enhanced patient profile will help to improve clinical judgments. Prospective Memory, or the ability to realize future intentions, has emerged in the literature as an important function that concerns the practical uses of a particular constellation of cognitive abilities. PM is especially notable for the influence it may have on everyday functioning and basic well-being, especially in patient populations that often have significant PM demands (e.g., medication adherence) concomitant with reduced capacity for the cognitive abilities which may be required for successful PM (Kliegel, Jager, Altgassen, & Shum, 2008). While the consequences of inadequate PM function can be disruptive, it is rarely assessed in clinical practice, and there is relatively little research available regarding the nature and consequences of PM deficits in distinct patient populations. PM has also proven difficult to assess using objective neuropsychological tests, and thus patient self-report has been proposed as a valuable supplement to (or substitute for) objective measures (Thone-Otto & Walthier, 2008).

Because individuals with MS frequently have a neuropsychological profile that includes generally intact everyday functioning concurrent with *some* cognitive deficits, this population is particularly appropriate to examine in terms of PM impairments. Between 50 and 72% of individuals with MS experience cognitive impairment in wide-ranging domains (Bobholz & Rao, 2003; Shevil & Finlayson, 2006). The population of

MS sufferers is relatively young and active compared with many other neurocognitively impaired populations, and individuals with MS are often keenly aware of their cognitive difficulties (Malcomson, Lowe-Strong, & Dunwoody, 2008; Marrie, Chelune, Miller, & Cohen, 2005; Yorkston, Johnson, Klasner, Amtmann, Kuehn, & Dudgeon, 2003). The current project aimed to 1) initiate a systematic approach to examining PM in the MS population, using a theoretical model (Kliegel, Mackinlay, & Jager, 2008), objective measures of PM (the Memory for Intentions Test (MIST) and an experimental paradigm, the Complex Prospective Memory Task), and a novel subjective measure of PM (the Prospective Memory Complaints Questionnaire (PMCQ)); and 2) collect user feedback to begin to validate a newly-developed questionnaire (the PMCQ) that seeks to gather and analyze self-reported PM difficulties.

1.2 Background: Prospective Memory and Everyday Functioning

Prospective Memory (PM) is the term that has been traditionally applied to the concept of realizing delayed, or future, intentions. As Freud pointed out more than one hundred years ago, the factors inherent in both our successful and unsuccessful attempts at accomplishing future objectives are often a mystery to us (Freud, 1901). More recently, research has begun to explore the complex stages of processing that must usually occur to successfully complete a delayed objective. Researchers such as Burgess, Dumontheil, Gilbert, Okuda, Scholvinck, & Simons (2008) and Moscovitch (2008) discuss PM as a *function* rather than a *construct*. The difference, they maintain, is that a *function* is a set of context-dependent real-world behaviors that relies on multiple subordinate *constructs*, such as attention and working memory, which are more specialized cognitive processes (Burgess et al., 2008). Thus, research on prospective memory as a function is (or should

be) more concerned with the practical, everyday uses of the functional ability rather than focusing on component cognitive constructs, which may not provide a truthful picture of the purpose and process of cognitive abilities (Moscovitch 2008).

As one might expect, these “practical uses” are countless, and PM demands occur across the breadth of everyday human experience. Activities of daily living (ADLs), such as paying bills on time, often require intact PM abilities, as do many occupational (e.g., attending meetings and appointments, multitasking), social (e.g., returning messages from friends or picking someone up at the airport), and health-related (e.g., medication adherence or attending medical appointments) activities. PM requirements, and their chance of success or failure, are complicated by general conditions in one’s life, especially those (such as raising children) in which extremely complex multitasking becomes of central importance (Burgess et al., 2008). Failure in any of the above domains is by no means homogeneously significant to one’s life, but runs the gamut from being “highly embarrassing...[or] frustrating” to “life-threatening” (Kliegel, Jager, et al., 2008, p. 284). In healthy individuals, the occasional PM failure is likely only to inconvenience oneself or cause others to become annoyed, while in many patient populations, tasks such as managing complex medication regimens are essential to health and safety, and poor PM function imposes extra responsibilities on caregivers (Kliegel, Jager, et al., 2008).

1.2.1 A Theoretical Model of Prospective Memory

The complexity of PM function necessitates establishing a theoretical framework to guide hypotheses. Several models, most coming from the cognitive psychology literature, have been suggested to explain how PM occurs, including Shallice and

Burgess's (1991) Supervisory Attentional System (SAS) theory, the Preparatory Attentional and Motivational Processes theory (PAM; Smith & Bayen, 2004) and Kliegel, Martin, McDaniel, and Einstein's Multi-Phasic Process framework (Kliegel, Mackinlay, & Jager, 2008; Kliegel, Martin, McDaniel, and Einstein, 2002). Most research concerning the cognitive process of PM focuses on what has been termed the "initiation" of the delayed intention. In other words, both the SAS and the PAM theories, along with most laboratory investigations of PM, are most concerned with how it is that one becomes aware that it is time to enact one's intention (Hertzog, 2008; Simons, Scholvinck, Gilbert, Frith, & Burgess, 2006). To this end, these theories often focus on the distinction between *time-cued* and *event-cued* PM tasks, since different aspects of environmental monitoring may be involved when one's task must be initiated at a specific time (e.g., pick up a friend at the airport at 7:15) rather than in response to a specific event (e.g., stop to buy milk when passing a convenience store).

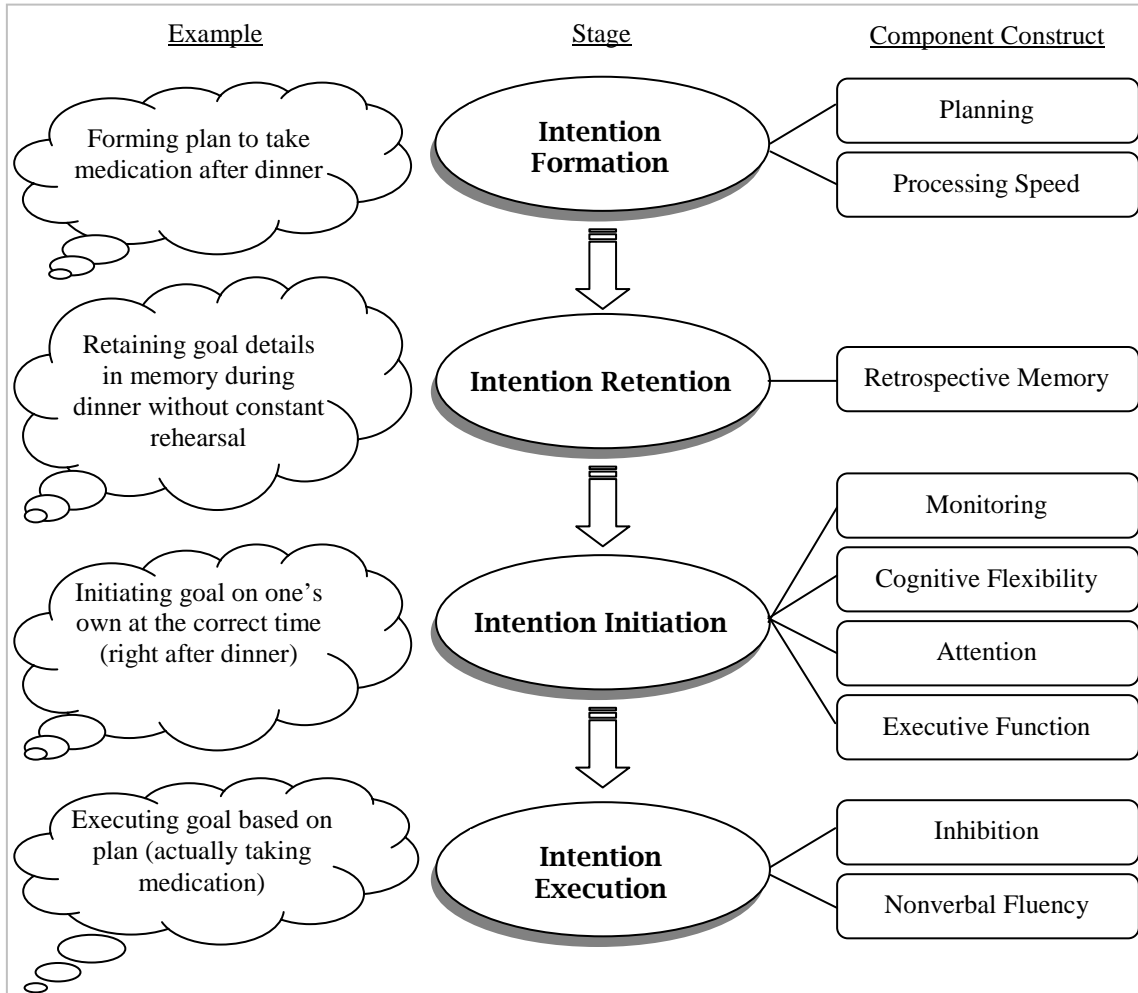
While the "initiation" aspect of PM is clearly an integral step in the process of realizing a delayed intention, it is neither the only time when PM errors can occur nor necessarily the most important point in the process, although it has apparently proven to be the most convenient to study. In contrast, Kliegel, Martin, McDaniel, and Einstein's (2002) Multi-Phasic Process model, while broader and potentially more difficult to examine empirically in a single study, seeks to specify all of the stages of processing that are required for successful PM. The stages of this model include *Intention Formation* (forming a plan of what is to be enacted), *Intention Retention* (retaining the intention in memory), *Intention Initiation* (recognizing the circumstances in which the intention should be performed), and *Intention Execution* (actual performance of the intention) (see

Figure 1 for a graphical representation). A major strength of this model is that it speculates as to what cognitive constructs may contribute to PM function at each stage. Despite fairly extensive inquiry in the literature, the word “speculate” may still be apt. Though there is general agreement on what component constructs are *likely* to contribute to each stage of PM, studies of patients who perform well on neuropsychological measures of these constructs but poorly on measures of PM are not uncommon (Burgess et al, 2008; West, McNerney, & Krauss, 2007).

The most common component constructs mentioned in the literature, according to which stage of the multi-phasic model they are thought to influence, are outlined in Figure 1. Intention formation is thought to rely on planning abilities and encoding efficiency or processing speed. Retrospective episodic memory is the key ability underlying intention retention. As was mentioned previously, intention initiation has been the most thoroughly studied stage, and is likely to require some combination of monitoring, cognitive flexibility, attention, and especially executive function. Intention execution has been correlated with inhibition and nonverbal fluency (Burgess et al., 2008; Kliegel, Jager, et al., 2008; Kliegel, Mackinlay, et al., 2008).

Perhaps the most useful aspect of the Multi-Phasic Process model is that when PM failures occur, the (relatively more) specific stages or component of the failure can be identified and analyzed. Much more research is needed to determine both the accuracy of this model with regard to true PM function and what underlying constructs are important to each step in the process (e.g., executive planning to Intention Initiation, or inhibitory control to Intention Initiation) (Kliegel, Jager et al., 2008). However, it is the expansive scope of the Multi-Phasic Process theory that makes it extremely valuable to a

preliminary investigation of PM.



Example from Kliegel, Mackinlay, et al. (2008). Model components from Kliegel, Jager, et al. (2008); Kliegel, Mackinlay, et al. (2008); and Burgess et al. (2008).

Figure 1: Cognitive Components of Prospective Memory Multi-Phasic Model

1.2.2 Measuring Prospective Memory

There is remarkably little to say with regard to assessing PM, because there are almost no standardized measures to do so. While there are nearly as many experimental PM paradigms as there are PM experiments, these experimental paradigms are often

time-consuming and hardware-intensive, and their psychometric properties are rarely reported; thus, while very useful in empirical investigations of the theoretical bases of PM, they may not be particularly useful clinically (Kliegel, Jager, et al., 2008).

Unfortunately, while experimental paradigms often have strong theoretical foundations, the same cannot be said for even the more popular PM assessment tools (Thone-Otto & Walthier, 2008). The Rivermead Behavioral Memory Test (RBMT; Wilson, Cockburn, & Baddeley, 1985) includes two PM tasks, but these have only been standardized in the context of the entire test, and thus a PM score is not easily obtained. Two recently-developed measures that have shown promise are the Cambridge Test of Prospective Memory (CAMPROMT; Wilson, Emslie, Foley, Shiel, Watson, Hawkins, et al., 2005) and the Memory for Intentions Test (MIST; Raskin & Buckheit, 2010). Each takes less than an hour to administer, consists of both time-cued (e.g., “Switch to another pen in 7 minutes...”) and event-cued (e.g., “When I hand you a red pen...”) tasks, and has been standardized, although the CAMPROMT’s standardization is more comprehensive at this point (Thone-Otto & Walthier, 2008). Both of these tests show potential but suffer from inadequate theoretical support and lack of standardization in patient groups other than TBI (Kliegel, Jager, et al., 2008).

The limited number of well-validated, clinically useful PM assessment tools is partly due to the unique challenges posed by the complexity of PM function and our lack of understanding of the cognitive correlates of successful PM. A binary assessment of a PM task attempt (i.e. the success or failure of the intended action) confers only a limited picture of PM function, and thus objective measures such as the CAMPROMT and the MIST must be supplemented with a close examination of the patient’s daily functioning,

which may be difficult to obtain (Thone-Otto & Walthier, 2008). A thorough analysis of the specific cause of a PM failure (using an empirically-based theoretical model) would give clinicians insight into a patient's clinical profile (Kliegel, Jager et al., 2008; Ellis & Freeman, 2008). To this end, it has been suggested that questionnaires may be effective means by which to assess PM function while retaining the context of the behavior. Questionnaires are currently the most commonly-used procedure for evaluating PM (Thone-Otto & Walthier, 2008). However, the degree to which even the more popular PM questionnaires actually measure current conceptions of PM is debatable. Often they include tasks that are no longer thought to fit under the rubric of PM (such as remembering to brush one's teeth, which is a more routine, crystallized task; see the Comprehensive Assessment of Prospective Memory; Waugh (1999)) or focus only on specific components of PM, such as memory for the details of the intention (the "retrospective component;" see the Prospective and Retrospective Memory Questionnaire; Smith, Della Sala, Logie, & Maylor, 2000). The major disadvantage of all self-report measures is the potential for inaccurate reporting, which is even more of a concern in cognitively impaired populations. However, authors of both reviews (Thone-Otto & Walthier, 2008) and empirical studies (Crawford, Henry, Ward, & Blake, 2006; Hannon, Adams, Harrington, Fries-Dias, & Gipson, 1995) support the use of questionnaires as measures of PM in particular. In any case, self-report measures of PM surely provide the clinician with information that may not be available from objective cognitive tests alone (Sullivan, Edgley, & Dehoux, 1990).

Currently, prospective memory is not commonly assessed in clinical contexts, despite the fact that problems completing delayed intentions are frequently noted in

numerous patient populations. As Kliegel, Jager, et al. (2008) illustrate in their excellent overview of investigations of PM in clinical populations, a wide range of patient groups have been examined in terms of potential PM deficits, including substance abuse, psychiatric disorders, developmental disorders, viral infections, and neurological disorders. The results of these studies are enlightening and contribute considerably to exposing PM as a significant problem in clinical populations. A closer look at their survey, however, reveals the lack of depth in the clinically-based PM literature. Outside of dementia and TBI, no disorder has garnered more than a handful of publications that focus on PM impairments. The studies that do exist employ a variety of methods (usually experimental paradigms) to examine PM, many of which fall far short of today's standards or include manipulations that are no longer believed to be valid. This deficiency of research is surprising, given the sheer number of disorders associated with cognitive deficits that putatively contribute to PM ability (Kliegel, Jager et al., 2008).

1.3 Background: Multiple Sclerosis and Associated Cognitive Deficits

Multiple Sclerosis (MS) is thought to be an autoimmune disease in which the sufferer's immune system attacks the myelin sheath of neurons in the central nervous system, causing diffuse white matter damage and widespread disruption of neural transmission. Symptoms of the disease are extremely varied, but generally fall into the broad categories of motor impairments, sensory impairments, emotional problems, bowel and bladder difficulties, and cognitive impairments, as well as pain and fatigue. Several subtypes of the disease have been identified based on the rate and pattern of progression, which usually happens in discrete episodes called relapses or exacerbations. Prevalence rates for MS vary; a 2001 study of worldwide MS prevalence by Rosati found rates

between 2 and 150 per 100,000, but it is generally agreed that MS is one of the most common neurological diseases of early and middle adulthood (Engel, Greim, & Zettl, 2007). Because MS sufferers are relatively young and active compared with many other neurocognitively impaired populations, they often retain a strong desire to be active and engaged in work and other activities. A significant portion of the MS population is in the prime of their working lives (in terms of age), and several studies have looked qualitatively at these individuals' perceptions of their occupational limitations. Even if "work" is given the broader definition of any activity done to accomplish some goal despite obstacles, it is clear that ability to work and maintain productivity is a major concern for this population. Many of their concerns are related to the presence or anticipation of cognitive decline (Malcomson, Lowe-Strong, & Dunwoody, 2008; Shevil & Finlayson, 2006; Yorkston, Johnson, Klasner, Amtmann, Kuehn, & Dudgeon, 2003).

Although MS is noteworthy because of the sheer number of potential symptoms, researchers have recently become increasingly interested in the cognitive symptoms of the disorder. There is some disagreement about the prevalence of cognitive impairments in MS; the common belief seems to be that roughly 50% have impairments (Bobholz & Rao, 2003), but other estimates are as high as 72% (Shevil & Finlayson, 2006). Memory difficulties are a common finding and include retrospective memory (in this case encompassing short term and long term memory) and working memory (Thornton & Raz, 1997). Other domains shown to be impaired include processing speed and immediate memory (Marrie, Chelune, Miller & Cohen, 2005), attention, visuospatial abilities, and executive abilities (Engel, Greim, & Zettl, 2007; Bobholz & Rao, 2003).

It is also worth bearing in mind that MS, by definition, affects tissue throughout

the central nervous system. While it has traditionally been thought to affect mainly the white matter, recent investigations have implicated deep grey matter structures as well, including medial temporal lobe structures and the thalamus (Benedict, Ramasamy, Munschauer, Weinstock-Guttman, & Zivadinov, 2009). Benedict et al. (2009) demonstrate the detrimental effects of frontal-subcortical axis degeneration on memory, processing speed, and visual perception. This study provides evidence of the consequences of damaged neural connections, which may especially (or exclusively) impair functions that rely on separate structures working in concert.

1.3.1 Background: Prospective Memory in Multiple Sclerosis

Given the range of cognitive deficits demonstrated in MS, and considering the apparent contributions of most of these cognitive abilities to PM, it is not unreasonable to expect PM deficits in individuals with MS. This has been found to be the case in the very few studies that have examined PM function in MS (see Kliegel, Jager, et al., 2008, for a review; Bruce, Hancock, Arnett, & Lynch, 2010; Kardiasmenos, Clawson, Wilken, & Wallin, 2008; Rendell, Jensen, & Henry, 2007; Bravin, Kinsella, Ong, & Vowels, 2000). Interestingly, even studies that have ruled out deficits in component constructs have identified PM problems (Rendell, Jensen, & Henry, 2007), and West, McNerney, & Krauss (2007) reported a case study of a potential circumscribed PM deficit in an individual with MS. These findings are puzzling but speak to the complexity of PM function as more than the sum of its parts, as well as to the need for further study in patient groups such as MS and more sensitive (and perhaps population-specific) measures of PM.

In light of the earlier discussion regarding the use of self-report measures to

assess PM function, and the complications inherent in such an assessment, the fact that individuals with MS are often keenly aware of their cognitive difficulties is worthy of mention. Many would argue, and logic dictates, that a memory-impaired person is not able to accurately perceive his or her own memory deficit, and this phenomenon is apparent in cognitively-impaired patient populations such as patients with Alzheimer's disease. However, at the early stages of decline, cognitive impairments that are too subtle to be picked up by neuropsychological (and also, importantly, imaging) study may be evident to the patient themselves in a subjective sense. Marrie et al.'s 2003 study using 136 individuals with MS showed that there is an intriguing, and non-linear, relation between cognitive decline and subjective memory complaints (as measured by a self-report memory inventory), in that those with the fewest deficits (i.e. normal function) and those with the most deficits (i.e. severe impairments) are unlikely to report subjective cognitive complaints, whereas individuals with mild impairments are able to accurately report on their experience. Of special note, this study also controlled for depression, which is associated with subjective cognitive complaints across patient populations (and probably in the general population as well). Additionally, the authors controlled for fatigue and physical impairment, both of which are particularly important issues in the MS population (Marrie et al., 2003). The fact that these authors were able to tease apart such significant and interrelated factors is remarkable.

Several other studies have corroborated Marrie et al.'s (2003) assertion that individuals with MS can be relied upon to provide accurate information regarding their deficits. Studies by Solari, Amato, Bergamaschi, et al. (1993) and Goodin (1996) showed that patient self-report of deficits predicted performance on objective scales of

impairment. More recently, Benedict & Zivadinov (2006) developed and used the Multiple Sclerosis Neuropsychological Screening Questionnaire (MSNQ) as a brief, reliable screening tool for cognitive and psychiatric dysfunction in MS. The measure includes both patient and informant forms, and in their 2006 study, scores on both forms significantly correlated with patient performance on a battery of neuropsychological tests. A previous study by this group using the same questionnaire had failed to find correlations between patient-report and objective test performance, but did find correlations with informant report (Benedict, Munschauer, Linn, Miller, Murphy, Foley, & Jacobs, 2003). Bruce, Bruce, Hancock, & Lynch (2010) found that perceived memory impairment was not associated with any neuropsychological testing measure, but that the relationship was mediated by dissociative experiences. As these examples indicate, findings in these types of studies are not perfectly consistent, and the studies which have found subjective reports of individuals with MS to be reliable are by no means conclusive. While studies such as these are potentially limited by the inclusion of participants with more serious impairments, they specify the need to use caution when interpreting the results of subjective assessments of cognitive impairment, with increased caution required as impairment levels increase.

1.4. Significance of the Present Study

The current study sought to initiate a systematic approach to examining PM in the MS population, using a Multi-Phasic Process-based theoretical model (Kliegel, Mackinlay, et al. 2008; Kliegel, et al., 2002). It was hoped that the use of this model as the basis for PM assessment would facilitate the collection of specific information regarding exactly what skills or components influence a patient's PM performance; thus,

for example, if a patient has the most trouble with the “intention initiation” stage of PM, we may be able to rule out selective retrospective memory problems as the underlying cause of a patient’s PM difficulties and focus on what abilities may have a greater contribution, such as attention or executive function.

Before clinicians can appropriately interpret the results of PM assessment using self-report and/or neuropsychological testing, it is important to understand to what degree PM failures are truly problematic for individuals with MS. The MS population is an ideal one with which to assess subjective PM complaints due to the reasons described above: they are often young and engaged (and thus have many PM demands), are frequently well-aware of their cognitive deficits (thus, self-report should be reliable), and suffer from a constellation of cognitive symptoms that are likely to be integral to successful PM (thus, we can expect PM deficits in many individuals with MS). To gather preliminary information regarding PM impairments, the Applied Neuro-Technologies Laboratory has developed a questionnaire to capture detailed information regarding specific PM difficulties in the MS population. Previous studies of this type, as well as previous subjective PM measures, have suffered from poor theoretical support and insufficient attention given to the full range of potential cognitive correlates of PM. To address these concerns, the Prospective Memory Complaints Questionnaire (PMCQ) was developed as a theoretically-based measure designed to garner information regarding the frequency of PM problems, how personally significant these problems are, and what particular stages of processing are most important when failures occur in individuals with MS (see Figure 2 for a sample item; see Appendix A for the complete questionnaire). The preliminary information gathered with this measure is an important first step to characterizing PM

difficulties in MS, and healthy controls also completed the survey to determine whether PM problems in the MS population are quantitatively and/or qualitatively different than PM problems in healthy adults. Additionally, in this study we began to examine the relation between subjective reports and objective measures of PM by comparing self-report data to a standardized measure of PM function as well as a theoretically-based experimental PM paradigm, the Complex Prospective Memory Task. The current study represents the first investigation to systematically assess subjectively-reported impairments in PM based on a process model, in any patient group. The overarching goal is to use information about PM impairments to inform a more comprehensive depiction of functional impairment in MS in order to improve clinical judgments.

I did not take out the garbage on trash day, even though it needed to go out.				
A	Please rate how often this has occurred in the last month			
	0	1	2	3
	Never	Sometimes	Often	Almost Always
B	I did not take out the garbage on trash day, even though it needed to go out because...			
	<input type="checkbox"/> I did not make a plan to take the garbage out			
	<input type="checkbox"/> I forgot some important detail about trash day			
	<input type="checkbox"/> I did not take out the garbage in time			
C	Please rate how distressing this was to you			
	0	1	2	3
	Not at all distressing	A bit distressing	Moderately distressing	Very distressing

Figure 2: PMCQ Sample Item

2. METHODS

2.1 Study Overview

This study was a preliminary exploration of PM difficulties in a sample of individuals with MS as compared to healthy controls. Data was collected during a two-hour study visit in which individuals with MS and controls completed a standardized objective PM assessment, an experimental PM paradigm, and a new self-report measure, the Prospective Memory Complaints Questionnaire (PMCQ) in an interview format. Demographic information and several measures of psychosocial function were also collected, including information pertaining to each patient's MS diagnosis. The primary goal of the current study was to use theoretical rationale to characterize PM problems in individuals with MS, using both objective and subjective measures of PM. A secondary goal was to assess the usefulness of the PMCQ as a measure of everyday PM function.

2.2 Participants

The groups consisted of a sample of individuals with diagnosed MS of any type ($N = 27$), and a sample of healthy controls (HCs; $N = 20$).

2.2.1 Recruitment

The MS participants were recruited from local chapters (PA and NJ) of the National Multiple Sclerosis Society and a local neurology clinic, as well as from a database of individuals with MS involved in other studies in the Applied Neuro-Technologies Lab. Healthy Control participants were recruited through flyers posted locally and given to former lab participants, and from a database of HC individuals involved in other studies in the Applied Neuro-Technologies Lab. All participants were required to be between 21 and 60 years of age, because of the rarity of receiving an MS

diagnosis before 21 and to reduce the potential effects of aging on cognitive performance. Participants had to meet the following exclusion criteria: 1) no significant alcohol/drug history, defined by current treatment or hospitalization; 2) no significant neurological diagnosis, defined by diagnosis and/or treatment of a major neurological illness (e.g. TBI, seizure disorder); 3) no significant psychiatric history, defined by diagnosis and/or treatment of a major psychiatric illness (e.g., bipolar disorder). MS participants were required to have carried their diagnosis of MS for at least one year, must not have had a relapse within the past 30 days and could not have been undergoing steroid treatment, because of the probability of acute symptoms during these periods and the influence of these medications on cognitive performance.

In the MS group, twenty-seven out of 33 individuals who underwent initial assessment protocol met the inclusion and exclusion criteria specified previously and consented to participate in the study. In the HC group, 20 out of 47 individuals who underwent initial assessment proceeded to study enrollment. Of the MS individuals not meeting criteria, one individual exceeded the age requirement, and two individuals were not on a stable regimen of medications. Three individuals met criteria to participate, but declined entry into the study. Of the HC individuals, 27 individuals were excluded because they were unsuitable matches for the MS sample, either because of age (i.e., too young) or gender (i.e., male).

2.2.2 General demographics

The MS sample consisted of 27 participants with a diagnosis of MS confirmed through participants' treating neurologist. The sample was 96% female ($n = 26$) and 4% male ($n = 1$), relatively consistent with reported gender differences in MS disease

prevalence, indicating higher rates among females (Milo & Kahana, 2010). Participants' mean age was 47.7 years ($SD = 7.90$), and mean education was 15.2 years ($SD = 2.20$). The sample was 85.2% Caucasian ($n = 23$), 7.4% African-American ($n = 2$), and 7.4% Hispanic ($n = 2$), consistent with reports of higher MS disease prevalence in Caucasian individuals.

The HC sample consisted of 20 participants without a diagnosis of MS. The sample was 95% female ($n = 19$) and 5% male ($n = 1$). Participants' mean age was 48.8 years ($SD = 8.37$), and mean education was 15.6 years ($SD = 2.44$). The sample was 65.0% Caucasian ($n = 13$) and 35.0% African-American ($n = 7$).

2.2.1 Power Analysis

The proposed project was a preliminary and exploratory analysis. To satisfy one of the primary objectives, to characterize PM deficits in individuals with MS as compared to healthy controls, we employed separate methods to analyze results of the objective and subjective PM measures. To examine group differences in PM functional assessment (MIST) scores, planned analyses included an independent-samples t -test. Based on a power analysis using the program G*Power (Faul, Erdfelder, Buchner, & Lang, 2009) and the average calculated effect size from the three available studies which examined PM in MS (Kardiasmenos et al., 2008; Rendell et al., 2007; Bravin et al., 2000), and assuming an alpha of .05 and power of .80, 27 participants were projected to be required in each group to obtain statistical significance. To examine group differences in subjective PM ratings, planned analyses included an independent-samples t -test using scores from the Frequency scale of the PMCQ (see Section 2.3.2, below). Based on objective PM assessment data (since this type of analysis has not been conducted

previously), a medium effect size (identical to that expected in the previous analysis) with an alpha of .05 and power of .80, it was estimated that this analysis would also require 27 participants per group to obtain statistical significance.

Though the preceding power analyses do not address all of the analyses conducted in the current investigation (see Section 2.5, below), they do address all analyses that have any previous literature whatsoever on which to derive effect size estimates. Thus, based on the results of this power analysis, the target group size was 27 per group.

2.3 Assessment Measures

A list of all planned assessment measures is provided in Table 1.

Table 1: Test Battery

Measure	Description	Reference
Neuropsychological tests		
Memory for Intentions Test (MIST)	The MIST is a test of eight prospective memory tasks. Each of the eight tasks is similar to a real-world task that one might have to perform in daily life. It includes both time- and event-cued tasks, and both long and short time delays. It also includes a 24-hour delayed task. It is particularly appropriate for individuals with neurological disorders.	Raskin & Buckheit, 2010
Complex Prospective Memory Task (CPM)	The Complex Prospective Memory Task is a research paradigm using a modified version of the Six Elements Test first proposed by Shallice and Burgess (1991), in which participants have six minutes to perform two parallel versions of three types of tasks. The PM-specific modifications include manipulations in which participants are asked to explicitly plan their strategy in advance, recall their plan when prompted, and self-initiate the task at a specified time.	Kliegel, McDaniel, & Einstein, 2000
Multiple Sclerosis Functional Composite (MSFC)	The Multiple Sclerosis Functional Composite (MSFC) is a composite score composed of three measures of functions commonly impaired in MS: lower extremity function (measured with the Timed Walk Test (TWT)), upper extremity function (measured with the Nine-Hole Peg Test (9-HPT)), and cognitive function (measured with an MS-specific version (2- and 3-second trials) of the Paced Auditory Serial Additional Test (PASAT)).	Fischer, Rudick, Cutter, & Reingold, 1999),
Questionnaires		
Prospective Memory Complaints Questionnaire (PMQC)	The PMQC consists of 25 items grouped into 4 domains: Medical/Health, Vocational, Social, and Everyday Activities. Each item describes a possible PM failure and asks participants to: a) rate how often this problem occurs for him or her, on a 0-3 scale; b) choose at which stage of processing the error occurred; and c) rate how distressing the failure was, on a 0-3 scale. Ratio scores (scale score / total items endorsed) will be computed for parts a and c, and responses to part b will be analyzed quantitatively.	McKeever & Schultheis, unpublished
Multiple Sclerosis Quality of Life-54 (MSQoL-54)	The MSQOL-54 is a 54-item questionnaire assessing health-related quality of life, and includes items that tap directly into the physical, social, sexual, and fatigue- and pain- related symptoms of MS.	Vickrey et al., 1995
Beck Depression Inventory – II (BDI-II)	The BDI-II contains 21 self-report items assessing depression symptom severity based on the DSM-IV criteria. Though neurovegetative symptoms of MS have been shown to elevate BDI-II score, evidence is equivocal, and research has shown that all BDI-II items do indeed tap depression in MS (Moran & Mohr, 2005).	Beck, Steer, & Brown, 1996
Fatigue Severity Scale (FSS)	The FSS is a 9-item self-report inventory commonly used in individuals with MS to evaluate their subjective level of fatigue over the past week using a 7-point Likert scale.	Krupp et al., 1989
Visual Analog Scale of Fatigue (VAS-F)	The VAS-F is a visual analogue scale used to assess levels of state fatigue. Participants mark their current level of fatigue on a line 10 centimeters long. It will be administered at the beginning and end of the testing day to monitor the effects of fatigue during testing.	Kos et al, 2006

2.3.1 Demographic Information

Demographic variables of age, gender, occupational status, medications, and years of education were collected from all participants. Variables collected from MS

participants included MS subtype, duration of diagnosis, and duration of symptoms. HCs were selected to match the distributions of the MS group's demographic variables (age, gender, and years of education only).

2.3.2 *Questionnaire (PMCQ)*

The Prospective Memory Complaints Questionnaire (PMCQ) was developed for this study because of the scarcity of theoretically-based and comprehensive measures of PM currently available. The measure consists of 25 items grouped into 4 domains: Medical/Health, Vocational, Social, and Everyday Activities. Each item describes a possible PM failure an individual might experience and asks respondents to a) rate how often this problem occurs for him or her; b) choose at which stage (see Kliegel, et al.'s (2002) model) the error occurred; and c) rate how distressing the failure was. It includes comprehensive instructions to ensure that respondents understand what is being asked, and includes a cover page to collect demographic information (age, type of MS, checklist of symptoms, etc.) as well as information regarding what strategies or external memory aids the respondent may commonly use (for an example of a PMCQ item, see Figure 2, above; see Appendix A for the complete questionnaire). In this preliminary study, the PMCQ was administered in an interview-type format. This decision was made due to the fact that this is the first time the measure was used, and extensive notes were taken regarding factors such as participant confusion about certain items in order to make adjustments and improve to the measure.

The PMCQ was modeled after several previous PM self-report measures (Smith, Della Sala, Logie, & Maylor, 2000; Waugh, 1999; Hannon et al., 1995) and a previous memory questionnaire used in MS (Sullivan et al., 1990). However, the PMCQ is unique

in that it 1) was theoretically developed using the Multi-Phasic Process model of PM, 2) makes use of only the most current conceptions of PM tasks, and 3) includes a rating not only of the frequency of problems but also their personal significance to the respondent.

Because there are three elements to each PMCQ item (see Figure 2), scoring of the PMCQ items was divided into several scales. The “Frequency” scale was calculated from the sum of responses to the frequency (A) element divided by the total number of responses to the overall questionnaire, to account for items that were not applicable to the respondent. The “Stage” scale consisted of three sub-scores, determined by the total number of endorsements on each of the three stage options (element B) (i.e., one score for the “form a plan” option (Plan sub-score), one score for the “forgot my plan” option (Recall sub-score), and one score for the “initiate my plan” option (Initiation sub-score)). The “Distress” scale was calculated, similarly to the Frequency scale, from the sum of responses to the distressfulness (C) element divided by the total number of responses to the questionnaire. Domain sub-scores were calculated separately for each of the four domains (Medical/Health, Vocational, Social, and Everyday Activities), and consisted of the sum of the endorsements from the Frequency (A) and Distress (C) elements for the set of items corresponding to each domain. The Medical/Health domain included 4 items, the Vocational domain included 6 items, the Social domain included 6 items, and the Everyday Activities domain consisted of 9 items.

2.3.3 Complex Prospective Memory Task

The Complex Prospective Memory (CPM) Task (Kliegel, McDaniel, & Einstein, 2000) is a modified version of the Six Elements Test (mSET) first proposed by Shallice and Burgess (1991). Participants are given six minutes to perform two parallel versions of

three types of tasks (word task, arithmetic task, picture naming task) for a total of six tasks. Rules are given that govern how the tasks must be completed, but otherwise the manner in which the tasks are completed is up to the participant. The PM-specific version included manipulations in which participants were asked to explicitly plan their strategy in advance, recall their plan when prompted, and self-initiate the task at a specified time. Four scores are produced for the complete CPM task, corresponding to the four phases of PM (Intention Formation [Plan], Intention Retention [Recall], Intention Initiation [Initiation], and Intention Execution [Execution]). The Plan and Recall phases are verbally produced by the participant and recorded, and the contents of each phase is scored based on criteria given in Kliegel, et al. (2000). The Initiation portion of the task requires participants to begin the mSET in response to a specific cue (after completing their date of birth on the Participant Information Form), and one point is given for a) remembering the correct task, and b) doing so at the correct time, for a maximum possible score of 2 points. The Execution portion is simply the participant's actual performance on the mSET task (part of the Behavioral Assessment of the Dysexecutive Syndrome battery; Wilson, Alderman, Burgess, Emslie, & Evans, 1996).

2.3.4 Standardized Prospective Memory Measure

To obtain an objective and standardized measure of PM function, the Memory for Intentions Test (MIST; Raskin & Buckheit, 2010) was administered. While it has been used in other patient populations, to our knowledge this test has been used only once in the MS population (Bruce, Hancock, Arnett, & Lynch, 2010). The MIST is a test of eight prospective memory tasks. Each of the eight tasks is similar to a real-world task that one might have to perform in daily life; for example, one item states, "in 2 minutes, ask me

what time this session ends today” (Woods, Moran, Dawson, Carey, & Grant, 2008). It includes both time- and event-cued tasks, and both long (15-minute) and short (2-minute) time delays. It is particularly appropriate for individuals with neurological disorders, and takes approximately 30 minutes to administer.

2.3.5 Other Measures

Testing included several tests traditionally used to estimate the contribution of MS symptoms to neuropsychological test performance, as well as a measure of depression, which has been frequently noted to have a significant effect on self-report measures and be a concern for the MS population (Middleton, Denney, Lynch, & Parmenter, 2006). A general depiction of subjectively-reported MS symptom severity and its effects on quality of life was assessed with the Multiple Sclerosis Quality of Life-54 measure (MSQOL-54; Vickrey, Hays, Harooni, Myters, & Ellison, 1995). Objective MS symptom severity was measured with the Multiple Sclerosis Functional Composite (MSFC; Fischer, Rudick, Cutter, & Reingold, 1999), which is a composite score composed of three measures of functions commonly impaired in MS: lower extremity function (measured with the Timed Walk Test (TWT)), upper extremity function (measured with the Nine-Hole Peg Test (9-HPT)), and cognitive function (measured with an MS-specific version (2- and 3-second trials) of the Paced Auditory Serial Additional Test (PASAT)). State and overall symptomatic fatigue were measured with the Visual Analog Scale of Fatigue (VAS-F; Kos, Nagels, D'Hooghe, Duportail, & Kerckhofs, 2006) and the Fatigue Severity Scale (FSS; Krupp, LaRocca, Muir-Nash, & Steinberg, 1989), respectively. Depression severity was measured using the Beck Depression Scale - II (BDI-II; Beck, Steer, & Brown, 1996). The FSS, BDI-II and MSQOL-54 were

completed at the end of the testing session.

2.4 Procedures

To determine eligibility, a pre-study phone screening interview was conducted. Using a predetermined script, the researcher asked several questions to ensure that all of the exclusion and inclusion criteria were met. Following the pre-screening phone interview, if eligible, the participant was invited to participate and given written informed consent including HIPAA approved by the Drexel University Institutional Review Board (IRB). After obtaining informed consent, eligible participants proceeded to study enrollment.

All participants participated in one session lasting approximately two hours. All testing was conducted in the Schultheis Applied Neuro-Technologies Laboratory at Drexel University. At the beginning of the testing session, participants were administered an initial VAS-F scale to obtain a pre-testing rating of fatigue, and the Plan phase of the CPM task was then administered. Next, participants were asked to provide a brief medical and psychosocial history, followed by the measures composing the MSFC and the Recall phase of the CPM task. The PMCQ questionnaire interview then took place, followed by the remaining portions of the CPM task, followed by the MIST. The remaining questionnaires (the FSS, MSQoL-54, and BDI-II) were then completed. Participants were offered a short break after roughly one hour of testing, as long as it did not occur during a test-required delay. At the end of the study participants completed a final VAS-F, and were debriefed and compensated for their time.

2.5 Hypotheses and Plan of Analysis

Preliminary analyses were conducted to compare demographic and psychosocial variables between the two groups and ensure an equal distribution of these variables. Independent-samples *t*-tests for continuous variables or chi-square tests of independence for categorical variables were used to examine whether the groups' distributions differ significantly on these variables. When significant differences were found, these variables were used as covariates in subsequent analyses to control for their potential influence. Several changes from the original project proposal were instituted, most notably: a) hypotheses were refined and updated after reconsideration of the specificity/testability of the original text; b) because statistically significant differences between the groups were identified on psychosocial and symptom severity variables, Analyses of Covariance were employed instead of *t*-tests to statistically control for these variables; and c) where statistically significant differences were not identified between the groups on main study variables, additional analyses (stepwise linear multiple regressions) were employed to explore patterns of performance in each group separately.

The data were checked to determine to what degree the assumptions for each statistical test were violated. If assumptions were not met, data transformations or other remedial procedures were undertaken to account for the violations. Analyses addressed the aims of the study. See Table 2 for a description of all study variables.

Table 2. Study Variables

Measure/Variables	Function Measured
<u>MIST</u>	
Total Score percentile (PMT%)	Standardized objective PM performance
<u>CPM Task</u>	
Plan Stage Score	Intention Formation stage performance
Recall Stage Score	Intention Retention stage performance
Initiation Stage Score	Intention Initiation stage performance
mSET Profile Score	Intention Execution stage performance
<u>PMCQ</u>	
PM Aids used	Self-reported (SR) # of PM aids used
Total Items Answered	# of items endorsed as applicable to the participant
Frequency Scale Score	SR PM error frequency†
Distress Scale Score	SR PM error-related distress†
Plan Stage sub-score	SR Intention Formation errors
Recall Stage sub-score	SR Intention Retention errors
Initiation Stage sub-score	SR Intention Initiation errors
Medical Domain sub-score	SR medically-related item errors
Vocational Domain sub-score	SR vocationally-related item errors
Social Domain sub-score	SR socially-related item errors
Everyday Activities Domain sub-score	SR everyday activities-related item errors
<u>Questionnaires</u>	
FSS Average Score	Average SR symptomatic fatigue
BDI-II Score	SR Depression level
MS-QoL Overall QoL	Overall SR quality of life
MS-QoL Physical Composite Score	Overall SR physical symptom-related quality of life
MS-QoL Mental Composite Score	Overall SR mental symptom-related quality of life
<u>MSFC Score</u>	MS symptom severity (composite score)

† = Corrected for Total Items Answered

Aim 1. To identify and define PM deficits in individuals with MS with respect to a theoretical model of PM using subjective and objective measures.

Hypothesis 1: Individuals with MS perform more poorly on objective tests of PM than healthy controls.

To examine objective PM performance, Analyses of Covariance (ANCOVAs) were performed to assess group differences in performance between the MS group and

the HC group on the MIST and on each portion of the CPM task. Analyses were covaried for depression (BDI-II score), fatigue (FSS Average Score), symptom severity (MSFC score), and quality of life (MSQoL-54 Overall Quality of Life). For the MIST, MIST Total Score percentile (PMT%) was used as the dependent variable. For the CPM task, Plan Score, Recall Score, Initiation Score and Execution Score (mSET Profile Score) were used as dependent variables. It was hypothesized that individuals with MS will score significantly lower on the MIST and significantly lower on the CPM tasks than HCs.

Hypothesis 2: Individuals with MS self-report committing more subjective PM errors than healthy controls.

To examine subjective PM performance, an ANCOVA was performed to assess group differences in self-ratings from the Frequency scale of the PMCQ between the MS group and the HC group. Analyses were covaried for depression (BDI-II score), fatigue (FSS Average Score), symptom severity (MSFC score), and quality of life (MSQoL-54 Overall Quality of Life), and PMCQ Frequency Scale Score was entered as the dependent variable. It was hypothesized that individuals with MS would score significantly higher on the PMCQ-Frequency scale.

Hypothesis 3: Individuals with MS self-report experiencing more subjective distress related to PM errors than healthy controls.

To examine the significance of PM problems to participants, an ANCOVA was performed to assess group differences in self-ratings from the Distress scale of the PMCQ between the MS group and the HC group. Analyses were covaried for depression (BDI-II score), fatigue (FSS Average Score), symptom severity (MSFC score), and quality of life

(MSQoL-54 Overall Quality of Life), and PMCQ Distress Scale Score was entered as the dependent variable. It was hypothesized that individuals with MS would score significantly higher on the PMCQ-Distress scale.

Hypothesis 4: Individuals with MS self-report a different pattern of PM Stage errors than healthy controls.

To examine patterns of PM failures, a Bonferroni-corrected independent-samples *t*-test will be performed for each PMCQ Stage sub-score to assess group differences in self-ratings from the Stage scale of the PMCQ between the MS group and the HC group. Though research on the cognitive deficits in MS is inconclusive with regard to which stage of the multi-phasic process model is expected to be most impaired, some research has shown the retrospective component may be the most difficult for individuals with MS (Bravin et al., 2000). Thus, the preliminary hypothesis was that the MS group would endorse significantly more items from the Recall stage option, and no significant differences would be identified for the other two options. Additionally, because the PMCQ items are divided into four domains of functioning (Medical, Vocational, Social, Everyday Activities), *t*-tests will also be performed for each Domain sub-score to assess differences between the groups.

Aim 2. To examine and improve the utility of the PMCQ as a subjective measure of PM.

Hypothesis 5: The PMCQ will be a useful and appropriate measure of subjective PM function.

To evaluate the usefulness of the PMCQ, qualitative user feedback will be collected during PMCQ administration, and preliminary psychometric and qualitative

characteristics will be assessed. Though this is the first time the PMCQ has been employed in any population, and thus its value as a measure of PM is uncertain, previous research has established the usefulness of subjective report in estimating both PM function in varied patient groups and cognitive difficulties in the MS population. The current study was used as an opportunity to critically examine this novel measure and collect user feedback from participants during the testing session.

3. RESULTS

3.1 Analytical Strategy

All analyses were performed using PASW 19.0. Analyses in the current study used descriptive analyses, comparisons of group means, and stepwise multiple linear regression. All between-group analyses used presence of MS diagnosis as the grouping variable (i.e., MS group versus Healthy Control (HC) group). Descriptive analyses were performed for demographic variables, neuropsychological variables, and psychosocial outcome variables. Means and standard deviations (or percentage/frequencies for categorical variables) for variables of interest are reported for each group. Demographic psychosocial, and symptom severity variables found to be statistically different across groups were entered as covariates in Analyses of Covariance (ANCOVAs) and in Block 1 in stepwise regression analyses.

Scores on the MIST were converted to standardized scores to facilitate examination of the distribution of scores. The distribution of all variables was tested for normality using skewness and kurtosis statistical tests. The data were examined for presence of outliers, which identified several extreme values across variables of interest.

These values were excluded from all analyses because of their potential for skewing measures of central tendency and introducing systematic error on variables of interest.

Non-directional hypotheses were tested using two-tailed tests. The criterion for statistical significance was $p < .05$ unless otherwise noted.

3.2 Characteristics of the samples

3.2.1 Demographics Comparison

A series of independent-samples t -tests were conducted to examine demographic differences between the two groups. The MS sample and the HC samples did not differ significantly on age ($t(54) = 0.44, p = .664$), education ($t(45) = 0.61, p = .545$), or work status (full time versus unemployed or part time; $\chi^2(1, N = 47) = 0.01, p = .905$). The groups differed significantly on racial distribution ($\chi^2(2, N = 47) = 6.66, p = .036$); see section 2.2.2 (General demographics) for a description of the racial distribution of the samples.

3.2.2 Clinical characteristics

Verified by records from their treating neurologist, 92.6% ($n = 25$) of participants had a confirmed diagnosis of Relapsing Remitting MS disease type, and 7.4% ($n = 2$) were diagnosed with Secondary Progressive MS disease type. Average disease severity (negative values = more impairment) as measured with the MSFC was 0.05 ($SD = .62$) for the MS group and .47 ($SD = .47$) for the HC group; these values were statistically significantly different, $t(43) = 2.49, p = .028$. In the MS group, participants had been diagnosed with MS for an average of 9.81 years ($SD = 8.32$), had experienced symptom onset an average of 15.44 years ago ($SD = 10.46$), and were on a stable regimen of medications at the time of the study.

3.2.3 Psychosocial outcome measures

Depression symptoms were measured with the BDI-II. The average BDI-II score was 14.15 ($SD = 10.20$) in the MS group and 4.30 ($SD = 4.77$) in the HC group, a statistically significant difference, $t(45) = 4.00, p < .001$. Average level of reported fatigue interference with daily functioning, as reported on the Fatigue Severity Scale (FSS), was 4.09 ($SD = 2.01$) in the MS group and 2.43 ($SD = .92$) in the HC group, a statistically significant difference, $t(44) = 3.361, p = .002$. Overall quality of life as measured by MSQOL-54 Overall QoL was 65.93 ($SD = 22.47$) in the MS group and 79.83 ($SD = 13.7$) in the HC group, a statistically significant difference, $t(43) = 2.36, p = .023$. Thus, as expected, group differences were identified on measures of symptom severity, depression, fatigue, and quality of life, and therefore these variables will be used as covariates or entered in the first block of stepwise regressions in subsequent analyses.

3.3 Results of Aim 1

In general, Aim 1 focused on identifying between-group differences (MS versus HC) on several measures of PM function, controlling for the psychosocial and symptom severity variables described above. Additional exploratory analyses were also conducted; these additional analyses, which included within-group statistics (stepwise linear regressions) on each of the groups separately, were employed with the goal of investigating what factors predict objectively- and subjectively-measured PM function in the MS and HC samples. Because one of the study's overarching aims was to examine whether any of several aspects of PM (such as component processes or PM errors) differ in the MS population as compared to the healthy population, a comparison of the factors impacting PM in these two samples is of particular interest to the current analysis.

3.3.1 Hypothesis 1: Individuals with MS perform more poorly on objective tests of PM than healthy controls.

MIST. Descriptive statistics for overall objective PM measures are summarized in Table 3. Where possible, raw scores were converted to age- and education-standardized scores to facilitate comparisons between tests. Results of ANCOVA on age- and education-standardized scores on the MIST (PMT%) did not reveal a significant effect of group on MIST performance, $F(5,35) = 2.009, p = .102$, observed power = .60. To examine within-group differences, stepwise multiple linear regression analyses were performed on each group separately, using MIST PMT% as the dependent variable and demographic (age, education), psychosocial (BDI-II, FSS Average Score, 3 MSQoL-54 Summary Scores), disease severity (MSFC Score), and PM variables (PMCQ Total Aids used, CPM Task Plan, Recall, Initiation, and Execution scores) were entered as predictor variables. Regressions revealed that in the MS group, MIST performance was significantly predicted by a model containing CPM Plan Score, CPM Execution Score, number of PM aids reported, and BDI-II Score, and the model explained 68.7% of the variance in MIST PMT%, $F(4,16) = 8.773, p = .001, R^2 = .687$. The regression model's beta values revealed CPM Plan Score ($\beta = 0.76, p = .001$), BDI-II Score ($\beta = -0.53, p = .002$), PM aids reported ($\beta = 0.53, p = .004$), and CPM Execution Score ($\beta = -0.43, p = .048$) to be significant predictors of MIST PMT%.

In the HC group, MIST performance was significantly predicted by a model containing CPM Initiation Score, CPM Recall Score, age, and number of PM aids reported, and the model explained 71.8% of the variance in MIST PMT%, $F(4,11) = 10.562, p = .001, R^2 = .718$. The regression model's beta values revealed age ($\beta = 0.48, p$

= .008), PM aids reported ($\beta = -0.40, p = .015$), CPM Recall Score ($\beta = 0.37, p = .024$), and CPM Initiation Score ($\beta = 0.35, p = .033$) to be significant predictors of MIST PMT%. In summary, there were no significant group differences on MIST total score, and distinct variables predicted MIST total score for each of the groups: [CPM Plan Score + BDI-II score + number of PM aids reported + CPM Execution Score] in the MS group and [Age + number of PM aids reported + CPM Recall Score + CPM Initiation Score] in the HC group.

Table 3. Objective PM Measure Scores

Measure	MS Group		HC Group		Effect Size (d)
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	
MIST PM Total Score (Raw)	40.27	6.89	41.7	5.67	0.228
MIST PM Total Score (%ile)	61.5	29.96	65.5	29.27	0.135
CPM task Plan score	8.36	4.31	9.30	3.87	0.230
CPM task Recall score	8.56	3.87	9.25	4.77	0.160
CPM task Initiation score	1.65	0.48	1.58	0.75	0.114
CPM task Execution score	3.29	1.00	3.69	0.48	0.541

Complex Prospective Memory (CPM) Task. Analyses of the CPM task were completed for all four task variables (Plan, Recall, Initiation, and Execution). Results of ANCOVA of scores on all four variables did not reveal any significant group differences on any of the CPM variables when controlling for BDI-II score, FSS Average Score, MSFC score and MSQoL-54 overall QoL score. Follow-up stepwise multiple linear regression analyses were then performed identically to those above but removing CPM task variables as predictors.

For CPM Plan Score, regressions revealed that in either group, none of the predictor variables significantly predicted CPM Plan Score.

For CPM Recall Score, regression revealed that in the MS group, none of the predictor variables significantly predicted CPM task Recall Score. In the HC group, CPM Recall Score was significantly predicted by a model containing MSQoL-54 Physical Composite score, and the model explained 31.3% of the variance in CPM Recall Score, $F(1,14) = 6.385, p = .024, R^2 = .313$. The regression model's beta values revealed MSQoL-54 Physical Composite score ($\beta = -0.56, p = .024$) to be a significant predictor of CPM Recall Score.

For CPM Initiation Score, regressions revealed that in either group, none of the predictor variables significantly predicted CPM Initiation Score.

For CPM Execution Score, regression revealed that in the MS group, CPM Execution Score was significantly predicted by a model containing level of education, and the model explained 33.9% of the variance in CPM Execution Score, $F(1,22) = 11.262, p = .003, R^2 = .339$. The regression model's beta values revealed education ($\beta = -0.58, p = .003$) to be a significant predictor of CPM Execution Score. In the HC group, none of the predictor variables significantly predicted CPM Execution Score.

In summary, there were no significant group differences on CPM Plan, CPM Recall, CPM Initiation, or CPM Execution Scores. In the MS group, CPM Execution Score was predicted by education level. In the HC group, CPM Recall Score was predicted by MSQoL-54 Physical Composite Score.

3.3.2 Hypothesis 2: Individuals with MS self-report committing more subjective PM errors than healthy controls.

PMCQ. Descriptive statistics for subjective PM measures are summarized in Table 4. Results of ANCOVA of Frequency Scale scores on the PMCQ did not reveal a significant effect of group on PM problem frequency, $F(5,34) = 1.011, p = .427$. To examine within-group differences, stepwise multiple linear regression analyses were performed on each group separately, using PMCQ Frequency Score as the dependent variable and demographic (age, education), psychosocial (BDI-II, FSS Average Score, 3 MSQoL Summary Scores), disease severity (MSFC Score), and PM variables (PMCQ Total Aids used, CPM Task Plan, Recall, Initiation, and Execution Scores) were entered as predictor variables. Regressions revealed that in the MS group, self-reported frequency of PM errors was significantly predicted by a model containing CPM Recall Score, and the model explained 33.7% of the variance in PMCQ Frequency Score, $F(1,20) = 10.172, p = .005, R^2 = .337$. The regression model's beta values revealed CPM Recall Score ($\beta = 0.58, p = .005$) to be a significant predictor of PMCQ Frequency Score. In the HC group, none of the predictor variables significantly predicted PM problem frequency. In summary, there were no significant group differences self-reported PM error Frequency Score, and in the MS group, PMCQ Frequency Score was predicted by CPM Recall Score, but no significant predictors emerged in the HC group.

Table 4. Subjective PM Measure (PMCQ) Scores

Measure	MS Group		HC Group		Effect Size (d)
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	
<u>Summary Variables</u>					
Total Items Answered**	22.19	2.47	19.78	2.37	0.996
Frequency Scale Score	0.39	0.16	0.37	0.19	0.114
Distress Scale Score	0.36	0.31	0.41	0.34	0.154
<u>Stage Sub-Score Variables</u>					
Plan Stage	2.59	1.89	2.67	1.71	0.044
Recall Stage*	1.26	1.63	0.39	0.70	0.747
Initiation Stage	3.44	1.93	3.11	1.88	0.173
<u>Domain Sub-Score Variables</u>					
Medical Domain*	2.56	3.40	0.72	1.18	0.803
Vocational Domain	3.89	3.98	2.89	3.53	0.266
Social Domain	2.96	2.14	3.28	3.39	0.116
Everyday Activities Domain	7.19	4.15	8.06	4.93	0.192

** = significantly different at Bonferroni-corrected $p < .004$

* = significantly different at $p < .05$

3.3.3 Hypothesis 3: Individuals with MS self-report experiencing more subjective distress related to PM errors than healthy controls.

Results of ANCOVA on Distress Scale scores on the PMCQ did not reveal a significant effect of group on PM problem distress, $F(5,34) = 0.477, p = .791$. To examine within-group differences, stepwise multiple linear regression analyses were performed on each group separately, using PMCQ Distress Score as the dependent variable and demographic (age, education), psychosocial (BDI-II, FSS Average Score, MSQoL Summary Scores), disease severity (MSFC Score), and PM variables (PMCQ Total Aids used, CPM Task Plan, Recall, Initiation, and Execution Scores) were entered as predictor variables. Regressions revealed that in the MS group, distress related to self-reported PM errors was significantly predicted by a model containing CPM Recall Score, and the model explained 33.3.% of the variance in PMCQ Distress Score, $F(1,20) =$

9.989, $p = .005$, $R^2 = .333$. The regression model's beta values revealed CPM Recall Score ($\beta = 0.58$, $p = .005$) to be a significant predictor of PMCQ Distress Score. In the HC group, none of the predictor variables significantly predicted PM problem distress. In summary, there were no significant group differences in self-reported PM error Distress Score, and in the MS group, PMCQ Distress Score was predicted by CPM Recall Score, but no significant predictors emerged in the HC group.

3.3.4 Hypothesis 4: Individuals with MS self-report a different pattern of PM Stage errors than healthy controls.

As an exploratory analysis, a series of Bonferroni-corrected independent-samples t -tests were conducted on the remaining PMCQ variables: the Stage Sub-Score variables (Plan stage, Recall stage, and Initiation stage), the Domain Sub-Score variables (Medical, Vocational, Social, and Everyday Activities domains), total items answered (i.e., NOT rated "N/A") and reported number of PM aids used. Results revealed significant differences between the MS and HC groups for only total items answered at the Bonferroni-corrected significance level ($p < .004$), $t(43) = 3.260$, $p = .002$, $d = 0.996$. Two other variables did not reach this level of significance but were significantly different at the $p < .05$ level: Recall Stage score, $t(43) = 2.131$, $p = .039$, $d = 0.747$; and Medical Domain score, $t(43) = 2.194$, $p = .034$, $d = 0.803$. In summary, compared on all PMCQ scales, the groups only differed significantly on the total number of PMCQ items they endorsed, with MS participants endorsing a significantly higher proportion of PMCQ items than HCs. Potential trends (i.e., group differences significant at $p = .05$) on endorsements of Recall Stage errors and Medical Domain errors revealed that MS participants may have reported more errors occurring in the Recall stage of PM (e.g., "I

forgot some important detail about the PM task”) and may have reported more PM errors on medically-related PMCQ items (e.g., missing a doctor’s appointment or medication regimen errors).

3.4 Results of Aim 2

3.4.1 Hypothesis 5: Analysis of PMCQ as a measure of PM function

The utility of the PMCQ as a measure of PM function was examined both quantitatively (i.e., correlation with objective PM measures) and qualitatively (i.e., collective user feedback).

Quantitative analysis. Correlation analyses were performed to examine associations between PMCQ variables and objective measures of PM (MIST scores and CPM task scores). Significant correlations between PMCQ scores and objective measures are presented in Table 5. Of note, no PMCQ variables were correlated with any MIST variables. In summary, the strongest correlations were observed between the Vocational Domain Sub-score on the PMCQ and CPM Plan Score, and between the Social Domain Sub-score of the PMCQ and CPM Recall Score.

Table 5. Correlations between PMCQ Scores and Objective PM Scores

Measure 1	Measure 2	Pearson’s <i>r</i> value	<i>p</i> - value
PMCQ Frequency Score	CPM Plan Score	.309	.044
PMCQ Frequency Score	CPM Recall Score	.320	.036
PMCQ Distress Score	CPM Recall Score	.339	.026
PMCQ Initiation Score	CPM Plan Score	.304	.047
PMCQ Initiation Score	CPM Recall Score	.319	.037
PMCQ Voc. Domain Score	CPM Plan Score	.418	.005
PMCQ Social Domain Score	CPM Plan Score	.334	.029
PMCQ Social Domain Score	CPM Recall Score	.368	.015

Because a secondary PMCQ variable (number of PM aids reported) was a significant predictor of MIST performance in both groups, exploratory analyses were conducted to examine correlations between this variable and MIST supplementary scale scores. In the MS group, the strongest correlation ($r = .53, p = .009$) was identified between aids reported and MIST Recognition Memory Percentile. In the HC group, the strongest correlation ($r = -.66, p = .003$) was identified between aids reported and MIST Verbal Response Percentile.

To examine reliability of the questionnaire using internal consistency, Cronbach's Alpha (α) was computed for the set of all 25 PMCQ items, and for each set of items comprising the four domain sub-scales. Only the Frequency scale data were used, because of the inability of the α method to process missing data points. Overall, the PMCQ was found to be highly internally consistent (25 items; $\alpha = .94$). The Medical Domain subscale consisted of 4 items ($\alpha = .60$), the Vocational Domain subscale consisted of 6 items ($\alpha = .79$), the Social Domain subscale consisted of 6 items ($\alpha = .20$), and the Everyday Activities Domain subscale consisted of 9 items ($\alpha = .65$). Overall, the PMCQ appears to demonstrate strong reliability, except for the Social Domain scale. Follow-up analyses suggest that several specific items should be removed from the questionnaire (most notably, items 14 and 22, which contributed no variance).

Qualitative Analysis. Based on user feedback, tentative conclusions can be made about the PMCQ measure. Several items were not endorsed by many participants, and were noted to probably be obsolete. The fact that individuals with a chronic disease like MS have more medically-related tasks to which they need to attend compared to healthy individuals was pointed out by several participants, and thus it is expected that different

patterns of item endorsement would be observed across medical and non-medical populations, and likely also across different disease populations. Additionally, many of the individuals with MS indicated that before their diagnosis and/or before significant disease progression, they would have had many other obligations which would have increased their prospective memory task load (e.g., more work-related PM demands before their disease forced them out of work). It was also indicated by many MS participants that they had intentionally reduced their potential PM demands because of concerns about cognitive dysfunction. Both of these factors would be reflected by potentially lower scores on the PMCQ despite significant PM problems in associated domains.

4. DISCUSSION

This study sought to examine prospective memory function in individuals with multiple sclerosis as compared to healthy controls. Specific goals were to initiate a theoretically-based approach to examining PM in the MS population, and to examine the utility of a standardized objective measure of PM (the Memory for Intentions Test (MIST)), an experimental PM paradigm (the Complex Prospective Memory (CPM) task) and a novel subjective measure of PM (the Prospective Memory Complaints Questionnaire (PMCQ)) for understanding PM difficulties in individuals with MS as compared to healthy individuals. Additionally, the study sought to collect user feedback to begin to validate the PMCQ as a measure of self-reported PM difficulties. Impaired PM function in individuals with MS has been reported in the literature in very few empirical studies to date (Kardiasmenos, Clawson, Wilken, & Wallin, 2008; Rendell,

Jensen, & Henry, 2007; Bravin, Kinsella, Ong, & Vowels, 2000). However, the current study's employment of a theoretical model of PM, the Multiphasic Process model, permitted the current analyses to take into account the *reasons* for PM errors, rather than simply examine the *incidence* of errors in a binary fashion.

4.1 Main Findings

MIST. Contrary to hypotheses, and despite statistically controlling for symptom severity, depression, fatigue symptoms, and quality of life variables, no significant differences were identified in objective, age- and education-normed PM ability (i.e., overall MIST performance). Our analyses identified disparate patterns of factors related to PM ability in each sample. For the control group, performance on PM recall and initiation, as well as age and reported number of PM aids used predicted MIST performance. In contrast, for the MS sample, MIST performance was predicted by depression level, PM planning ability, PM task execution (i.e., the actual mSET task), and reported number of PM aids used. Interestingly, while total reported PM aids used was related to objective PM ability in both groups, the prediction occurred in the opposite direction for each group. One way to interpret this finding is that healthy participants demonstrated awareness of their PM ability, as those that reported needing more help completing PM tasks in their everyday lives (e.g., post-it notes, calendars or asking for help) performed more poorly on the MIST. Conversely, individuals with MS demonstrated a lack of this awareness, as those that reported using fewer PM aids performed more poorly on the MIST. However, this interpretation assumes that self-reported number of aids used is a suitable measure of one's awareness of PM deficits. While this PMCQ item may tap into this phenomenon to some degree, the manner in

which the item is presented introduces several confounds. For one, it does not query the total number of aids used but the number of *types* of aids used; thus, no data is available about the degree (e.g., frequency) one uses aids such as datebooks or sticky notes.

Secondly, the options this item provides conflate internally-mediated aids (e.g., mental rehearsal) with externally-mediated aids (e.g., electronic reminders). Thus, use of this variable as a predictor of PM ability is somewhat flawed and difficult to interpret.

Secondary analyses explored correlations between this variable and other variables of interest within each group. The strongest relationships were seen between aids reported and recognition memory on the MIST (+ relationship) in the MS group and between aids reported and verbal-item performance on the MIST (- relationship) in the HC group; these findings indicate that the relationships described above may be mediated by recognition memory ability (in the MS group) and memory for verbal PM information (in the HC group). Again, these findings are very preliminary and difficult to interpret without context.

The result that older HCs demonstrated better MIST performance may reflect a phenomenon often observed in the literature dubbed the “age prospective memory paradox,” wherein older adults perform better than younger adults on more naturalistic PM tasks (Bailey, Henry, Rendell, Phillips, & Kliegel, 2010). Thus, this finding is counterintuitive but not entirely unexpected. In addition to these factors, PM recall and initiation abilities also predicted MIST performance in the HC group, demonstrating retrospective memory and ability to actually initiate a task at the correct time (in response to a cue, in this case) as significant factors related to overall PM function in this group. By contrast, in the MS group, depression level, PM planning and execution abilities were

significant predictors of MIST performance. The PM task execution results actually revealed that, after controlling for CPM Plan Score, BDI-II Score, and number of PM aids reported, participants that scored higher on the CPM Execution task (the mSET) performed more poorly on the MIST; this finding is difficult to interpret and may be spurious. Of note, PM planning ability was the strongest identified predictor in this group.

Overall, the findings in the MS group appear to indicate that in the MS sample, ability to plan an intention was a better predictor of PM performance than retrospective memory or the ability to initiate correctly in response to a cue. One hypothesis is that, in the healthy population, the “intention formation” stage happens automatically without much cognitive control, and thus retaining the intention details and detecting the cue correctly are more significant processes, while in MS the ability to formulate an intention adequately requires more conscious processing, and individuals with even subtle cognitive deficits cannot rely on their retrospective memory and initiation (e.g., attention-switching) abilities alone to help them successfully complete PM tasks. This hypothesis is partly supported by previous literature that demonstrates processing speed deficits in MS (Bruce et al., 2010) as well as the importance of processing speed to PM planning abilities (Kliegel, Jager, Altgassen, & Shum, 2008; West & Craik, 2001); however, it is still extremely preliminary.

These findings suggest that future studies would benefit from including measures of neuropsychological constructs that may impact PM ability or individual stages of processing, such as information processing speed or set-shifting capacity. Such investigations could shed light on which constructs are actually essential (or supportive)

to PM function, and provide context for the current study's interesting but complex findings. It is possible that the Multi-Phasic Process model of PM simply does not apply to individuals with MS as it does with other populations, and thus future investigations should explore this possibility as well. The finding that depression score predicted objective PM performance on the MIST is intriguing, but it is difficult to identify the mechanism of action of such an association. Perhaps depressed individuals with MS simply have more on their minds and thus fewer cognitive resources to devote to PM tasks, even in the laboratory.

Complex Prospective Memory (CPM) Task. The other objective measure of PM function used in this study, the CPM task using the modified Six Elements Task, revealed similar patterns to those identified with the MIST. No overall group differences were identified for any of the four stages of the task (Plan, Recall, Initiation or Execution). Overall, few variables significantly predicted performance on these tasks in either group. In the HC group, the only significant prediction occurred for PM recall performance, which was predicted only by self-reported physical disability factors identified on a quality of life measure, such that those reporting more physical disability performed more poorly on recall of their CPM plan. This finding is difficult to interpret and may be spurious. In the MS group, the only variable that predicted PM task execution was education level, such that higher educational attainment was associated with better scores on this measure (the mSET).

Overall, performance on objective measures of PM function in the MS and HC groups revealed several interesting patterns and indicated that the intention formation stage may be particularly important to PM task success in individuals with MS, but that

healthy individuals may be able to rely on their recognition memory or executive functions (e.g., attention-shifting or cue detection/vigilance) to successfully complete PM tasks. However, additional research will be required to further explore these hypotheses.

PMCQ. Although novel, the PMCQ permitted examination of several aspects of PM function. In the current study, group comparisons of subjectively-reported PM errors failed to identify group differences in PM error frequency as measured by the PMCQ, even when controlling for symptom severity, depression, fatigue, and quality of life variables. When examined separately, the MS group's performance demonstrated that PM recall ability alone predicted frequency of self-reported PM errors such that as recall performance increased, frequency of reported errors increased. While counterintuitive, this finding may indicate that individuals with MS with better retrospective memory ability are more accurately able to report on their PM errors than those with poorer retrospective memory. In the HC group, none of the proposed factors predicted self-reported PM error frequency, which may be a result of a restricted range of performance on many study variables in this sample. Regardless, these results did not indicate that individuals with MS experience more frequent self-reported PM errors than healthy individuals, and thus Hypothesis 3 was not supported.

Overall, group comparisons revealed that there were no differences in subjectively-reported distress related to PM errors between the samples. Within the groups separately, self-reported PM-error distress showed an identical pattern to Frequency scale analyses in both groups (see discussion above), which may indicate that these two scales tap into the same behavioral phenomenon and thus share variance. This may indicate that querying the level of distress experienced during PM errors does not

offer much additional information above and beyond querying error frequency alone; conversely, it could demonstrate that individuals experiencing more subjective distress report more frequent cognitive problems. Further research is needed to elucidate this relationship.

Secondary analyses of PMCQ sub-scale variables were conducted to examine group differences on variables such as total PMCQ items endorsed, reported PM aids used, and Stage and Domain sub-scores. Significant group differences were identified only for total PMCQ items endorsed (i.e., total number of queried PM tasks that were applicable to the participant and not rated “N/A”), such that individuals with MS reported engaging in more of the PM tasks presented in the questionnaire than did HC individuals. This likely reflects the greater number of medically-related PM tasks required of individuals with a chronic disease (and this conclusion is partially supported by analysis of the Medical Domain sub-scores, which revealed a trend, with a large effect size, signifying that MS participants may have reported more errors on medically-related items), but is interesting in light of the feedback of several MS participants indicating reduced everyday PM demands because of not working, reduced social engagements, among other factors. While very preliminary, this finding is important, as it indicates that PM demands are a significant aspect of the lives of those living with MS, perhaps even to a greater degree than those in the normal population. While not statistically significant at the Bonferroni-corrected level, the finding that individuals with MS may have reported more retrospective memory-related PM errors than healthy individuals may represent a greater concern with cognitive abilities, particularly memory problems, in the MS

population than in the healthy population (Shevil & Finlayson, 2006). Of note, this group difference exhibited a medium-to-large effect size.

One of the main aims of the current study was to assess the utility of the PMCQ as a measure of PM function in the MS population and controls. A promising finding emerged in that the PMCQ was found to be highly internally consistent, and each of the Domain Sub-scales (except for the Social Domain) demonstrated strong reliability characteristics. On the other hand, while providing much data about subjective PM concerns, the PMCQ was not found to be highly associated with objective PM performance or even corresponding PM component stages, at least as measured on the MIST and the CPM task. Perhaps due to inadequate statistical power, the Stage sub-scales of the PMCQ were not reliably associated with performance on objective PM stages of planning, recall, and initiation. Thus, the PMCQ was not supported as a valid way to assess component stages of the PM process in either individuals with MS or healthy individuals. There are several possible explanations for this finding, including a) that either the PMCQ, the MIST, the CPM task, or some combination of these measures was not sensitive enough to detect PM impairments in these high-functioning groups; b) if PM impairments were present in either group, both PM function and self-report of it were both compromised enough to obscure patterns; or c) the PMCQ or the Multi-Phasic Process model itself is flawed and is not a valid way to examine real-world PM function. Unfortunately, the data collected in this study cannot fully tease these possibilities apart. Several of these hypotheses will be addressed in subsequent sections.

4.2 Prospective Memory in Multiple Sclerosis

One of the immediate questions raised by these data concerns the lack of replication of previous research. Clearly, the current study's negative findings with regard to objective PM differences between MS and HC groups is at odds with several prior research studies, which did identify PM impairments in MS. Bravin et al. (2000) conducted the first study of PM in MS with a considerably less educated sample than that of the current study (Mean education = 11.2 years compared to 15.2 years in the current sample), and found that PM differences between the groups, identified using nonparametric statistics, were driven nearly entirely by retrospective memory deficits. In the only two other studies examining PM in MS specifically (Kardiasmenos, Clawson, Wilken, & Wallin, 2008; Rendell, Jensen, & Henry, 2007), the same PM measurement methodology (the Virtual Week board game task) was used, and impairments were identified in the MS groups compared to control groups. The MS samples in these studies appeared to be more closely matched to the current sample's demographic characteristics. Interestingly, the latter study demonstrated that initiating a specific planning strategy (implementation intentions) increased the performance of the MS group nearly to that of controls on more difficult PM subtasks; this effect lends support to our finding that the planning stage in particular is related to overall PM task success in MS. One other study (Bruce et al., 2010) did not utilize a control group and made use of an outdated version of the MIST, and thus it is difficult to put PM performance results in any useful context.

With these previous studies in mind, several explanations are possible for the current study's inability to identify objective PM differences between the MS and HC groups. Perhaps the most likely explanation is that the MIST (as opposed to the Virtual

Week) is not a sensitive enough measure to capture PM impairments in a high functioning sample such as the current MS group. The fact that, on average, both the MS and HC groups performed well on the MIST (percentiles = 61.5 and 65.5, respectively) lends support to this possibility, and begs the question of whether this issue may have been present in the data collected on the PMCQ and the CPM task as well. On the other hand, the Virtual Week, which is the basis for nearly all of the current conclusions about PM deficits in MS, may be systematically biased against individuals with MS in some way that is not a direct result of PM function deficits. Some authors have criticized the associative learning aspects that half of the tasks require (Hadjiefthyvoulou, Fisk, Montgomery, & Bridges, 2011). Associative learning deficits have been identified in MS (Basso, Lowery, Ghormley, Combs, & Johnson, 2006), and thus may confound the use of this measure in individuals with MS. Another problem with the Virtual Week is that nearly every investigation following Rendell & Craik's (2000) original use of the task has used a "modified" version, and modifications are often significant (e.g., computerized version rather than actual board game; Rendell, Phillips, Henry, Brumby-Rendell, de la Piedad Garcia, Altgassen, & Kliegel, 2011). Though the Virtual Week has been shown to be sensitive to PM deficits in aging and psychiatric populations (Rendell, Jensen, & Henry, 2007), more research should be conducted with this measure in concordance with other PM measures, particularly in MS, and further investigation of cognitive correlates of Virtual Week performance should be conducted as well. Overall, these issues signify the need for more sensitive measures (and models) of PM to detect subtle PM impairments which may nevertheless be behaviorally significant.

4.3 Remaining Questions Regarding Measurement of PM in MS

One of the questions the current study set out to answer was a fundamental one: How does one measure prospective memory function in MS? Unfortunately, the findings did not provide a conclusive answer, likely because of either a) sample characteristics (e.g., no actual PM deficits present in our sample), b) measure characteristics (e.g., measures were not sensitive enough to detect subtle impairments), or c) both (a) and (b). One of the major reasons to measure PM in patient populations is its relevance to everyday function, as well as the fact that PM errors may be significant even in less impaired populations (Kliegel, Jäger, Altgassen, & Shum, 2008). It is possible that subtle real-world PM problems are so inseparable from their contexts that they cannot be measured with standardized objective measures; if so, self- or informant-report may be the only valid way to measure them. On the other hand, perhaps measuring stages of PM processing individually (e.g., “PM planning,” à la the Multi-Phasic Process model), each as they relate to overall PM task performance (and thus NOT merely as distinct neuropsychological phenomena) could prove to be a useful way to examine PM in different patient populations, especially if particular deficits were identified as characteristic of different disorders (e.g., Kliegel, Eschen, & Thöne-Otto, 2004).

In light of previous literature, it was not wholly unexpected that subjectively-reported PM ability did not correlate well with objective, standardized PM assessment (e.g., Bruce, Bruce, Hancock, & Lynch, 2010). However, it is still worthwhile to consider why this relationship was not more robust. While the MIST is able, at least in theory, to tease apart many significant aspects of PM (e.g., time vs. event cueing, long and short delays), the theoretical basis on which it was developed may simply be too different from

the theoretical model utilized in this study, the Multi-Phasic Process model. The current study's objective measure of PM stages, the CPM task, also did not show robust correlations between corresponding objective PM stage scores and self-reported PM stage errors on the PMCQ, which is likely a result of the "unrefined" nature of both measures, which have thus far been used infrequently (or not at all, in the case of the PMCQ). It is encouraging, however, that several PMCQ scales, such as the vocational and social domain scales did correlate with objectively-measured PM stages (i.e., the plan and recall stages of the CPM). It is worth noting that even thoroughly-studied neuropsychological constructs often do not show strong relationships across measurement methods (i.e., objective versus subjective), which is not surprising for constructs such as retrospective memory, for obvious reasons. Prospective memory is likely to be even more complex and is definitely not as well understood, and thus preliminary inquiries like the current study are needed to determine what aspects of PM are more and less accessible to different measurement methods. As of now, clinicians should use caution when interpreting either type of measure, as performance-based measures of PM may not yet be sensitive enough to detect subtle or context-dependent PM impairments, and self-report measures of PM may be confounded by the impairments themselves (Thone-Otto & Walthier, 2008; Marrie et al., 2003).

4.4 Limitations

Several limitations to the current study deserve consideration. Though sample sizes in each group met (or nearly met, in the HC group) target sample sizes predicted by power analyses, power to detect differences on many of the measures used in this study was limited by a small sample size. Though medium and large effect sizes are reported in

the literature for the effects of MS diagnosis on PM ability (Kardiasmenos et al., 2008; Rendell et al., 2007; Bravin et al., 2000), PM deficits (if they existed) in our sample of MS participants were too subtle to be discerned by the measures utilized. Notably, our sample of individuals with MS was relatively high-functioning, and it may be that an increase in sample size and range of impairment would have allowed significant differences to emerge. However, an advantage of having a high-functioning clinical population is the ability to examine subtle cognitive phenomena, and the MS population in particular was chosen in this study because of their significant engagement and often intact cognitive functioning, as measured by traditional neuropsychological variables. In general, the conclusions generated from this study may be limited to the current high-functioning sample of individuals with MS, and multiple aspects of PM function may differ in individuals with MS with varying levels of cognitive, physical or other impairment. Other limitations to this study are largely related to the exploratory nature of the research itself, in that the study was limited by the use of: a) a new measure of PM function, the PMCQ; b) a model of PM, the Multi-Phasic Process (MPP) model, that has not yet been fully validated; and c) an experimental (and thus also not fully validated) PM paradigm, the CPM task. While an exploration of subjective (PMCQ) and objective (CPM task) measures of PM informed by a theoretical model (the MPP model) was the overarching goal of this study, such an exploration provides little empirical basis to put findings in context.

4.5 Strengths

On the other hand, several strengths of this study arose from its exploratory nature. Because the study controlled for so many psychosocial variables (e.g., depression,

quality of life, fatigue, demographic variables) that have been found to be important in the MS population, conclusions could be drawn about the impact, or lack thereof, of these variables on PM ability in both the MS and HC samples. Thus, while depression did predict scores on self-report inventories and on the MIST in the MS group, neither symptom severity, fatigue, quality of life, nor demographic variables such as age or education level were able to significantly predict objective PM performance in individuals with MS, demonstrating the independence of these psychosocial constructs from PM function in this population. Many of the questions raised by this study about the use of the MPP model, the MIST, the CPM task, and self-reported PM difficulties (e.g., whether these theories or measures are applicable to this population in the same ways as in the normal population) could not have been addressed as broadly in a more rigidly structured study. Likewise, external validity of findings is likely enhanced by the use of both objective and subjective measures, and internal validity was enhanced by the use of such a well-matched control group. The PM literature (Thone-Otto & Walthier, 2008) has identified the necessity of using both performance-based and self-report measures of PM ability because of the complexity and real-world applicability of PM, and while this study did not identify particularly high correlations between these two types of measures, it did not refute this association either, but demonstrated the possible utility of either type of assessment independently.

4.6 Future Directions

The current study provided a set of new research questions and indicated the necessity of further study of PM in MS in general. The Multi-Phasic Process model of PM, while intuitively constructed, is still in the early stages of empirical validation in the

literature, and it should continue to be fine-tuned with respect to the relative importance and operational definition of each stage in the process. This study points to the need for better variable specifications within clinical populations, even those with only subtle cognitive impairments, and perhaps most importantly, better measures of performance for each proposed PM stage. There is clearly room for measure development using both objective and subjective means, especially with regard to sensitivity to subtle PM deficits, which are complex and elusive. Closely related to this need is the need for more neuropsychological explorations of the component cognitive constructs of PM, which are far from being fully understood. PM function should be examined in samples with greater variability in factors such as disease severity and cognitive function than were present in the current sample, as well as in more clinical populations. It may also be worthwhile to begin establishing a composite measure of PM that could be used to integrate both subjective and objective measurements. Such a composite could also give differential weight to distinct aspects of PM function (e.g., time- versus event-cued tasks or tasks with different intervening durations). Lastly, researchers should seek to examine the contributions of PM factors and abilities to functional outcomes, such as vocational success or social engagement.

4.7 Conclusion

Overall, the current theoretically driven exploratory analysis of objective and subjective prospective memory difficulties in both individuals with and without multiple sclerosis identified discrepant predictors of PM performance between the groups, despite nonsignificant overall differences in performance when controlling for symptom severity, depression, symptomatic fatigue, and quality of life reports. While much further research

is needed before all of the complex factors impacting PM performance in the MS population are well understood, the utility of breaking PM down into hypothesized stages of processing was demonstrated, as was the utility of using both objective and subjective measures of PM. Ideally, further study can clarify the relationships detected in this study and provide guidelines for assessment and remediation of PM difficulties in MS, other clinical populations, and even the general populace.

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Appendix A: The Prospective Memory Complaints Questionnaire

Date Completed: _____

Age: _____ Gender: M F Years of Education: _____

Date of MS Diagnosis: _____ Type of MS: _____

Date of Last Exacerbation or “flare up”: _____

Difficulties Due to MS (check all that apply):

- | | |
|---|---|
| <input type="checkbox"/> Upper extremity difficulties | <input type="checkbox"/> Walk with a cane |
| <input type="checkbox"/> Lower extremity difficulties | <input type="checkbox"/> Use a scooter to get around |
| <input type="checkbox"/> Fatigue | <input type="checkbox"/> Depression or other mood symptoms |
| <input type="checkbox"/> Cognitive impairment | <input type="checkbox"/> Vision difficulties |
| <input type="checkbox"/> Urinary or bowel difficulties | <input type="checkbox"/> Sensory difficulties other than vision |
| <input type="checkbox"/> Sexual difficulties | <input type="checkbox"/> Speech difficulties |
| <input type="checkbox"/> Sleeping difficulties | <input type="checkbox"/> Appetite difficulties |
| <input type="checkbox"/> Coordination or balance difficulties | <input type="checkbox"/> Pain |
| <input type="checkbox"/> Numbness or tingling | <input type="checkbox"/> Nausea |
| <input type="checkbox"/> Other : _____ | |

Have you been diagnosed with any disorder in addition to MS? _____

Please answer the following question:

- “To help myself remember to do things, I often ...” (check all that apply):
 - Use External memory aids (post-it notes in strategic places, a planner or calendar)
 - Use Extra mental effort (trying very hard to remember, concentrating)
 - Maximize my alertness (try to be well-rested, avoid things which impair my judgment or alertness)
 - Use Mental Rehearsal (mental repetition of plan or intention)
 - Use Mental Exercise/Training (trying to exercise my memory)
 - Request assistance from others
 - Other: _____
 - Use nothing; I just remember spontaneously

Please note: Your answers to this page and the following survey are totally anonymous, and there are no wrong answers; we are interested in *your personal experience*. Thank you for your input!

PROSPECTIVE MEMORY (PM) COMPLAINTS QUESTIONNAIRE

Introduction

The following questionnaire will ask you about difficulties that you may have with a kind of memory called *Prospective Memory*. Prospective Memory is the type of memory you use to remember to do things at some point in the future, such as remembering to take out the garbage on trash day or remembering to keep appointments.

We think that successful Prospective Memory happens in several stages:

- First, you must actually think about, or plan, having to do something (for example, you may notice the trash getting full and make a mental note to put the garbage out on Tuesday morning).
- Second, you must remember the important details: you have to know when (Tuesday morning) and what to do (take out the garbage).
- Third, you must notice that it is the right time (on Tuesday morning) and actually complete your task.

Instructions

- This survey has 25 items about common Prospective Memory difficulties.
- Each item has 3 parts.
- Please respond to each question by indicating how much it applies to you.
- Here is a sample item, with example responses filled in:

1. **I did not take out the garbage on trash day, even though it needed to go out.**

A	Please rate how often this has occurred in the last month			
	0	1	2	3
	Never	Sometimes	Often	Almost Always
B	I did not take out the garbage on trash day, even though it needed to go out because...			
	<input checked="" type="checkbox"/> I did not make a plan to take the garbage out			
	<input type="checkbox"/> I forgot some important detail about trash day			
	<input type="checkbox"/> I did not take out the garbage in time			
C	Please rate how distressing this was to you			
	0	1	2	3
	Not at all distressing	A bit distressing	Moderately distressing	Very distressing

- For **A**, please circle the number which describes how often this problem has happened to you in the past month. Circle only one choice.
- For **B**, please clearly mark the box (✓ or x) which best describes why this happened. Check only one box, or none if you did not have this problem in the past month. See Introduction (above) for more explanation.
- For **C**, please circle the number which describes how distressing this problem was for you personally. Circle only one choice.

Medical / Health

1. **I missed a doctor's appointment.**

Please rate how often this has occurred in the last month			
0	1	2	3
Never	Sometimes	Often	Almost Always
I missed a doctor's appointment because...			
<input type="checkbox"/> I did not make plans for how to get to the doctor's office			
<input type="checkbox"/> I forgot some important detail about the appointment			
<input type="checkbox"/> I forgot to go to the doctor's office at the right time			
Please rate how distressing this was to you			
0	1	2	3
Not at all distressing	A bit distressing	Moderately distressing	Very distressing

2. **I did not take my medication when I should have**

Please rate how often this has occurred in the last month			
0	1	2	3
Never	Sometimes	Often	Almost Always
I did not take my medication when I should have because...			
<input type="checkbox"/> I did not make a plan for remembering to take it			
<input type="checkbox"/> I forgot some important detail about the medication			
<input type="checkbox"/> I did not notice it was time to take my medication			
Please rate how distressing this was to you			
0	1	2	3
Not at all distressing	A bit distressing	Moderately distressing	Very distressing

3. **I did not attend a fitness program at the gym I had planned to attend**

Please rate how often this has occurred in the last month			
0	1	2	3
Never	Sometimes	Often	Almost Always
I did not attend a fitness program at the gym I had planned to attend because...			
<input type="checkbox"/> I did not make plans for how to get there			
<input type="checkbox"/> I forgot some important detail about the program or class			
<input type="checkbox"/> I did not notice it was time to go to the gym			
Please rate how distressing this was to you			
0	1	2	3
Not at all distressing	A bit distressing	Moderately distressing	Very distressing

4. **I did not refill my prescription before I ran out of medication**

Please rate how often this has occurred in the last month			
0	1	2	3
Never	Sometimes	Often	Almost Always
I did not refill my prescription before I ran out of medication because...			
<input type="checkbox"/> I did not make plans for how to get more medication			
<input type="checkbox"/> I forgot some important detail about ordering more medication			
<input type="checkbox"/> I did not notice it was time to order more medication			
Please rate how distressing this was to you			
0	1	2	3
Not at all distressing	A bit distressing	Moderately distressing	Very distressing

Vocational

5. **I did not bring an important item to work with me**
- | Please rate how often this has occurred in the last month | | | |
|--|-------------------|------------------------|------------------|
| 0 | 1 | 2 | 3 |
| Never | Sometimes | Often | Almost Always |
| I did not bring an important item to work with me because... | | | |
| <input type="checkbox"/> I did not make a plan for how to remember the item | | | |
| <input type="checkbox"/> I forgot some important detail about the item | | | |
| <input type="checkbox"/> I did not get the item before I left home | | | |
| Please rate how distressing this was to you | | | |
| 0 | 1 | 2 | 3 |
| Not at all distressing | A bit distressing | Moderately distressing | Very distressing |
6. **I did not bring an important item home from work**
- | Please rate how often this has occurred in the last month | | | |
|--|-------------------|------------------------|------------------|
| 0 | 1 | 2 | 3 |
| Never | Sometimes | Often | Almost Always |
| I did not bring an important item home from work because... | | | |
| <input type="checkbox"/> I did not make a plan for how to remember the item | | | |
| <input type="checkbox"/> I forgot some important detail about the item | | | |
| <input type="checkbox"/> I did not get the item before I left work | | | |
| Please rate how distressing this was to you | | | |
| 0 | 1 | 2 | 3 |
| Not at all distressing | A bit distressing | Moderately distressing | Very distressing |
7. **I did not attend an important work meeting I meant to attend**
- | Please rate how often this has occurred in the last month | | | |
|---|-------------------|------------------------|------------------|
| 0 | 1 | 2 | 3 |
| Never | Sometimes | Often | Almost Always |
| I did not attend an important work meeting I meant to attend because... | | | |
| <input type="checkbox"/> I did not make plans for getting to the meeting on time | | | |
| <input type="checkbox"/> I forgot some important detail about the meeting | | | |
| <input type="checkbox"/> I did not notice it was time to go to the meeting | | | |
| Please rate how distressing this was to you | | | |
| 0 | 1 | 2 | 3 |
| Not at all distressing | A bit distressing | Moderately distressing | Very distressing |
8. **I did not make an important work call I had intended to make**
- | Please rate how often this has occurred in the last month | | | |
|---|-------------------|------------------------|------------------|
| 0 | 1 | 2 | 3 |
| Never | Sometimes | Often | Almost Always |
| I did not make an important work call I had intended to make because... | | | |
| <input type="checkbox"/> I did not make a plan for when to make the call | | | |
| <input type="checkbox"/> I forgot some important detail about the call | | | |
| <input type="checkbox"/> I did not notice it was time to make the call | | | |
| Please rate how distressing this was to you | | | |
| 0 | 1 | 2 | 3 |
| Not at all distressing | A bit distressing | Moderately distressing | Very distressing |

13. **I did not give someone a message or news when I meant to**
- | Please rate how often this has occurred in the last month | | | |
|--|-------------------|------------------------|------------------|
| 0 | 1 | 2 | 3 |
| Never | Sometimes | Often | Almost Always |
| I did not give someone a message or news when I had intended to do so because... | | | |
| <input type="checkbox"/> I did not make a plan for giving the message or news | | | |
| <input type="checkbox"/> I forgot some important detail about the message | | | |
| <input type="checkbox"/> I did not notice it was time to give the message | | | |
| Please rate how distressing this was to you | | | |
| 0 | 1 | 2 | 3 |
| Not at all distressing | A bit distressing | Moderately distressing | Very distressing |
14. **I did not pick someone up whom I had told I would**
- | Please rate how often this has occurred in the last month | | | |
|--|-------------------|------------------------|------------------|
| 0 | 1 | 2 | 3 |
| Never | Sometimes | Often | Almost Always |
| I did not pick someone up whom I had told I would because... | | | |
| <input type="checkbox"/> I did not make a plan for picking them up | | | |
| <input type="checkbox"/> I forgot some important detail about picking them up | | | |
| <input type="checkbox"/> I did not notice it was time to pick them up | | | |
| Please rate how distressing this was to you | | | |
| 0 | 1 | 2 | 3 |
| Not at all distressing | A bit distressing | Moderately distressing | Very distressing |
15. **I did not return a borrowed item to someone when I meant to**
- | Please rate how often this has occurred in the last month | | | |
|--|-------------------|------------------------|------------------|
| 0 | 1 | 2 | 3 |
| Never | Sometimes | Often | Almost Always |
| I did not return a borrowed item to someone when I meant to because... | | | |
| <input type="checkbox"/> I did not make a plan for returning the item | | | |
| <input type="checkbox"/> I forgot some important detail about the item or the owner | | | |
| <input type="checkbox"/> I did not notice it was time to return the item | | | |
| Please rate how distressing this was to you | | | |
| 0 | 1 | 2 | 3 |
| Not at all distressing | A bit distressing | Moderately distressing | Very distressing |
16. **I did not pay someone back when I meant to**
- | Please rate how often this has occurred in the last month | | | |
|--|-------------------|------------------------|------------------|
| 0 | 1 | 2 | 3 |
| Never | Sometimes | Often | Almost Always |
| I did not pay someone back when I meant to because... | | | |
| <input type="checkbox"/> I did not make a plan for paying the person back | | | |
| <input type="checkbox"/> I forgot some important detail about the money or lender | | | |
| <input type="checkbox"/> I did not notice it was time to pay the person back | | | |
| Please rate how distressing this was to you | | | |
| 0 | 1 | 2 | 3 |
| Not at all distressing | A bit distressing | Moderately distressing | Very distressing |

Everyday Activities

17. **I did not stop at the store for something when I meant to**
- | Please rate how often this has occurred in the last month | | | |
|--|-------------------|------------------------|------------------|
| 0 | 1 | 2 | 3 |
| Never | Sometimes | Often | Almost Always |
| I did not stop at the store for something when I meant to because... | | | |
| <input type="checkbox"/> I did not make a plan for going to the store
<input type="checkbox"/> I forgot some important detail about what I needed or where to go
<input type="checkbox"/> I did not notice it was time to go to the store | | | |
| Please rate how distressing this was to you | | | |
| 0 | 1 | 2 | 3 |
| Not at all distressing | A bit distressing | Moderately distressing | Very distressing |
18. **I did not give a pet its meal**
- | Please rate how often this has occurred in the last month | | | |
|---|-------------------|------------------------|------------------|
| 0 | 1 | 2 | 3 |
| Never | Sometimes | Often | Almost Always |
| I did not give a pet its meal because... | | | |
| <input type="checkbox"/> I did not make a plan for feeding the pet
<input type="checkbox"/> I forgot some important detail about feeding the pet
<input type="checkbox"/> I did not notice it was time to feed the pet | | | |
| Please rate how distressing this was to you | | | |
| 0 | 1 | 2 | 3 |
| Not at all distressing | A bit distressing | Moderately distressing | Very distressing |
19. **I did not water a plant when it needed watering**
- | Please rate how often this has occurred in the last month | | | |
|--|-------------------|------------------------|------------------|
| 0 | 1 | 2 | 3 |
| Never | Sometimes | Often | Almost Always |
| I did not water a plant when it needed watering because... | | | |
| <input type="checkbox"/> I did not make a plan for watering the plant
<input type="checkbox"/> I forgot some important detail about watering the plant
<input type="checkbox"/> I did not notice it was time to water the plant | | | |
| Please rate how distressing this was to you | | | |
| 0 | 1 | 2 | 3 |
| Not at all distressing | A bit distressing | Moderately distressing | Very distressing |
20. **I did not turn off an appliance (stove, toaster, curling iron) for more than an hour**
- | Please rate how often this has occurred in the last month | | | |
|---|-------------------|------------------------|------------------|
| 0 | 1 | 2 | 3 |
| Never | Sometimes | Often | Almost Always |
| I did not turn off an appliance for more than an hour because... | | | |
| <input type="checkbox"/> I did not make a plan for remembering to turn off the appliance
<input type="checkbox"/> I forgot some important detail about turning off the appliance
<input type="checkbox"/> I did not notice it was time to turn off the appliance | | | |
| Please rate how distressing this was to you | | | |
| 0 | 1 | 2 | 3 |
| Not at all distressing | A bit distressing | Moderately distressing | Very distressing |

21. **I did not return a book/movie to the rental facility**
- | Please rate how often this has occurred in the last month | | | |
|---|-------------------|------------------------|------------------|
| 0 | 1 | 2 | 3 |
| Never | Sometimes | Often | Almost Always |
| I did not return a book/movie to the rental facility because... | | | |
| <input type="checkbox"/> I did not make a plan for returning the item | | | |
| <input type="checkbox"/> I forgot some important detail about the item or due date | | | |
| <input type="checkbox"/> I did not notice it was time to return the item | | | |
| Please rate how distressing this was to you | | | |
| 0 | 1 | 2 | 3 |
| Not at all distressing | A bit distressing | Moderately distressing | Very distressing |
22. **I missed paying a bill on time and was charged a late fee**
- | Please rate how often this has occurred in the last month | | | |
|---|-------------------|------------------------|------------------|
| 0 | 1 | 2 | 3 |
| Never | Sometimes | Often | Almost Always |
| I missed paying a bill on time and was charged a late fee because... | | | |
| <input type="checkbox"/> I did not make a plan for paying the bill | | | |
| <input type="checkbox"/> I forgot some important detail about the bill or due date | | | |
| <input type="checkbox"/> I did not notice it was time to pay the bill | | | |
| Please rate how distressing this was to you | | | |
| 0 | 1 | 2 | 3 |
| Not at all distressing | A bit distressing | Moderately distressing | Very distressing |
23. **I left the house, only to remember later that I forgot something important (wallet, phone, keys, etc)**
- | Please rate how often this has occurred in the last month | | | |
|---|-------------------|------------------------|------------------|
| 0 | 1 | 2 | 3 |
| Never | Sometimes | Often | Almost Always |
| I left the house, only to remember later that I forgot something important because... | | | |
| <input type="checkbox"/> I did not make a plan for how to remember the item I meant to bring | | | |
| <input type="checkbox"/> I forgot some important detail about the item I meant to bring | | | |
| <input type="checkbox"/> I did not take the item with me before leaving | | | |
| Please rate how distressing this was to you | | | |
| 0 | 1 | 2 | 3 |
| Not at all distressing | A bit distressing | Moderately distressing | Very distressing |
24. **I did not move my car/add money to my parking meter and got a ticket (or towed)**
- | Please rate how often this has occurred in the last month | | | |
|---|-------------------|------------------------|------------------|
| 0 | 1 | 2 | 3 |
| Never | Sometimes | Often | Almost Always |
| I did not add money to my parking meter because... | | | |
| <input type="checkbox"/> I did not make a plan for remembering when to move/feed the meter | | | |
| <input type="checkbox"/> I forgot some important detail about parking the vehicle | | | |
| <input type="checkbox"/> I did not notice it was time to move/feed the meter | | | |
| Please rate how distressing this was to you | | | |
| 0 | 1 | 2 | 3 |
| Not at all distressing | A bit distressing | Moderately distressing | Very distressing |

25.	I did not set my alarm to wake me for something important			
	Please rate how often this has occurred in the last month			
	0	1	2	3
	Never	Sometimes	Often	Almost Always
	I did not set my alarm to wake me for something important because...			
	<input type="checkbox"/> I did not make a plan for setting the alarm			
	<input type="checkbox"/> I forgot some important detail about the alarm or the event it signaled			
	<input type="checkbox"/> I did not set my alarm in time			
	Please rate how distressing this was to you			
	0	1	2	3
	Not at all distressing	A bit distressing	Moderately distressing	Very distressing

