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PROSPECTIVE MEMORY AND MEDICATION ADHERENCE IN

SCHIZOPHRENIA: INFLUENCING FACTORS AND AWARENESS OF ABILITES

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PROSPECTIVE MEMORY AND MEDICATION ADHERENCE IN SCHIZOPHRENIA: INFLUENCING FACTORS AND AWARENESS OF ABILITES

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PROSPECTIVE MEMORY AND MEDICATION ADHERENCE IN SCHIZOPHRENIA: INFLUENCING FACTORS AND AWARENESS OF ABILITES

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Adherence to antipsychotic medication in schizophrenia has been shown to predict symptom exacerbations; however, adherence remains poor in this population. The concept of taking medication on a maintenance regime is an example of prospective memory (PM). The current investigation is comprised of three studies in which 59 outpatients diagnosed with schizophrenia completed a comprehensive assessment including measures of PM, executive functioning, comprehension of medication instructions, insight into the need for medication, and environmental variables supporting adherence. An objective measure of medication adherence was also collected during a one-month baseline period. In study 1, medication adherence was conceptualized as a PM task and variables for predicting adherence based on PM literature were examined. Of the hypothesized variables, the interactive effect of PM ability and comprehension of medication instructions was the only predictor of adherence to antipsychotic medication. Comprehension of medication instructions alone was the only predictor of adherence to total psychotropic medication regime. Study 2 investigated the role of executive

functions in the awareness of PM deficits and use of compensatory strategies. Results indicated that patients with poorer executive skills were less reliable in their report of PM ability compared to performance on PM measures. However, both fair and poor executive functioning groups reported similar use of compensatory strategies. Lastly, the third study manipulated the specificity of retrieval context for a 5-day habitual PM task intended to mimic medication-taking. The aim of this investigation was to examine the effect of retrieval context specificity and executive functioning on task performance. Results demonstrated that patients categorized as fair executive functioning completed significantly more days of the habitual task than patients categorized as poor executive functioning. There was no difference in performance between patients receiving greater retrieval context specificity versus patients receiving a general context. However, there was a trend for individuals with fair executive functioning to benefit from greater retrieval context specificity, implying that a minimum level of executive skill may be necessary for individuals to recognize the risk of a restricted retrieval interval and/or mobilize additional resources for encoding. Clinical implications are discussed.

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Chapter 1: Introduction and Background Information

1.1 Background and Significance of Proposed Research

Although it is estimated that schizophrenia affect only 1-2% of the population, its symptomatology, chronicity, associated cognitive deficits, and resulting personal and social costs cause many to consider schizophrenia one of the most devastating diseases of our time (Warner, 1995). Aside from the personal cost to individuals and family members affected by schizophrenia, it is estimated that the direct and indirect financial costs of schizophrenia in the United States alone is 50-60 billion dollars annually (Torrey, 1988; Wyatt et al., 1995; Trauer et al., 1998). A substantial portion of this cost is accounted for by the numerous hospitalizations required by patients with the disease as it is estimated that more than 25% of all hospital beds in the United States are occupied by patients with schizophrenia (Davies & Drummond, 1990). Adherence to antipsychotic medication has been shown to predict symptom exacerbations and subsequent need for hospitalization (Wieden & Glazer, 1997). Though it was once predicted that the unveiling of atypical antipsychotic medications would improve medication adherence by reducing unwanted side effects of medication and decreasing the need for concomitant medications to treat these side effects, adherence remains poor in this population. Recent research assessing medication adherence in this population indicates that as few as 40% of outpatients with schizophrenia adhere to prescribed antipsychotic medication regimes (Velligan et al., 2003; Gilmer et al., 2004). A number of psychosocial interventions have been proposed to improve medication adherence among individuals with schizophrenia (Dolder et al, 2003). However, interventions with the most promise

tend to be labor intensive and/or costly as they combine education, behavioral prompts for taking medication, positive reinforcement, and social support. Clearly, a method of identifying patients in the greatest need of such treatments would prove financially advantageous.

Though the basic concept of taking medication on a maintenance regime is an undeniable example of everyday prospective memory ability, a number of internal and external variables interact in performing this task. The use of memory strategies or an environment that supports medication adherence may improve adherence in individuals with poor prospective memory (PM) ability. Likewise, those with adequate PM ability may choose not to take medication, or be unable to take medication due to environmental variables. Cognitive deficits, financial factors, poor social support for taking medication, and poor insight into the fact that they have a psychological illness and the need for medication are all likely to affect medication adherence in this group. Having a better understanding of the relationship these variables play in patients' level of adherence improves our ability to appropriately identify and treat individuals at the greatest risk of relapse.

1.2 Prospective Memory and Everyday Functioning

A growing body of research has focused on an aspect of memory processes termed prospective memory. Prospective memory (PM) is the mechanism by which an individual is able to remember to perform some intended future action. PM research has grown in popularity over the past two decades largely for its relevance in day-to-day functioning and the fact that it is characterized by intentions that are personally

motivating to remember (Conway, 1991; Larrabee & Crook, 1989). In spite of the latter, Einstein and McDaniel (1996) report that more than 50% of memory complaints are prospective in nature. Mundane, everyday tasks, as well as complex tasks that require an individual to follow a sequence of activities by responding to a number of temporal and environmental cues utilize PM. Without adequate PM ability, activities of daily living such as cooking, doing laundry, paying bills, and taking medication may become increasingly difficult and jeopardize independent living (Maylor, 1990; Einstein & McDaniel, 1996). The necessity of PM in everyday functioning has prompted many researchers to refer to this ability as "everyday memory" (Kinsella et al., 1996; Marsh, Hicks, & Landau, 1998). Though PM includes a retrospective memory (RM) component (the content of the intended action), recollection of the action is not facilitated by an explicit request to retrieve the intention. Rather, PM largely relies on internal processes for self-generating cues and vigilance for detecting associative cues in the environment which would indicate the correct time to perform the intended action (Einstein & McDaniel, 1996; McDaniel & Einstein, 2000).

1.3 Subtypes of Prospective Memory

There are two primary subtypes of PM discussed in the literature: event- and time-based (Sellen, Louie, Harris, &Wilkins, 1997; Park, Herztog, Kidder, Morrell, & Mayhorn, 1997). Within these, some researchers have also begun to examine habitual PM which can further specify the frequency with which certain time- and event-based tasks are intended to be performed. In addition, a distinct subtype of event-based PM, activity-based PM, is also discussed in the literature (Kvavilashvili and Ellis,1996; Shum

et al., 2004). However, regardless of the subtype, the goal of any PM task is to remember to perform some intended future action. What differs among time- and event- based PM tasks is the cue that should prompt retrieval of the memory to perform the action. In event-based PM, the cue for remembering is an event such as seeing a certain person, doing a specific activity, or being in a particular setting. Time-based PM is different in that there are no obvious external cues to prompt the remembering of a specific intention. In these tasks, it is important to perform a particular activity at a certain time. With time-based tasks, the individual must rely on internal processes to monitor the passage of time and/or to self-initiate the checking of time (looking at their watch) (Einstein & McDaniel, 1996). This makes prospective time estimation or time production a crucial component of time-based PM. The heavy reliance on internal processes makes time-based tasks more difficult and prompts many individuals to convert time-based tasks to event-based tasks, which has been shown to increase success in remembering (Maylor, 1990).

Kvavilashvili and Ellis (1996) discuss habitual PM which can be a further specification of either time- or event-based PM. In general, most time- and event-based tasks consist of a single episode of forming an intention and remembering to execute the intention on a single occasion in the future. However, some PM tasks require remembering to execute an intended action on multiple occasions in the future. These tasks, where one intends to carry out an activity on a regular time interval (such as taking medication every 4 hours) or every time a specific cue is encountered (buying a paper on the way to work every morning), can be termed habitual PM tasks.

As the cue for remembering to execute an intended action in activity-based PM is an external cue in the environment, activity-based PM, proposed by Kvavilashvili and Ellis (1996), is a specific subdivision of event-based PM. However, unlike general event-based tasks where the occurrence of the external cue is likely to interrupt an ongoing activity, the cue to retrieve an intention for activity-based PM tasks naturally occur at the end of another activity. Examples of activity-based tasks might include putting on one's seat belt after sitting down in your car, or turning off the oven after one is finished cooking. As the cue always coincides with the end of another activity, and one is not required to interrupt an ongoing activity, activity-based PM is considered less cognitively demanding than general event-based PM tasks.

Chapter 2: Prospective Memory: Conceptual Framework and Influencing Factors

2.1 A Conceptual Framework of Prospective Memory

PM appears to be at the crossroad of memory, attention, and execution of action. Though the use of a single term, PM, to describe the process of remembering to do a specific action in the future may seem to indicate a single specific ability, PM is a process that supports the realization of delayed intentions through a number of phases. These phases are not simply prospective in nature, but also include retrospective aspects of memory. In addition, neurocognitive abilities such as vigilance, executive functions, and time estimation influence PM along with a host of other environmental and individual factors. Ellis (1996) offers a conceptual framework for understanding the phases of PM tasks. She explains that there are five distinct phases including: (1) formation and encoding of the intention and action, (2) a retention interval, (3) a performance interval, (4) initiation and execution of the intention, and (5) evaluation of the outcome.

The formation and encoding phase is actually retrospective in nature and includes the entire content of the intention. For successful realization of an intention, the specific action (what one is to do) must be encoded along with intent to perform it (that one wants to do this). Finally, the appropriate retrieval context (when should one perform the task) must be encoded. The retention interval represents the period of time between encoding the intention and the appropriate time to execute the action. During this period, an intention may be recollected, but correct performance of the intention can not take place due to a mismatch between the current situation and the encoded retrieval context. When

the appropriate retrieval context matches the current situation, the PM task enters the performance interval. During this period one must recognize the current situation as the retrieval context and recall the intention to perform a specific action. The next phase includes the initiation and execution of the action. Finally, some evaluation of the outcome must take place to determine if the current state is a match or mismatch to the goal state. Though this final phase occurs after an intention has either been successfully completed or failed, it is crucial in preventing unwanted repetitions of a successfully completed PM task or to ensure that future attempts are made to complete a failed task.

2.2 Neurocognitive Correlates of Prospective Memory

Theorists have always hypothesized that the complex nature of PM required a significant contribution of the frontal lobe. Specifically, it is thought that a heavy reliance on the integrity of the frontal lobe is an area of distinction between RM and PM (Glisky, 1996). The frontal lobes are responsible for formulating plans, initiating actions, monitoring ongoing behavior, supervising non-routine activities, evaluating outcomes, and involved in the selection of cognitive plans of action and behavior selection (Damasio & Anderson, 1993; Cohen & O'Reilly, 1996). Based on this, the connection seems clear between the frontal lobe and PM, which requires these specific activities (Mantyla, 1993; Glisky; Bisiacchi, 1996; Cohen & O'Reilly; McDaniel, Robinson-Riegler, & Einstein, 1998). Though investigations of the neuropsychology of PM have only occurred in the last decade, the intuitive hypothesis that the frontal lobe plays a critical role in the realization of PM intentions has been supported.

2.2.1 Neurocognitive measures

The role of the frontal lobe in mediating the prospective component of PM activities has been supported by investigations examining the relationship between clinically validated measures of neurocognitive abilities. Though not all studies find identical results due to differing methodologies including the use of a wide array of PM tasks, varied measures of executive functions/working memory/memory, the inclusion of different clinical populations, and variations in power due to sample size, the literature consistently reports correlations between measures of PM and executive functions/working memory (Groot et al., 2002; Ritch et al., 2003; Ritch & Tucker, 2004; Shum et al., 2004; Knight, Harnett & Titov, 2005; Carey et al., 2006). In addition to functions largely mediated by the frontal lobe, studies also report significant correlations between verbal memory (mediated predominately by regions within the temporal lobe) and PM task performance highlighting the RM component in PM tasks.

2.2.2 Normal brain development and known abnormalities

Normal brain development is marked by continued growth of the frontal lobe throughout the second decade of life (Klingberg et al., 1999). Therefore, PM tasks, with their hypothesized heavy reliance on abilities mediated by the frontal lobe should demonstrate a main effect for age. A number of studies investigating the development of PM across childhood have consistently reported that older children out-perform younger children and adults out-perform children on both time- and event-based PM tasks (Kerns, 2000; Kvavilashvili, Messer & Ebdon, 2001, Ward et al., 2005).

In addition, PM has been shown to be impaired in individuals with illnesses that adversely affect the functions of the frontal lobe. Individuals with depression, Alzheimer's disease, ADHD, and traumatic brain injuries of the frontal lobe have all exhibited significant deficits in PM when compared to control subjects (Rude, Hertel, Jarrold, Covich, & Hedlund, 1999; Smith, Della Sala, Logie, & Maylor, 2000; Ritch, Tucker, & Vaurio, 2004; Shum, Valentine, & Cutmore, 1999). In the case of each of these conditions, abnormalities in the functioning of the frontal lobes are apparent (Beblo, Baumann, Bogerts, Wallesch, & Herrmenn, 1999; Johannsen, Jakobsen, & Gjedde, 2000; Schweitzer et al., 2000; Swanson et al., 1998).

2.2.3 Double dissociation studies

In double dissociation studies, the performance of a patient or group of patients with circumscribed damage to different brain regions is compared in hopes of demonstrating that specific functional loss is related to localization of lesions and not simply a part of a generalized impairment following non-specific brain compromise. The findings from double dissociation studies investigating the cognitive and neuroanatomical correlates of PM support the hypothesis that frontal functioning plays a key role in PM performance.

Umeda, Nagumo, & Kato (2006) trained two patients with brain damage, one with bilateral damage to the medial temporal lobe (MTL) and the other with lesions on the forebrain and right medial frontal lobe, in a sequence of specific event-based PM tasks over the course of three months. Though both patients improved over time, the primary improvement for the patient with MTL damage was in recognizing the

appropriate time when something should be performed. Conversely, the primary improvement for the patient with forebrain and right medial frontal lesions was for remembering the content ("what" aspect) of the tasks. Results support the hypothesis that the MTL plays a primary role in the retrospective component of PM, but that the prospective component is primarily related to intact frontal lobe functioning.

Complimentary findings were reported in a large scale study examining the correlates of multi-tasking in 60 normal controls and 60 subjects with various circumscribed cerebral lesions (Burgess et al., 2000). In this investigation, deficits in aspects of the multi-tasking task that are related to PM including planning, overall task performance/completion, and the maintenance of an intention were related to frontal lesions. Specifically, patients with lesions of the dorsolateral prefrontal cortex (DLPFC) performed significantly worse than all other lesion and control groups on prospective planning; patients with lesions of the medial aspects of Brodman areas (BA) 8, 9, and 10 (within the frontal lobe) demonstrated significant difficulty with overall task performance; and lesions to BA 10 were specifically associated with poor intention maintenance.

In an analogue dissociation study, McDaniel et al. (1999) divided subjects into four groups based on frontal lobe function and MTL function: high/high, high/low, low/high, and low/low. Patients were categorized into groups based on composite scores of multiple neuropsychological tests well accepted as measures of frontal and MTL functioning, and were then compared on their performance of event-based PM tasks with both high and low salient cues. Results indicated that poor frontal lobe functioning,

regardless of MTL status, resulted in poor performance on the PM tasks. Though there was a nominal advantage for high MTL function to improve performance on PM tasks, the difference between the groups was not significant. As self-initiated monitoring is considered a function of the frontal lobe important to PM, and this is highest when task cues are low in salience, an interaction was expected between cue salience and frontal lobe status with the low frontal group expected to demonstrate the largest increase in performance when cue salience was increased. However, the findings indicated that all groups demonstrated roughly equivalent improvement on PM when cue salience was increased. This implies that the primary role of the frontal lobe in PM may not involve monitoring, but rather one's ability to initiate probing of memory once a cue is recognized and in coordinating multiple tasks.

2.2.4 Event-related brain potentials (ERPs)

In an investigation of event-related brain potentials (ERPs), PM cue detection was associated with neural systems essential to processing the features of the stimulus cue (occipital-parietal region for a visual discrimination task); whereas, the right frontal region was related to monitoring and strategic search for the to-be-remembered intention (West, Herndon, & Crewdson, 2001). Another ERP investigation lends further support to the role of the frontal lobe in PM tasks by demonstrating that normal controls experience sustained negativity over the frontal-polar region (BA 10 bilaterally) between intention formation and realization implicating this area in the maintenance of intentions (West & Covell, 2001). In the same study, the only difference between older subjects (who have been shown to experience more PM failures) compared to younger subjects on ERPs

during a PM tasks, was a reduction in the magnitude of the sustained negativity in the frontal-polar region. The authors hypothesize that the relatively reduced efficiency of the frontal lobe in older adults may result in a loss of the intention or insufficient attentional modulation of the neural systems needed to process the cue. This hypothesis was supported by findings that show that the PM errors made by older adults tend to be primarily errors of omission.

2.2.5 Functional Magnetic Resonance Imaging (fMRI)

Though one can not directly compare electrophysiological and neuroimaging findings, fMRI studies investigating the neuroanatomical architecture of PM components build on earlier ERP data. den Ouden et al. (2005) observed activation in the right frontal polar region along with the right parietal cortex and precuneus when subjects simultaneously kept an intention in mind while performing an ongoing task. At the point that PM cues where recognized, activation for the lateral aspects of BA 10 increased significantly and medial aspects of BA 10 decreased. Simmons et al.(2006) manipulated cue identification and the intention retrieval aspects of PM tasks by creating two PM tasks, each with a high demand on one component process and a low demand on the other component process, to examine the neural basis subserving each process. Regardless of the manipulation, similar hemodynamic changes in the anterior portion of the prefrontal cortex (BA 10) were observed indicating this region is critical to both aspects of PM. Specifically, lateral BA 10 activation was highest when there were increased demands on intention retrieval, and medial aspects of BA 10 were highest in association with cue identification. In both of the above studies, results support the hypothesis that the medial

frontal polar region is associated with attention to external stimuli when the goal is cue recognition ("when" aspect of PM content), while the lateral aspects of the frontal polar region are associated with attention to internal cognitions ("what" aspect of PM content).

2.3 Other Factors Influencing the Realization of Delayed Intentions

In addition to the neurocognitive variables shown to correlate and predict performance on PM tasks, several other factors related to the individual, the environment, and the nature of the PM tasks itself influence task performance.

2.3.1. Factors influencing encoding of the delayed intention

Before anything else can occur, the content of the delayed intention (the "what", "that", and "when") must be encoded. In relation to the content of the action ("what" element), the complexity of the intended action influences task performance in that tasks with greater complexity are less likely to be performed correctly. Essentially, these tasks are negatively impacted by retrospective memory failure; the content of the action was not encoded (Ellis, 1996; Morrell, Park, and Poon, 1989). First, complexity in terms of whether the task is routine or novel influences encoding demands. The performance of novel tasks requires a greater level of planning to occur during encoding in terms of how the action will be completed. Failure to recognize the need for planning with novel tasks may result in poor encoding of the content of the intention, or an inability to execute the task if remembered (Morrell, Park, and Poon). Next, Ellis (1996) discusses that complexity of a task can also be influenced by the need for enabling actions to occur prior to being able to complete the intended action. Enabling actions include actions that make the intended action possible. For example, if one would like to remember to write a

history paper on Thursday night, one may also need to go to the library and check out and read literature on the topic, and buy computer hardware and paper to save and print the document before they begin writing on Thursday night. These tasks enable one to successfully complete the task of writing the paper and constitute several mini-PM tasks that must be successfully performed. A failure to complete enabling actions often prohibits successful completion of the original intention. As the number of enabling actions increases, the encoding and retention demands naturally increase making successful completion of the original intention less likely.

The actual desire to perform a task ("that" element) is influenced by the strength of the intention. The strength of the intention is affected by the tasks personal importance, the expected benefit of completing the task, or the cost of not completing the task (Cicogna & Nigro, 1998; Kliegel et al., 2001). Also influencing the strength of the intention is the source of the intention (self or another), who the beneficiary will be (self or another), and the status of the other individual to the person performing the task if another person is the source or beneficiary (Meacham, 1988). Tasks that are *personally* important, have perceived high benefit/cost, or are important to individuals of high status to the person performing the task are more likely to be successfully completed (Ritch, Tucker & Vaurio, 2004; Cicogna & Nigro, 1998). As the level of importance is a subjective judgment by the subject, research has demonstrated that certain personality traits such as conscientiousness and neuroticism also predict subjective memory complaints and PM task performance (Pearman & Storandt, 2005).

An important aspect of a delayed intention that influences the encoding of retrieval context is opportuneness or the number of available performance intervals for a task. As with complexity, tasks that are more restricted in terms of when they can be appropriately performed (needing to call someone at exactly 3 p.m. on Friday compared to needing to call someone any time before 5 p.m. Friday) require additional planning during encoding. Though specific contexts are more cognitively demanding in terms of encoding, a study examining this aspect demonstrated that tasks with specific retrieval contexts are more likely to be performed than tasks with more general retrieval contexts (Ellis, 1988). The increase in success related to retrieval context specificity is hypothesized to be the additional planning that occurs at the point of forming the intention. McDaniel & Einstein (2000) theorize that one way in which this benefits retrieval is that there is a more similar match between the *imagined* retrieval context and the *actual* retrieval context causing a greater sense of familiarity when the appropriate context is encountered sparking a search of memory to understand why the context is familiar. In addition, tasks with specific retrieval contexts are likely to result in a reorganization of one's daily activities at the superordinate level (Meacham, 1982). In planning for the activity, subjects generally create a temporal representation of their day with the intended action forming a break between other typical activities of the day. With the normal routine overridden, the intention becomes more salient and easier to retrieve (Ellis & Shallice, 1996). Also, as the intended action is now planned to occur at a boundary between other activities, it is now an activity-based PM task which is less cognitively demanding (Kvavilashvili & Ellis, 1996). The issue of specificity of retrieval

context seems especially relevant to medication adherence where prescription instructions may vary for the same medication from “one tablet twice a day” to “one tablet at 8 a.m. and one tablet at 8 p.m.”

2.3.2. Environmental factors influencing successful completion of delayed intentions

During retention intervals, memory for the content of the delayed intention must somehow be kept online. One way this can occur is through recollections of the intention. Recollections are believed to refresh the content of the intention, alert the subject to the possibility of failure thereby increasing the importance of the task, and provide an opportunity for additional planning (Ellis, 1996). Though number of recollections in general positively correlates with task performance, the relationship between recollections and task performance is strongest in the period of time directly prior to the performance interval (Einstein et al., 1995). In a series of experiments by Marsh, Hancock, & Hicks (2002) where the cognitive demand of an ongoing task was manipulated during the retention and performance interval of PM tasks, PM task performance covaried with the cognitive demands of the ongoing task. In all manipulations, increased cognitive demands in the ongoing task decreased performance on the PM task. A possible explanation for these findings may be that the cognitive demands of the ongoing task reduce cognitive resources thereby reducing recollections of the PM task prior to the performance interval.

In addition to the idea that cognitively demanding ongoing tasks reduce recollections by way of consuming limited cognitive resources, the specific characteristics of an ongoing task have also been shown to interfere with cue detection in

the retrieval context. Marsh, Hick, & Cook (2005) demonstrated that, when the activities of an ongoing task utilize the same cognitive processes that are necessary to identify the cue for the intention (visual ongoing task and a visual cue for intention), the result is a reduction in PM task performance. Reduced PM task performance was not observed when the ongoing task utilized cognitive processes different from those necessary to identify the cue for the PM task (visual ongoing task and an auditory cue for intention).

Other factors that influence task performance are situational variables outside the subject's control which prohibit the performance of a delayed intention (Marsh, Hicks, & Landau, 1998). For example, a subject may intend to pick up their prescription today, but did not have enough money to pay for the prescription or they do not have transportation to get to the pharmacy. These situations do not represent an error in PM per se, but they result in a failure to complete an intended future action all the same. Hence, they are important to consider in everyday PM tasks such as medication adherence as they may constitute a better predictor of the behavior than PM ability alone.

Finally, task importance is not static. As situational variables change and new intentions are formed, subjects are continually re-evaluating the importance of intended tasks and reprioritizing delayed intentions. Situational variables, new information and changing attitudes that result in fluctuation of task importance influence the likelihood that a task will be completed (Marsh, Hicks, & Landau, 1998; Cicogna & Nigro, 1998).

2.3.3. Personality traits influencing delayed intentions

Though little research has been performed to investigate the relationship between personality variables and PM, some trends have emerged in the literature regarding

subjective memory complaints and PM performance. In three studies, Goschkle & Kuhl (1993) found that subjects who demonstrate a tendency to experience involuntary intrusions regarding future goals and past failures (state-oriented disposition) keep delayed intentions in a higher state of activation than subjects who rarely experience these intrusions (action-oriented disposition). In these investigations, state-oriented subjects demonstrated an intention superiority effect for words associated with a to-be-executed task regardless of whether the cue for performing the task was prompted by an associative cue in the environment (event-based) or needed to be completely internally monitored (time-based PM). Action-oriented subjects only demonstrated an equivalent intention superiority effect when the cue for performing the delayed intentions was based entirely on internal monitoring.

In regard to memory complaints by older adults (mean age of 73), which included both subjective difficulty with retrospective and prospective memory tasks, self-discipline (a facet of conscientiousness) and self-consciousness (a facet of neuroticism) accounted for 29% of the variance after controlling for anxiety (Pearman & Storandt, 2005). Though subjective complaints and the above personality variables did not correlate with objective measures of memory utilized in the investigation, two additional facets of conscientiousness were related to actual PM performance: competence and order. These findings indicate that subjects who feel capable and effective, and describe themselves as having the ability to organize belongings and activities are more effective at successfully completing PM tasks. These individuals may be more likely to assign

greater importance to delayed intentions and be able to set up and utilize compensatory strategies to aid in remembering such intentions.

2.4 Measuring prospective memory

Though no one disputes the ecologically valid nature of PM, there continues to be no standard measure of PM for clinicians to accurately and efficiently assess PM ability. Laboratory-based studies have often utilized tasks where subjects are asked to remember to perform various actions when specific temporal and environmental cues are encountered (Marsh, Hancock, & Hicks, 2002; Carey et al., 2006). Naturalistic studies have asked subjects to identify their personal intentions for the future and have followed up at a later date to determine the number of intentions completed (Marsh, Hicks, & Landau, 1998). Self-report studies have utilized questionnaires where subjects report their subjective ability to remember to perform a variety of everyday activities requiring PM ability (Smith et al, 2000; Hannon et al. 1995). In all instances, these measures appear to tap the definition of PM outlined in the literature, but all have substantial problems associated with them as well. With PM, there appear to be multiple roads to failure as well as multiple roads to success.

Though laboratory measures allow for the greatest level of experimental control, a number of findings indicate that factors outside of raw PM ability influence performance on these measures (Ellis, 1996; Cicogna & Nigro, 1998; Pearman & Storadnt, 2005). First, performance of *naturally* occurring PM tasks are, by definition, personally motivating (Conway, 1991; Larrabee & Crook, 1989). Forgetting to wash one's clothing or pay a bill has a direct consequence/cost on the life of the individual. Experimental

tasks performed in and out of a laboratory rarely carry such personal weight. As the subjective importance, benefit, or cost assigned to the task by the subject is critical to encoding the "that" element, and the fact that investigators in a research study may not be considered important or of high personal status to the subject, performance on laboratory PM tasks is likely to differ from the performance of naturally occurring personal intentions. Therefore, a failure to perform an experimental task may not reflect poor PM ability, but rather reduced motivation for completing the action (Ritch, Tucker & Vaurio, 2004) or a difference in personality variables such as conscientiousness (Pearman & Storandt, 2005). In addition, the salience of the environmental cues selected, complexity of the task, and level of distraction or cognitive load associated with an ongoing task all have been shown to affect the performance of PM tasks (Marsh, Hancock, & Hicks, 2002; Marsh, Hick, & Cook, 2005). Therefore, it is difficult to compare across multiple studies of PM as different laboratory measures are unlikely to be equivalent even if they are purporting to measure the same aspect of PM.

Naturalistic studies of PM remedy the difficulty with motivation, as the to-be-performed intentions are the subjects own personally relevant intentions. However, Marsh, Hicks, & Landau (1998) demonstrated that only 13% of the unfulfilled planned intentions of normal college students were the result of a failure to remember the intention. Failure to perform self-reported intentions were largely the result of three situations: (1) participants reprioritized their activities, deeming the original intention less important or favorable than a new intention, (2) there was no longer a need to perform the intention, or (3) it was impossible to perform the intention due to situational variables.

Based on these findings, it cannot be concluded that a failure to perform an intended action is necessarily the result of a failure in PM.

Finally, self-report questionnaires, though they allow one to gather information on a number of PM tasks and related variables in a timely manner, are not necessarily an assessment of PM ability; rather, they offer the level of insight one has into their ability. Therefore, they only provide good information about an individual's PM ability if the individual has good insight into their ability or deficit. Subjects may guess about their ability to perform some tasks listed on questionnaires which they have never had a need to perform or which they do not perform because they do not deem them important. Also, psychological research clearly indicates that most people tend to be inaccurate in estimating their abilities on many cognitive tasks (Metcalfe, 1998; Pearman & Storandt, 2005). PM literature on this specific topic indicates that individuals with traumatic brain injury tend to significantly overestimate their PM ability compared to their scores on performance-based measures (Hannon et al., 1995; Knight, Harnett & Titov, 2005). In these studies, clinical subjects did not rate their expected task performance or their subjective PM ability as being any different from control subjects. However, performance-based measures demonstrated a significant difference between the groups with the clinical group performing more poorly. As executive control appears to play a significant role in PM ability as well as one's ability to make judgments, those with impaired PM may be the least reliable in their self-report of their own abilities (Glisky, 1996).

Chapter 3: Schizophrenia and Associated Features

3.1 The diagnosis of schizophrenia in the DSM-IV

Schizophrenia is a disorder that has been described throughout history with various labels. The terms "madness" appears in the Bible to label bizarre behaviors, Galen describes symptoms of schizophrenia using the term "dementia" from A.D. 130-200, and Kraeplin explicitly describes a number of the symptoms of schizophrenia as "dementia praecox" in 1899 (Comer, 1995). The term "schizophrenia" was coined by Bleuler in 1911 and translates in Greek to "split mind." Bleuler's reference to "split mind" was meant to describe the fragmented thought processes, the split between thoughts and emotions, and the withdrawal from reality that he observed in individuals with this disorder (Comer, 1995).

Today, we continue to use the term coined by Bleuler. However, the gold standard for discussing the symptoms and associated features of schizophrenia come from the Diagnostic and Statistical Manual of Mental Disorders—Fourth Edition (DSM-IV). According to the DSM-IV (1994), schizophrenia "involves a range of cognitive and emotional dysfunctions that include perception, inferential thinking, language and communication, behavioral monitoring, affect, fluency and productivity of thought and speech, hedonic capacity, volition and drive, and attention." (DSM-IV, 1994 pp. 274). Despite this comprehensive definition, a diagnosis of schizophrenia can be made with only one month of active phase symptoms over the course of a continuous six month period of prodromal and/or residual symptoms. The one-month active phase symptoms must include two (or more) of the following: delusions, hallucinations, disorganized

speech, disorganized or catatonic behavior, or negative symptoms. A diagnosis may be made based on only delusions or hallucinations if delusions are bizarre or hallucination keep a running commentary on the individual's behavior or include two or more voices speaking to each other. In addition, the symptoms must result in social or occupational dysfunction, and not be better accounted for by another disorder.

3.2 Associated features of schizophrenia

Outside of the characteristic symptoms of the disorder, patients with schizophrenia often display a number of associated features. For the purpose of the proposed research, the following section will specifically address associated laboratory findings regarding core cognitive deficits, and what these deficits indicate regarding brain abnormalities.

3.2.1. Cognitive deficits associated with schizophrenia

Individuals with schizophrenia demonstrate poorer performance on a number of cognitive tasks relative to controls. Studies incorporating comprehensive batteries of neurocognitive tests indicate a "generalized deficit" that spans abstraction-flexibility (executive functions), verbal intelligence, spatial organization skills, semantic memory, visual memory, verbal learning, language skills, visual-motor processing, auditory processing, motor skills, and attention-vigilance (Saykin et al., 1991; Braff et al., 1991). However, deficits in attention, memory, and executive functions are the most agreed upon in the literature (Randolph, Goldberg, & Weinberger, 1993; Gold & Harvey, 1993).

3.2.1.1. Attention

Impairments in attentional processes in schizophrenia have been well documented over the last century (Gold & Harvey, 1993). Though attention as a construct can include

a number of cognitive processes, individuals with schizophrenia have exhibited attentional deficits in both visual and auditory modalities of a wide range of paradigms including: continuous performance, backwards masking, span of apprehension, and test of auditory distractibility.

The most widely utilized measure of sustained attention is the Continuous Performance Test (CPT) (Rosvold et al., 1956). The CPT can be administered through visual or auditory modalities, and presents subjects with a series of stimuli and instructions to respond to specific targets when encountered. Complexity of the targets and length of the test can vary considerably depending on version. However, regardless of the version, the consistent impairment of individuals with schizophrenia compared to normal controls on the CPT suggests that sustained attention is a cardinal deficit in this disorder (Nuechterlein & Dawson, 1984; Ito et al., 1996).

Another area of attentional impairment in schizophrenia is slowed perceptual processing demonstrated in deficit performance on backwards masking tests. In tests of backwards masking, a target stimulus is presented briefly followed by the presentation of a mask which overlays to same location. Subjects are asked to identify the target over varying intervals between the presentation of the target and the mask. Numerous studies have documented that individuals diagnosed with schizophrenia consistently require intervals that are two to three time longer than normal controls to correctly identify the target (Green et al., 2003; Koelkebeck et al., 2005).

Processing capacity, as measured by span of apprehension tests is another deficit area for individuals with schizophrenia. The span of apprehension test requires subjects

to identify which of two target letters are present during a briefly shown array of letters. Normal controls consistently out-perform individuals with schizophrenia in their ability to identify the target stimulus in letter arrays with as few as two distracter letters, and the difference between groups continues to increase as letter arrays become increasingly complex (Asarnow & McCrimmsom, 1981; Ito et al., 1996).

Finally, impaired selective attention is another robust finding in the schizophrenia literature. Individuals with schizophrenia consistently perform more poorly than age matched-controls on tasks where they are required to attend to specific information while filtering out irrelevant information (Nuechterlein & Dawson, 1984; Hugdahl et al., 2003; Hotchkiss & Harvey, 1990).

The neuroanatomical structures associated with attentional control are many and widely distributed including: frontal, striatal, and thalamic brain regions (Gold & Harvey, 1993; Heilman, Watson & Valenstein, 1993). This being the case, in addition to the fact that attention deficits in schizophrenia has been demonstrated using a number of paradigms, it is difficult to draw specific conclusions regarding the neuropathophysiology of schizophrenia based on these (Randolph, Goldberg & Weinberger, 1993). However, though more general neurocognitive impairment appears to be acquired as symptoms of the disorder manifest (Randolph, Goldberg, & Weinberger, 1993), attentional impairment appears to precede symptoms of the disorder. Similar deficits have also been observed in populations at risk for schizophrenia (Nuechterlein & Dawson, 1984).

3.2.1.2. Memory

Memory dysfunction in schizophrenia is considered to be another core deficit in the disorder. In a study by Saykin et al. (1991) investigating multiple domains of cognitive functions, the authors report general neurocognitive impairment with patients performing at least one standard deviation below the mean on all neurocognitive domains. However, on this background of general impairment, measures of verbal memory (subtests of the Wechsler Memory Scale-WMS; California Verbal Learning Test-CVLT) and visual memory (WMS) stood out as a selective impairment with patients. On these tasks, patients performed approximately three standard deviations below the mean. In a more recent investigation utilizing scales from the Woodcock Johnson, additional support for a selective impairment in memory over and above other neurocognitive deficits was found (Binks & Gold, 1998). In fact, 49% of schizophrenics exhibit deficits typical of patients with clear organically based memory disturbance (Turetsky et al., 2002).

Though attentional difficulties can certainly impede memory performance, patients with schizophrenia tend to demonstrate impaired performance across a variety of memory tasks requiring differing levels of attentional demand (free recall as well as temporal order and frequency tasks). The lack of correlation between attentional demands and performance suggests that memory deficits are not simply secondary to impairments in attention and processing (Gold & Harvey, 1993).

These above findings contribute to the understanding of brain abnormalities in schizophrenia. The medial aspects of the temporal lobe and hippocampal regions of the

brain have long been associated with memory and learning. In addition, these areas are heavily interconnected with thalamic and frontal regions (see Poldrack & Gabrieli, 1997, for a review). The fact that patients with schizophrenia demonstrate such severe impairment on tests of both verbal and visual memory implicates these regions bilaterally in the neuropathophysiology of schizophrenia. Patients with schizophrenia exhibiting severe memory deficits display significantly reduced volume of the frontal and temporal lobes associated with enlarged ventricles, and significant reductions in regional cerebral metabolism in the superior temporal gyrus, the mid-temporal gyrus, parahippocampus, and hippocampus (Turetsky et al., 2002).

3.2.1.3. Executive Functions

Patients with schizophrenia also have demonstrated significant difficulty in tasks involving executive functions (or traditional frontal lobe functions) including abstract reasoning, novel problem solving, and initiation (Saykin et al., 1991; Goldberg et al., 1988; Popescu & Miclutia, 2006). One of the most widely used measures of executive skill is the Wisconsin Card Sorting Test (WCST). Though children aged 10 and above generally display adult levels of performance, a majority of patients with schizophrenia consistently demonstrate difficulty with problem solving, shifting cognitive set, and benefiting from feedback; chronic patients continue to demonstrate this deficit even after attempts to teach the task have been made (Goldberg et al., 1988).

Further evidence for the involvement of the frontal lobe in schizophrenia comes from the behavioral resemblance between schizophrenics and individuals with known frontal lobe disease. Behavioral manifestations of executive dysfunction common in both

populations include: poor planning, apathy, disinhibition, and self-monitoring deficits (Randolph, Goldberg & Weinberger, 1993). In addition, single photon emission computed tomography (SPECT) indicates that while normal controls display increased regional cerebral blood flow in the prefrontal region during trials of the WCST, schizophrenics do not (Liu et al., 2002). Similar patterns of "hypofrontality" have been demonstrated in schizophrenia patients compared to normal controls during another task requiring executive skill (contextual processing) using functional magnetic resonance imaging techniques (McDonald & Carter, 2003).

3.3. Functional significance of cognitive deficits

In addition to a variety of neurocognitive deficits, individuals with schizophrenia demonstrate impairment in adaptive and role functioning (Liberman & Corrigan, 1993). Though a clear understanding of how specific neurocognitive abilities predict areas of functioning is unlikely, due to the fact that no neuropsychological tests can measure any discrete ability and the fact that functional tasks are likely to be neurocognitively multidetermined (Bellack, 1992; Velligan et al., 2000), literature over the last two decades has attempted to elucidate the impact of cognitive deficits associated with schizophrenia.

In one of the first studies examining the relationship between neurocognitive ability and functional outcomes, Heaton and Pendleton (1981; as discussed in Green, 1996) found that individuals with a higher IQ demonstrated better functioning than lower IQ individuals. Since Heaton and Pendleton's finding of a global association between

neurocognitive status and functional outcome, the literature has continued to support this relationship (Harvey et al., 1998; Velligan et al., 1997).

Harvey et al. (1998) examined the relationship between positive symptoms, negative symptoms, neurocognitive impairment, social and adaptive functioning, and overall functional status among geriatric patients with lifelong schizophrenia. Overall functional status was defined by dividing the sample into three groups based on residential placement: (1) subjects requiring chronic residential care in a nursing home, (2) subjects requiring chronic residential care in a psychiatric hospital, or (3) subjects with a history of residing primarily in the community. Results indicated that the best predictor of adaptive functioning among the three groups was level of cognitive impairment. Primarily community dwelling patients demonstrated better cognitive functioning, less negative symptoms, and the least severe deficits in adaptive functioning among the groups. The variable that discriminated nursing home patients from chronically hospitalized patients was the severity of positive symptoms with chronically hospitalized patients experiencing greater levels of symptomatology. As the primarily community dwelling group was assessed during an acute exacerbation of their illness requiring hospitalization, the chronically hospitalized patients and the primarily community dwelling patients did not differ in severity of positive symptoms.

As there appears to be an association between symptomatology (predominantly negative symptoms) and adaptive functioning, Velligan et al. (1997) examined the triadic relationship between neurocognitive deficits, symptomatology, and adaptive functioning by proportioning the variance and using path analysis in two studies. According to the

proposed model, cognitive functioning contributes to adaptive functioning and positive and negative symptomatology. As a result of symptoms being, in part, brought about by cognitive deficits, symptomatology is also related to adaptive functions. In the above studies, step-wise multiple regression analyses revealed that only the variables measuring cognitive function entered into the equation accounting for 42% and 48% of the variance in scores of adaptive functioning. Results from the path analyses indicated that the data supported the full model. The data continued to fit models where paths from symptoms to adaptive functioning were removed, but the model no longer fit when the direct path from cognitive function to adaptive function was eliminated.

Though the above studies indicate a clear relationship between global measures of neurocognitive ability and functional outcome measures, understanding how specific neurocognitive deficits can predict specific areas of functional impairment would be important. In a review of prospective studies that assessed specific aspects of neurocognition and subsequently assessed community functioning, Green (1996) reports that consistencies between the relationship of specific neurocognitive abilities and specific areas of functional outcome emerged. In studies examining general measures of community outcome, outcome was best predicted by measures of delayed verbal memory and executive function (WCST). Measures of social problem-solving were predicted by secondary verbal memory, vigilance, and negative symptoms. Lastly, measures of social skills acquisition were best predicted by secondary verbal memory, immediate verbal memory, and vigilance. No significant relationship between psychotic symptoms and

functional outcome was found in any of the eight studies that evaluated psychotic symptoms.

Though Green's (1996) review indicates that there are in fact trends for specific neurocognitive abilities to predict certain areas of functioning, only three of the 17 studies included in the review had power at or above 0.80, and the analyses where not guided by specific hypotheses. However, using a priori hypotheses based on Green's review, Velligan et al. (2000) confirmed that secondary verbal memory was related to all domains of community outcome, vigilance predicted social effectiveness, and executive function predicted general measure of community outcome as well as work/productivity and the performance of activities of daily living (ADLs). In addition to the hypothesized relationships, measures of executive function were also associated with social competence, vigilance was significantly related to global outcome, and visual memory was significantly related to the performance of ADLs. Though there is overlap in neurocognitive test scores due to the fact that even simple tasks require multiple neurocognitive abilities to perform, the finding that vigilance is related to social domains and not work/productivity or the performance of ADLs, and that visual memory relates only to the performance of ADLs is evidence for some specificity (Velligan et al., 2000).

Chapter 4: Medication Adherence and Prospective Memory in Schizophrenia

4.1 Medication Adherence and Prospective Memory

Though one would be hard-pressed to find a PM researcher who would disagree with the statement that medication-taking is a PM task, little research has been conducted integrating findings from PM studies with research on medication adherence. Part of this may be explained by the complexity of the task itself. Another part may be explained by a misunderstanding of what a PM task includes. Park and Kidder (1996) discuss medication-taking as a task representing a long chain of cognitive and psychosocial behaviors. Therefore, it can not be thought of as an isolated act of cognition. Medication adherence is not a laboratory measure where extraneous variables can be easily controlled. Rather, like other real-world PM tasks, it is bound in daily activities and influenced by behavioral factors which are not cognitive in nature (Winograd, 1988). This, as described through the phases of PM tasks and the influencing factors in Chapter 2, is not unique to medication adherence; it simply is the nature of any real-world PM task.

Leventhal and Cameron (1987) proposed the self-regulatory model of medication adherence. The authors state that values, beliefs, and illness representations held by the patient are a critical part of understanding adherence. They posit that patients are problem-solvers who make decisions regarding whether to use medication and in what amounts. The authors explain that there are two factors that must be examined in understanding adherence. First, does the patient have an illness representation that is consistent with taking medication; second how distressing is the condition, and how

effective does the patient believe medication will be in alleviating the symptoms. If medication adherence is conceptualized as a PM task, this theory is consistent with findings that perceived task importance is critical in the realization of delayed intentions (Kvavilashvili, 1987; Cicogna & Nigro, 1998).

Research with older adults also highlights another important factor related to medication adherence. Morrell, Park, and Poon (1989) found that level of comprehension of medication instructions was a key factor in determining adherence behaviors. As medication regimes increase in complexity, older adults demonstrate more difficulty understanding how to take medication correctly. The inability to encode the task may result in an inability form an adequate plan of action. When elderly patients were given organizational devices that supported comprehension (e.g. filled medication containers), adherence behaviors were facilitated.

Also, the role of cognitive ability in general is important in issues related to medication adherence. Remembering to do something involves a retrospective memory component, vigilance, working memory, and planning (Bisiacchi, 1996; McDaniel et al., 1999). Though this is true of all categories of PM tasks (time-, event-, and activity-based), these cognitive skills are necessary to differing degrees for each task. The most cognitively challenging of the different categories of PM is time-based as it has the heaviest reliance on the frontal lobe. Taking medication is often seen as a time-based task. However, many individuals spontaneously convert time-based tasks, such as medication adherence, to an event-based task to reduce forgetting (Maylor, 1990; Gould, McDonald-Miszczak, & King, 1997). In addition, some medication instructions are

written as activity-based tasks ("take after eating"), requiring the least demand on cognition of all PM tasks (Kvavilashvili & Ellis, 1996). Therefore, it seems that factors related to the individual (propensity to convert tasks or use compensatory strategies) and the environment influence which cognitive skills will become most relevant and to what degree.

Lastly, factors that influence medication adherence may not be stable across individuals or even within individuals across different instances of taking medication (Park & Kidder, 1996). In an investigation of medication adherence across age (middle aged, younger-old, and older-old adults), Park et al. (1992) found that younger-old adults (60-75) demonstrated the highest level of adherence. These individuals were hypothesized to still harbor the necessary cognitive abilities and to have an appropriate illness representation believing that medication would be beneficial. The authors posit that middle-aged patients likely lacked the appropriate illness representation, making medication-taking less personally important to them. Older-old adults (75+) likely have an appropriate illness representation, but lack the cognitive skills. Therefore, though middle-aged and older-old adults performed more similarly, the variable with the largest impact on their performance differed. Therefore, measuring the influence of any *one* individual factor is unlikely to yield impressive results across a large sample.

4.2 Medication Adherence in Schizophrenia

Though data clearly indicates that schizophrenia patients who are adherent with antipsychotic medication experience fewer symptom exacerbations and hospitalizations (Davis et al., 1993; Gilmer et al., 2004), poor medication adherence remains a persistent

problem in schizophrenia. In a recent study examining medication adherence in 68 patients at 3-months post psychiatric hospital discharge, Velligan et al. (2003) found that only 40% of patients were adherent to prescribed oral antipsychotic medications 80% of the time as assessed by pill counts. In the same investigation, analysis of blood level data indicated that only 23% of patients were adherent. Additionally, these percentages did not include more than 16% of the original sample that were dropped from the study due to dangerousness, re-hospitalization, or jail. Very similar results using electronic refill records (41% adherence rate) were reported by Gilmer et al. (2004). Though the current estimates are surprisingly low, they are still likely to be overestimates of true rates of adherence as patients volunteering to participate in clinical research are likely to be more compliant that patients who refuse to participate in such investigations (Duncan & Rogers, 1998).

As the importance of medication adherence is well-known, researchers have attempted to isolate variables that might predict the variance in adherence. However, investigations have often been conducted in an ad hoc fashion with only a few variables collected in the course of investigating other hypotheses. In addition, more than 77% of all studies that have collected some measure of medication adherence have relied solely on subjective measures including: patient report, significant other report, provider report, and chart review (Velligan et al., 2006). These methods tend to exaggerate adherence or be markedly inaccurate as patients are often poor at reporting their true adherence and reports from others are often based on insufficient information or inferred based on symptoms (Velligan et al., 2006). Other problems with studies predicting medication

adherence are the varying definitions for what constitutes “adherence” versus “non-adherence”, and the use of a wide array of measures to assess similar constructs. Therefore, there are still no clear answers to questions of how medication adherence can be best predicted. Albeit these limitations, some variables that have shown promise in predicting adherence will be discussed.

Among the variables that have been examined in relation to medication adherence, insight is the most common. Though insight into the need and benefit of medication have been measured a number of ways, many studies do report a significant relationship between insight and medication adherence (Amador et al., 1993; Cuffel et al., 1996; Adams & Scott, 2000; Kamali et al., 2001). However, other studies have found that insight does not predict adherence, or only predicts adherence at certain time-points (Garavan et al., 1998; Yen et al., 2005). These discrepancies are likely the result of differing methodologies discussed earlier.

In addition to insight, Jarboe & Schartz (1999) and Donohoe et al. (2001) found evidence that better attention and visual memory are correlated with medication adherence. Other studies have found that factors related to social support for taking-medication (having a guardian, increased family involvement, good therapeutic alliance) and environmental factors that support medication-taking (having a stable living environment) also tend to be more common among patients reporting better adherence (Drake et al., 1991; Olfson et al., 2000; Farabee, Shen, & Sanchez, 2004). However, each of the above studies utilized unique variables, and these findings have not been replicated.

Research investigating the realization of delayed intentions indicates that PM often represents complicated tasks that are influenced by a number of factors, and medication adherence would not be an exception. However, few studies have been published examining the relationship between PM and medication adherence; no studies have been published examining this relationship in schizophrenia. As taking medication on a regular basis is clearly an example of a PM task, an investigation of raw PM ability and key factors known to influence the realization of delayed intention may yield clearer answers to how good medication adherence is achieved. In addition, the relationship between these variables and PM task performance are likely to fluctuate from task to task. Therefore, it is important to measure multiple factors simultaneously and in combination with each other to best predict this complex behavior.

4.3 Prospective Memory Deficits in Schizophrenia

In spite of enormous literature on the neurocognitive deficits associated with schizophrenia and the growing literature on PM, few published studies exist examining this particular ability in individuals diagnosed with schizophrenia. However, studies that do address questions related to PM ability in this population: (1) suggest that PM is reduced in individuals with schizophrenia, (2) lend support to the importance of the frontal lobe in PM tasks, and (3) suggest a unique deficit in internal source monitoring and discuss its relationship to PM.

Based on the associated features of schizophrenia and the neurocognitive abilities hypothesized to be important in PM, it is no surprise that *every* investigation of PM in schizophrenia has reported deficits in this ability compared to controls. Examinations of

time-based, event-based, activity-based, and habitual PM have all indicated that individuals diagnosed with schizophrenia perform significantly more poorly than controls (Elvevag, Maylor, & Gilbert, 2003; Shum et al., 2004; Twamley, Narvaez, & Jeste, 2005; Kumar, Nizamie, & Jahan, 2005).

In addition, findings in this population further support the hypothesized role of the frontal lobe (or executive skills) in PM. As discussed earlier, deficits in prefrontal lobe functioning in schizophrenia are well-known. Therefore, tasks with greater prefrontal demands should be the most impaired in this population. In examining PM performance in patients with schizophrenia across all tasks categories, Shum et al. (2004) found that the largest deficit was in time-based PM tasks. Time-based tasks are unique in the aspect that one must completely self-initiate the retrieval of an intention thus exerting a greater demand on the prefrontal lobe (Einstein et al., 1995). In addition, Kondel (2002) found that the ability to form specific intentions for a PM task was impaired in patients with executive dysfunction, but not in a subset of patients who demonstrated intact executive skills.

Beyond a general deficit in frontal lobe functions, one study suggests that performance on PM tasks and awareness of performance on PM tasks may be further affected by difficulties with internal source monitoring in patients with schizophrenia. When a task must be repeated on a regular basis, as in habitual PM tasks, it becomes increasingly important to discriminate between two internally generated processes: thinking about an action and carrying out an action. This ability can be termed internal source monitoring. Elvevag, Maylor, & Gilbert (2003) demonstrated that individuals

with schizophrenia were significantly more likely to report that they had completed a failed (omitted) PM task compared to control subjects. The investigators in this study can not differentiate whether these results are truly accounted for by a deficit in internal source monitoring or problems with temporal discrimination (remembering a previous action and attributing it to the current trial). However, this finding has serious implications for measuring medication adherence (a habitual task) in schizophrenia, as most studies rely solely on self-report measures of adherence (Velligan, 2006).

4.4 Awareness in PM Deficits

The feeling-of-knowing in retrospective memory can be seen when individuals fail to recall information, but believe that they will be able to recognize it when they encounter it at a later time (Perfect & Hollins, 1999; Knight, Harnett, & Titov, 2005). Though individuals are frequently correct, patients with frontal impairment demonstrate reduced accuracy in recognizing information for which they experienced a feeling-of-knowing (Squire, 1982; Janowsky et al., 1989). These individuals show little awareness of their own memory capabilities and have difficulty employing appropriate memory strategies. Further support for frontal involvement in this phenomenon was found in a recent fMRI study. Maril et al. (2003) found increased activation in the frontal and left parietal regions of the brain during successful recall and unsuccessful recall accompanied by a feeling-of-knowing. This activation was not seen during unsuccessful recall that was not accompanied by a feeling-of-knowing. In addition to poor accuracy of feelings-of-knowing, patients with frontal lesions also experience difficulty with recalling source information and accurate frequency of occurrence information (Glisky, 1996). Recall

from the previous section that patients with schizophrenia also display these difficulties during PM tasks.

An ability similar to the feeling-of-knowing may be important in PM. Accurate knowledge about what one will or will not be capable of remembering in the future, in addition to an examination of failure cost may be the basis for the decision to utilize compensatory behaviors to aid in PM tasks (Knight et al., 2005). Individuals who lack awareness of their PM deficit have no reason to employ these strategies (Hannon, 1995).

In patients with traumatic brain injury, individuals who exhibit an accurate awareness of their cognitive deficits and an ability to set realistic goals for rehabilitation, experience better treatment outcomes (Ownworth, McFarland, & Young, 2000). This finding may be explained by the fact that being wrong about one's cognitive abilities may lead to negative stressful outcomes when one fails to perform intentions that are personally important. Possibly recognizing a deficit motivates one to take action to improve the skill (as is the goal of cognitive rehabilitation), or to develop strategies to by-pass the deficit.

Patients with schizophrenia have demonstrated increased errors in reporting PM performance immediately following a laboratory habitual PM task (Elvevag, Maylor, & Gilbert, 2003). In addition, patients frequently self report better levels of medication adherence than objective measures reflect; even when they are aware that objective measures are being collected (Velligan et al., 2003). This appears to indicate that patients are not attempting to be dishonest, but rather that they truly lack awareness of their disability. Though executive functions of the frontal lobe are reduced in schizophrenia as

a whole, there is variability within this population. If awareness of PM ability is truly a product of frontal lobe functioning, then patient with less frontal dysfunction should demonstrate better accuracy in self-reporting PM ability.

Chapter 5: Hypotheses

The proposed research seeks to gain a better understanding of factors related to medication adherence in outpatients with schizophrenia. The act of taking medication on a regular basis can be conceptualized as a complex PM task involving a long chain of cognitive and psychosocial behaviors. Previous research indicates that PM involves a number of cognitive abilities with a heavy reliance on the functions of the frontal lobe. In addition to cognitive variables, a number of other factors have been found to influence the completion of delayed intentions. Many cognitive deficits have been associated with schizophrenia including deficits in attention, memory, and executive skills. These are precisely the cognitive variables implicated in PM. In addition, patients with schizophrenia frequently exhibit poor insight, reduced comprehension, difficulty with initiating activities, and tend to have fewer financial and social resources compared to non-clinical populations. Again, these factors are believed to impede PM task completion.

Predicting Medication Adherence

Though many researchers have attempted to isolate variables that may contribute to medication adherence in schizophrenia, none of these investigations have appeared to conceptualize medication taking as a PM task, comprehensively measuring factors known to influence the performance of delayed intentions. This is problematic as these variables may contribute to task performance in varying level from one task to the next. Therefore, isolating one variable from the others may produce only weak correlations with real-world PM tasks such as medication adherence. In addition, it is difficult to interpret

results from previous studies as the methods used to measure medication adherence have almost exclusively utilized subjective measures (mostly self-report) and have defined adherence in a multitude of ways.

In the present study, medication taking has been conceptualized as a PM task. Therefore, variables for predicting medication adherence have been drawn from the PM literature. Specifically, predictive variables will be examined using a variety of standardized measures, and an objective measure of medication adherence.

Specific Aim 1: Test the hypothesis that prospective memory ability, comprehension of medication instructions, insight into the need for medication, and resources supporting medication-taking are positively correlated with medication adherence among patients with schizophrenia and schizoaffective disorder.

Specific Aim 2: Test a model of medication adherence with PM ability, comprehension of medication instructions, insight into the need for medication, and resources supporting medication-taking as contributing variables. Each variable is hypothesized to make an independent contribution to the overall variance and it is hypothesized that the full model will account for a significant portion of the variance in medication adherence over and above any individual variable.

Investigating the Role of Executive Functions in Awareness of PM Deficits

Research demonstrates that the use of compensatory strategies aids in memory for intentions. However, individuals subjectively evaluate their need to utilize such strategies. Therefore, only individuals believing that there is a significant chance for failure would be motivated to employ compensatory strategies. It is indicated that

awareness/judgment of one's abilities is mediated by the frontal lobe; an area also heavily associated with PM ability in general. Additionally, once one determines that such strategies would be beneficial, they must utilize a number of executive skills to plan and initiate how they will remember; frontal lobe abilities again. Due to this overlap, it is likely that individuals in the most need of compensatory strategies may be precisely the individuals who are least likely to utilize them.

Specific Aim 3: To investigate the hypothesis that patients with poor executive functions are less reliable in their subjective assessment of PM ability than patients with better executive functions.

The sample will be divided into two groups based on a measure of executive functions: patients performing at or above a criterion score (fair executive), and patients performing below the criterion score (low executive). We will compare the two groups on a performance-based measure of PM (MIST) and self-reported PM ability (PMQ subscales 1-3). It is hypothesized that the low executive group will perform significantly more poorly on the performance-based assessment compared to the fair executive group. No difference is expected between the groups on subjective reporting of PM ability.

Specific Aim 4: To investigate the hypothesis that patients with better executive functions will report greater utilization of compensatory strategies for PM tasks.

The two executive functions groups will be compared on reported use of techniques to assist in recall (PMQ subscale 4). Our hypothesis predicts that patients in the high executive functions group will report significantly greater use of techniques to

assist in recall of PM tasks. However, this effect may be mediated by actual PM ability and awareness of PM ability.

Specific retrieval context

Though specific retrieval contexts result in a reduced window of opportunity for completing PM tasks, previous research with a normal population indicates that task performance is enhanced under these conditions compared to more general retrieval contexts. This result is hypothesized to be the product of additional encoding that occurs at the point of forming the intention. As the retrieval context is specific, individuals may visualize or give additional thought to the retrieval context causing a greater sense of familiarity when the context is encountered. This increased sense of familiarity may enhance one's ability to recognize the context as a cue for remembering to do something. Another explanation is that as the window of opportunity is restricted, an individual may become aware of the greater possibility of failure and reorganize their daily routine, possibly pairing the PM task with another task that occurs within the retrieval context. This mental reorganization makes the intention more salient and easier to retrieve. If this reorganization and pairing occurs, individuals should demonstrate greater consistency in the time of task completion of a habitual PM task.

Though instructions identifying a specific retrieval context should prompt additional planning at the point of forming the intention, this process is likely influenced by executive functions. Therefore, patients with poor executive skills may not benefit from specific retrieval instructions. Also, it is possible that individuals with higher

executive functions may not need specific retrieval instructions to engaging in the additional planning processes discussed above.

This information has important implications for medication adherence, as prescription instructions vary in specificity and patients with schizophrenia generally demonstrate reduced executive functioning. In the current investigation, we intend to examine the effect of retrieval context specificity on a habitual time-based PM task intended to mimic medication taking in patients with schizophrenia, and the effect of executive functions and response time variability on overall task performance.

Specific Aim 5: Test the hypothesis that specific retrieval contexts benefit the realization of delayed intentions among patients with schizophrenia and schizoaffective disorder. This will be accomplished by comparing the number of days completed and the time of task completion on the habitual PM task among two retrieval context conditions. It is hypothesized that:

1. Patients in the specific retrieval context group will be significantly more consistent in the time of task completion.
2. Patients in the specific retrieval context group will complete significantly more days of the assigned habitual PM task than individuals in the general retrieval context group.
3. Overall task performance will be significantly influenced by level of executive functions and variability in the time of completion.

Chapter 6: Methods

6.1 Participants

Participants included 59 outpatients with schizophrenia or schizoaffective disorder recruited to participate in a larger psychosocial treatment outcome study which included a one-month assessment and baseline period. All data for the current investigation was obtained during the one-month baseline period prior to randomization to psychosocial treatment interventions. Potential participants were identified through chart reviews conducted at three community clinics that are part of the Center for Health Care Services in San Antonio and the Austin-Travis County MHMR. After providing written informed consent, participants were interviewed by a master's level research associate utilizing the Structured Clinical Interview for DSM-IV (SCID)—Texas Medication Algorithm Project Version (Miller et al., 1999) to confirm clinic diagnosis. This version of the SCID is designed specifically for the Texas MHMR population from which participants were to be drawn. Prior to administering this interview, all raters were trained in a standardized training program to a reliability of .95 Kappa statistic for diagnoses of schizophrenia and schizoaffective disorder versus all other diagnoses.

In addition to diagnosis, patients were screened to ensure that they met the following inclusion criteria: (1) age between 18 and 60, (2) prescribed oral antipsychotic medication, (3) patient primarily responsible for taking their own medication, (4) able to read at a functional level as assessed by the Wechsler Test of Adult Reading and the ability to read and answer questions from the consent form, (5) no hospitalizations in the past three months, (6) no history of significant head trauma, seizure disorder, or mental

retardation, (7) no alcohol or drug abuse within the past three months, (8) no history of violence in the past 12 months, and (9) patient has a working telephone present in their living environment. Patients meeting entry criteria who agreed to participate in the larger treatment outcome study were compensated $50 for completing a five hour screening and baseline assessment, and $20 for one-month participation in a baseline adherence assessment including two or more pill-counts in their home.

6.2 Materials

Measures

A variety of measures were utilized to examine the specific aims of the proposed investigation. The following section will discuss measures relevant to all study aims followed by a description of the measures for specific aims. See Table 1 for a list of acronyms.

6.2.1 Measures Common to all Hypotheses

Demographic Variables

A number of demographic variables were collected during the initial screening visit and through chart review including: SCID diagnosis, age, gender, ethnicity, level of education, name of antipsychotic prescribed and dosing information for all psychotropic medications, and living arrangement. Complexity of medication regime was assessed by the total number of psychotropic medications prescribed.

Table 1

Table of Study Acronyms

Acronym	Title of Measure/Device	Description
WTAR	Wechsler Test of Adult Reading	Single word reading
MIST	Memory for Intentions Screening Test	Performance-based PM ability
PMQ	Prospective Memory Questionnaire	Self-reported PM ability
Habitual PM Task	Habitual Prospective Memory Task	Performance-based habitual PM ability
SUM-D	Scale to assess the Unawareness of Mental Disorder	Insight into having a mental illness & need for medication
TABS	Test of Adaptive Functioning in Schizophrenia	Performance-based; Comprehension of medication instructions
PEAS	Psychiatric Environmental Assessment Scale	Environmental variables supporting medication taking
WCST	Wisconsin Card Sorting Test	Executive functioning
PC	Pill Counts	Used to calculate adherence
MM	Med-eMonitor™	Device utilized to store medication and perform Habitual PM Task

Wechsler Test of Adult Reading (WTAR)

The WTAR (2001) is a test of single word reading requiring participants to read a list of words of increasing difficulty from a card. A score is given based on the number of words read correctly. As the WTAR is a test of single word reading, we intended to estimate reading level based on WTAR raw scores; however, the WTAR was normed as a brief measure of general intelligence and norms for grade level were not available. In addition, as the measure was designed to estimate IQ, not reading level, the list contained numerous irregular words making it difficult to assess functional reading when individuals performed poorly. This presented a problem in the current investigation for many of the participants who had limited education and/or low IQ likely as an associated feature of their illness, but have demonstrated the ability to read at a functional level. Therefore, individuals performing below the low average range for single word reading were asked to read the first page of the consent form out loud to study personnel and answer standardized questions regarding information contained on the first page. The Institutional Review Board of the University of Texas Health Science Center in San Antonio requires that all consent forms be written at a 6th grade reading level. Only participants able to successfully read the first page of the consent and correctly answer questions regarding its content were eligible to participate in the study.

6.2.2 Measures for Predicting Medication Adherence

Independent Variables

Memory for Intentions Screening Test (MIST)

The MIST (Raskin, 2005) is a brief performance-based measure of overall PM ability. During test administration, participants are provided with a clock and asked to complete eight PM tasks whilst attending to an ongoing distracter task (word search puzzles). The MIST includes both time-based and event-based tasks requiring either a verbal or action response over either a short- (2 minute) or long-delay (15 minute) interval. Some examples of items included on the MIST are: "In 2-minutes, please ask me what time the session ends today.", "When I hand you a post-card, please self address it.", and "In 15-minutes, use that paper to write down the number of medications you are currently taking." The timing for tasks instructions and task completion is standardized; therefore, the test lasts for exactly 25-minutes. During the MIST participants must keeps several sets of task instructions on-line for remembering with a maximum memory load of five in the 13th minute. A study examining the validity and reliability of the MIST indicated that it demonstrated convergent validity ($r = .86$) with like measures and good test-retest reliability ($r = .85$) (Raskin, 2005). Though a number of scores may be derived from the MIST, the variable of interest which was used in all analyses is the total performance score across all eight tasks.

Scale to assess Unawareness of Mental Disorder (SUM-D)

The SUM-D (Amador & Gorman, 1998) assesses several domains of insight in schizophrenia, and is one of the most commonly used measures to assess awareness deficits in this population. Specifically, it measures patient's awareness of (1) having a mental illness, (2) the effect of medication, (3) the consequences of mental illness, and (4) awareness and attribution for the specific symptoms of the illness. The SUM-D is a semi-structured interview where participants are asked questions regarding their insight into the above domains such as, "Do you have a mental illness?" Based on participant responses, the interviewer indicates the level of awareness for each domain using an anchored rating scale. Though a number of scores may be obtained from administration of the SUM-D, the variable of interest for the current study, included in the multiple regression analysis, was the sum of the items assessing the participant's awareness into having a mental illness and awareness into the need/usefulness of medication.

Test of Adaptive Behavior in Schizophrenia—Medication (TABS)

The TABS (Velligan et al., 2007) is a performance-based measure of functional ability requiring participants to initiate and perform tasks related to day-to-day community functioning. The TABS consists of subtests assessing functional ability across five domains: (1) medication-taking, (2) bathroom skills, (3) dressing skills, (4) grocery shopping, and (5) work and productivity. The medication-taking subtest was administered for the current study as a measure of comprehension of medication instructions. For the medication-taking subtest, participants must read the prescription labels of three medication bottles and correctly fill a medication container based on

prescription instructions. Patients receive credit for each day medication is correctly placed in the container, for correctly explaining how to take the medications, and for generating a solution to a medication problem (not enough medication for the entire week) and correctly completing actions to solve the problem. All scores are summed to yield a total score for the subtest.

The Psychiatric Environmental Assessment Scale (PEAS)

The PEAS (Velligan, Ritch, & Maples, In Preparation) is a newly developed 13-item scale assessing opportunities for and restrictions on independent functioning within the living environment on a series of 5-point anchored scales. Ratings are based on patient and caregiver interview and direct observations of the living environment. For the current investigation, data was collected for three items on the PEAS: financial resources, transportation resources, and social support for managing medication. Higher scores on all three items indicate greater resources. As part of the larger study, psychometric properties of the PEAS will be explored. However, preliminary data indicates acceptable inter-rater reliability and a relationship to functional outcome. A total score reflecting all resources supporting medication adherence was derived by summing the average of the financial resources rating and transportation resources rating (yielding an environmental resource factors) with the rating for social support for managing medication (social resource factor).

(Financial + Transportation)/2 + Social = Resources for Medication Adherence

Dependent Variables

Medication Adherence—Pill Counts (PC)

Study personnel traveled to patients' homes to complete pill counts of all psychotropic medication prescribed to patients at the beginning of the baseline period, and again at 1-month. Ratings of adherence to complete psychotropic medication regime as well as adherence to antipsychotic medication were calculated by dividing the number of pills missing from the baseline count by the number of pills that should have been taken based on prescription instructions during the 1-month period.

6.2.3 Measures for Investigating the Role of Executive Functions in Awareness of PM Deficits

Independent Variable

Wisconsin Card Sorting Test (WCST)—Nelson Modification

The WCST (Berg, 1948) is a widely accepted measure of executive functions. The WSCT was devised to study cognitive flexibility, the ability to perform a shift in mental set, planning and organization, and problem solving-ability. In this test, participants are asked to match cards to one of four stimulus cards according to a rule that must be deduced from the examiner's response to the participant's placement of the cards. During administration, the examiner changes the rule for matching by changing their pattern of response to the participant's placement of the cards. The variable of interest which was used to divide the sample into fair versus low executive skills was the number of categories achieved. In factor analytic studies, this variable loads with factors of "complex-intelligence" and "planning-organization" (.58) (Lezak, 1995).

The Nelson Modification of the WCST (Nelson, 1976) removes all ambiguous cards from the deck and is thus only recommended for populations with known executive dysfunction who would likely experience a floor effect with standard administration. Participants were regarded as "fair executive functioning" if they completed three or more categories. Participants completing two or fewer categories were regarding as "poor executive functioning."

Dependent Variables

Memory for Intentions Screening Test (MIST)

A complete description of the MIST is included in the previous section. The specific variable of interest will be the total PM performance score.

Prospective Memory Questionnaire (PMQ)

The PMQ (Hannon et al., 1995) is a 52-item self-report measure of one's everyday PM ability and use of techniques to assist in recall. Items on the PMQ are behaviorally anchored and rated on a 9-point Likert-type scale. The test is comprised of four subscales measuring different dimensions of PM: (1) long-term episodic tasks, (2) internally cued tasks (largely short-term episodic tasks), (3) short-term habitual tasks, and (4) techniques to assist recall. The PMQ yields subscale scores based on the average rating for the items within each subscale, and a total score based on the sum of the means for the first three subtests. The PMQ has demonstrated high internal consistency (coefficient alpha = .92 for total score and ranged from .78 to .90 for the subscale scores), and acceptable test-retest reliability (r = .88 for total score and .64 to .88 for subscale scores) (Hannon et al., 1995; Hannon et al., 1990).

6.2.4 Measures for Investigating the Benefit of Specific Retrieval Contexts in PM

Experimental Habitual Prospective Memory Task

In this task, all participants were randomly selected to receive one of two instruction sets asking them to press a specified button on the med-Emonitor (described below) once daily for five days. In instruction set "general," participants were asked to go to the monitor once every *evening* for the next five days and press the menu button and button A. In instruction set "specific," participants were asked to go to the monitor *at a specific time in the evening* for the next five days and press the menu button and button A. The specific time selected varied by patient to ensure that it was at a time when the patient was regularly home. Participants were asked to repeat the task instructions, and to demonstrate the task on the med-Emontior during the home-visit to ensure comprehension. All participants were provided with written instructions for completing the task. Any time participants pressed the sequence of buttons to complete the task, the monitor displayed a message reading, "Thank you for remembering. Your response was recorded." The med-Emonitor device recorded the date and time of each response. As an incentive to completing the tasks, participants were told that they would receive $1 in McDonald's gift certificates for every day they remembered to press the button on the monitor. In actuality, all participants received $5 in gift certificates at their next home visit regardless of task performance. The variables of interest included the number of days the task was completed and the times of task completion.

6.3 Procedure

After providing written informed consent, participants completed two, 2 ½-hour, screening and initial assessment sessions at their outpatient clinic. The current investigation was part of a larger treatment outcome study and the total time for completion of the tasks of interest was approximately 1 ½ hours. Measures administered during the screening and initial assessment sessions included the SCID, MIST, SUM-D, TABS, interview portion of PEAS, PMQ, and WCST; as well as a comprehensive battery measuring symptom severity, cognitive functions, and adaptive functioning specific to the larger treatment outcome study. Tasks relevant to the current investigation were interspersed with tasks related to the larger treatment outcome study. The order of presentation for the tasks was the same for all participants. Care was taken in planning the order of administration to minimize participant fatigue and ensure that no measure spoiled any other measure. Participants received $50 for completing the screening and initial assessment.

Following completion of the initial assessment, participants had a Med-Emonitor™ (MM) set-up in their home. The MM is an electronic device capable of storing up to a one month's supply of five different medications (Ruskin et al., 2003). Medication information is programmed into the MM to identify which medications are contained in each compartment. The MM records the times and dates medication compartments are opened, and automatically queries the participant as to the reason why the compartment was opened (i.e., taking medication and how many pills taken, refilling the compartment, or just checking and did not take any medication). In addition,

assessment instruments which the participant can respond to can be remotely programmed into the device. Data is automatically downloaded to a secure website when the MM is placed into a cradle connected to a telephone line. Though a rating of adherence could be obtained from the MM, the MM was developed as a clinical intervention tool and is currently being investigated to determine its utility as an objective measure of medication adherence.

Each participant was assigned an MM specialist to conduct the initial in-home visit. During the initial visit, the study personnel completed the observational portion of the PEAS, pill counts of the participant's medications, connected the cradle of the MM to the phone line, programmed the MM, assisted the patient in correctly filling the compartments, and explained the use of the monitor. At the one-month visit, the MM specialist completed another pill count and explained the Experimental Habitual PM Task. Results from this task were down-loaded daily, and participants were compensated for the task at the following home-visit. In addition to the scheduled monthly visit and pill count, the MM specialist was responsible for reprogramming the device as needed based on refills and changes in prescriptions, and communicating in-person or by phone with the participant to resolve any problems related to using the MM device. At the end of the 1-month period, participants were compensated $20 for the inconvenience associated with phone calls, home-visits, and use of the monitor. Therefore, patients were compensated $50 for the screening and initial assessment, $20 for using the monitor during the 1-month medication adherence phase, and $5 in gift certificates for the Experimental Habitual PM Task ($75 in all).

Chapter 7: Results

The purpose of this investigation was to explore the potential influence of PM ability, comprehension of medication instructions, insight into mental illness/benefit of medication, and resources supporting medication taking on medication adherence among stable outpatients diagnosed with schizophrenia or schizoaffective disorder. In addition, the study attempted to elucidate variables related to spontaneous use of compensatory strategies to improve completion of everyday PM tasks, and how general versus specific instructions for completing a habitual PM task may influence task completion. This chapter is organized as follows: 1) discussion of demographic variables, 2) means, standard deviations, and ranges for primary variables, 3) analyses for predicting medication adherence, 4) analyses for investigating the role of executive functions in awareness of PM deficits and use of compensatory strategies, and 5) analyses for investigating the benefit of specific retrieval contexts in habitual PM.

7.1 Demographic Variables

A number of demographic variables were collected during the initial screening visit and through chart review including: SCID diagnosis, age, gender, ethnicity, level of education, name and dosing information for psychotropic medications prescribed, and living arrangement. In summary, of the 59 participants, 47.5% were diagnosed with schizophrenia and 52.5% were diagnosed with schizoaffective disorder. In terms of gender, 47.5% were male and 52.5% were female. Ethnically, 35.6% were Hispanic, 33.9% were Caucasian, 27.1% were African-American, 1.7% were Middle-Eastern American, and 1.7% were Asian-American. Individuals living with family represented

49.2% of the sample, those living independently or as a head of household, 50.8%. The mean age of the sample was 44.5 years (SD = 9.97; range = 23-59) and the mean level of education was 12.5 years (SD = 2.52; range = 7-20). The mean raw score for WTAR reading was 30.45 (SD = 12.63; range = 4-50). For participants who completed the one-month baseline period, the mean number of antipsychotic medications prescribed per patient was 1.28 (SD = 0.54; range = 1-3; N = 50) and the mean number of all psychotropic medications prescribed was 2.98 (SD = 1.33; range = 1-7; N = 50). Please see section for Predicting Medication Adherence below for an explanation of reduced sample size.

One-way between-subjects ANOVAs were calculated to identify differences in levels of all measures of interest by diagnosis, ethnicity, gender, and living arrangement. These analyses produced significant main effects for diagnosis on the MIST ($F(1,57) = 7.67$, $p = .008$) and SUM-D ($F(1,56) = 5.25$, $p = .026$). Specifically, participants diagnosed with schizophrenia performed significantly more poorly on the performance-based measure of PM and exhibited less insight into having a mental illness and the benefit of medication. For statistically significant analyses utilizing the MIST and SUM-D, we examined the contribution of diagnosis and reported results with and without diagnosis as a covariate. No additional main effects were found for any of the other above listed demographic variables.

In addition, complexity of medication regime, age, and level of education were examined in a correlation matrix with the variables of interest (Table 2). There was a significant correlation between age and the PEAS (r = -.321, p = .015) indicating that

older individuals had fewer resources to support medication-taking. In addition, education was significantly correlated with the TABS (r = .297, p = .023) and the PMQ123 (-.421) indicating that higher levels of education yielded improved performance for comprehension of medication instructions and higher levels of self-reported PM abilities. Complexity of medication regime did not correlate with any of the variables of interest included in this investigation.

Table 2

Intercorrelations of Demographic and Primary Variables

	Complexity of Regime	Age	Education
AP Adherence	-.182	.232	-.021
Total Adherence	-.228	.276	.108
MIST	-.191	-.241	.197
TABS	-.197	.188	.297*
SUM-D	-.001	.116	.033
PEAS	.000	-.321*	-.070
PMQ123	.278	-.065	-.421**
PMQ4	-.021	-.090	.049
WCST Categories	-.166	-.168	.151
Habitual PM Task (Days)	-.056	.049	.109

* p < .05

** p < .01

7.2 Primary Variables: Means, Standard Deviations, and Ranges

Means, standard deviations, and ranges were computed for the primary variables and are presented in Table 3. The variables include: 1) percent adherence for antipsychotic medications, 2) percent adherence for all psychotropic medications, 3) MIST total scores, 4) TABS-Medication Subtest total score, 5) SUM-D score, 6) PEAS score, 7) WCST number of categories achieved, 8) PMQ mean of subtest 1-3 (self-reported PM ability), 9) PMQ subtest 4 (self-reported use of compensatory strategies), and 10) Number of days completed on the habitual PM task.

7.3 Predicting Medication Adherence

Nine participants recruited for the investigation dropped out prior to completing the one-month pill-count. Therefore, 50 participants had baseline medication adherence data and were used in the analyses. Adherence was measured for antipsychotic medication/s (AP adherence), as well as for adherence to all psychotropic medications prescribed (Total adherence). Ratings of adherence were calculated using the following equation.

(Number of pills taken / Number of pill should have taken) X 100 = Adherence Rating

Participants with Over Adherence

Of the 50 participants with baseline medication adherence data, 5 participants were over adherent for at least one antipsychotic medication and an additional 7 participants were over adherent for at least one other psychotropic medication. There is

Table 3

Means, Standard Deviations, and Ranges for Primary Variables

Variable	Mean	SD	Range	N
Antipsychotic Adherence	87.50	27.05	0-188.4	50
Total Psychotropic Adherence	87.43	23.44	27.7-188.4	50
MIST Total Scores	26.71	13.42	0-48	59
Schizophrenia	21.89	14.53	0-45	28
Schizoaffective	31.06	10.80	3-48	31
TABS-Medication Scores	15.16	5.44	0-22	58
SUM-D Total Scores	3.07	1.68	2-9	58
Schizophrenia	3.59	2.08	2-9	27
Schizoaffective	2.61	1.09	2-7	31
PEAS Total Scores	5.49	1.52	3-10	57
WCST Categories Achieved	2.09	1.70	0-5	54
PMQ Subscales 1, 2, & 3	8.59	3.87	3.68-22.04	58
PMQ Subscale 4	4.01	1.71	1.00-7.65	58
Habitual PM Task	3.98	1.53	0-5	44

controversy regarding how to handle the data of patients who demonstrate over adherence to medication. Some methods include: using adherence ratings as they are, cutting off all over adherence ratings at 100%, subtracting the adherence rating from 200 if participant ratings are over 100, and excluding over adherent participants from the analyses. Just

like participants who are under adherent, participants who are over adherent demonstrate an error in taking medication as prescribed; however, the type of error, factors related to over adherence, and the consequences are considerably different. Therefore, for the purpose of this investigation, all adherence ratings were calculated as discussed in the previous section including all participants with useable data; No further manipulations were performed. In addition, AP adherence data was re-analyzed excluding the participants who demonstrated over adherence to antipsychotic medications (AP excluding). This procedure was not done for the total adherence ratings as no participant was over adherent for all medications and over adherence on different psychotropic medications is likely to be related to a variety of variables other than those under investigation in this study.

As part of the analyses, a correlation matrix was computed to examine the relations among the primary variables (Table 4). Results indicated that AP adherence was not significantly related to any of the proposed independent variables. Total adherence was related to comprehension of medication instructions (TABS) ($r = .31$, $p = .03$), but not to any other proposed independent variable.

Standard Multiple Regression Analyses

Standard multiple regression analyses were conducted to assess the degree of impact of the model including PM ability (MIST), comprehension of medication instructions (TABS), insight into illness/benefit of medication (SUM-D), and resources supporting medication taking (PEAS) on the dependent variables of medication adherence. AP adherence, AP excluding, and Total adherence were regressed on the

Table 4

Intercorrelations of Primary Variables

Variable	1	2	3	4	5	6
1. AP Adherence	--	.92**	.05	.24	-.16	.01
2. Total Adherence	--	--	.13	.31*	-.16	.04
3. MIST	--	--	--	.52**	-.23	.02
4. TABS	--	--	--	--	-.18	-.10
5. SUM-D	--	--	--	--	--	-.20
6. PEAS	--	--	--	--	--	--

* $p < .05$

** $p < .01$

independent variables. This model yielded no statistically significant coefficient of multiple determination for AP adherence (adjusted $R^2 = -.003$), AP excluding (adjusted $R^2 = -.023$), and Total adherence (adjusted $R^2 = .029$). As comprehension of medication instructions (TABS) was the only variable related to any of the medication adherence variables, Total adherence was regressed on the TABS. This analysis yielded a statistically significant coefficient of determination (adjusted R^2) of .076 (p=.03), suggesting that 7.6% of the variance in total psychotropic adherence was accounted for by comprehension of medication instructions.

Post-Hoc Stepwise Multiple Regression Analysis

Though there were no a priori hypotheses that performance on the habitual PM task would predict medication adherence, performance on this task was examined in a correlation matrix with the other variables of interest. There was a significant correlation between performance on the habitual PM task and Total adherence ($r = .391$, $p = .009$), indicating that individuals with better performance on the habitual PM task demonstrated better Total adherence. There was no significant relationship between the habitual PM task and AP adherence ($r = .243$, $p = .113$). In a stepwise multiple regression analysis including performance on the habitual PM tasks and comprehension of medication instructions (TABS), the only variables with significant correlations with any of our measures of adherence, only performance on the habitual PM task entered into the equation accounting for 13.2% of the variance (adjusted $R^2 = .132$, $p = .009$) in overall adherence to complete psychotropic medication regimes.

Hierarchical Multiple Regression Analyses Examining Interactive Effects

Given that the contributions of the variables of interest are not likely to be stable across patients, 2-way interactive effects of the independent variables on medication adherence were also examined. Prior to conducting further regression analyses, all independent variables were centered by subtracting the sample mean from each participant's score. Multiplicative terms were then created by multiplying each of the centered independent variables with each other. Hierarchical regression analyses were conducted for all combinations of the independent variables. For each analysis the individual centered variables were entered in blocks 1 and 2 and the multiplicative term

of those variables was entered in block 3. In total, six hierarchical regression analyses (MIST*TABS, MIST*SUM-D, MIST*PEAS, TABS*SUM-D, TABS*PEAS, and PEAS*SUM-D) were conducted for each of the three dependent measures (AP adherence, AP excluding, and Total Adherence).

AP adherence, AP excluding, and Total adherence were regressed on the centered independent variables and multiplicative variables in the hierarchical regression analyses procedures described above. The model including the MIST, TABS, and MIST*TABS yielded a statistically significant coefficient of multiple determination for AP adherence (adjusted $R^2 = .104$, $p = .045$) and AP excluding (adjusted $R^2 = .116$, $p = .048$), suggesting that 10.4% of the variance in adherence to antipsychotic medication was accounted for by the 2-way interactive effects of performance-based PM ability and comprehension of medication instructions. The percentage of variance explained by these variables increased to 11.6% when individuals who were over adherent were excluded from the analysis. No other combinations of the independent variables resulted in significant coefficients of multiple determination for AP adherence or AP excluding. No combination of independent variables resulted in significant coefficients of multiple determination for Total adherence.

7.4 Investigating the Role of Executive Functions in Awareness of PM Deficits and use of Compensatory Strategies

Though it was attempted to gather complete assessment data for all 59 participants, some data was lost due to participant refusal and administration error. In

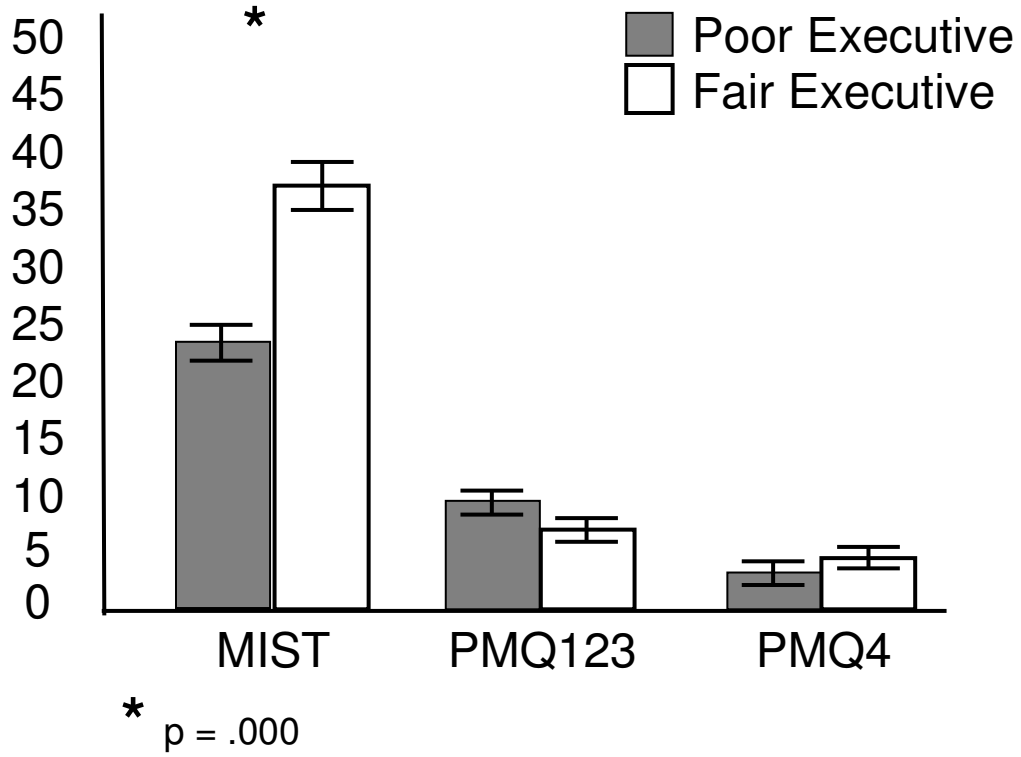
regard to hypotheses related to investigating the role of executive functions in awareness of PM deficits and use of compensatory strategies, all 59 participants completed the MIST, 58 participants completed the PMQ, and 54 participants had useable data from the WCST. Of the six participants with incomplete data, one refused to complete the PMQ, four requested to discontinue the WCST due to frustration with the task, and one participant's data on the WCST was lost due to administration error. All participants with useable data were included in the following analyses.

One-way between subjects ANOVAs were calculated to examine the effects of executive functions (fair vs. poor) on measures of PM including: the MIST (performance-based) and the PMQ123 (self-reported ability). The analyses produced significant main effects for group for the MIST ($F(1,52) = 15.09$, $p = .000$) but not for the PMQ ($F(1,51) = 1.876$, $p = .177$) (Figure 1). Individuals with fair executive functioning performed significantly better on a measure of PM ability; however, both fair and poor executive functioning groups self-reported similar levels of PM ability. Because diagnosis ($F(1,51) = 8.096$, $p = .006$) significantly contributed to the variance in MIST scores, an ANCOVA was calculated using diagnosis as a covariate in MIST scores. The results indicated that the above findings were essentially unchanged, with MIST scores ($F(1,51) = 14.99$, $p = .000$) showing a significant main effects.

A one-way between subjects ANOVA, comparing level of executive functions (fair vs. poor) on PMQ4 (reported use of techniques to assist in PM recall), produced no significant main effect ($F(1,51) = .447$, $p = .507$) (Figure 1). Pearson Correlation

Figure 1

Poor versus Fair Executive Functioning on Measures of PM



Coefficients were calculated to determine whether PMQ4 was related to MIST scores (performance-based PM ability) or PMQ123 (self-reported PM ability). The PMQ4 was significantly related to both the MIST ($r = .388$, $p = .003$) and the PMQ123 ($r = .423$, $p = .001$). The direction of the relationships indicates that individuals who *demonstrate* better PM ability report greater use of compensatory strategies, and individuals who *report* poorer PM ability report greater use of compensatory strategies.

7.5 Investigating the Benefit of Specific Retrieval Contexts in PM

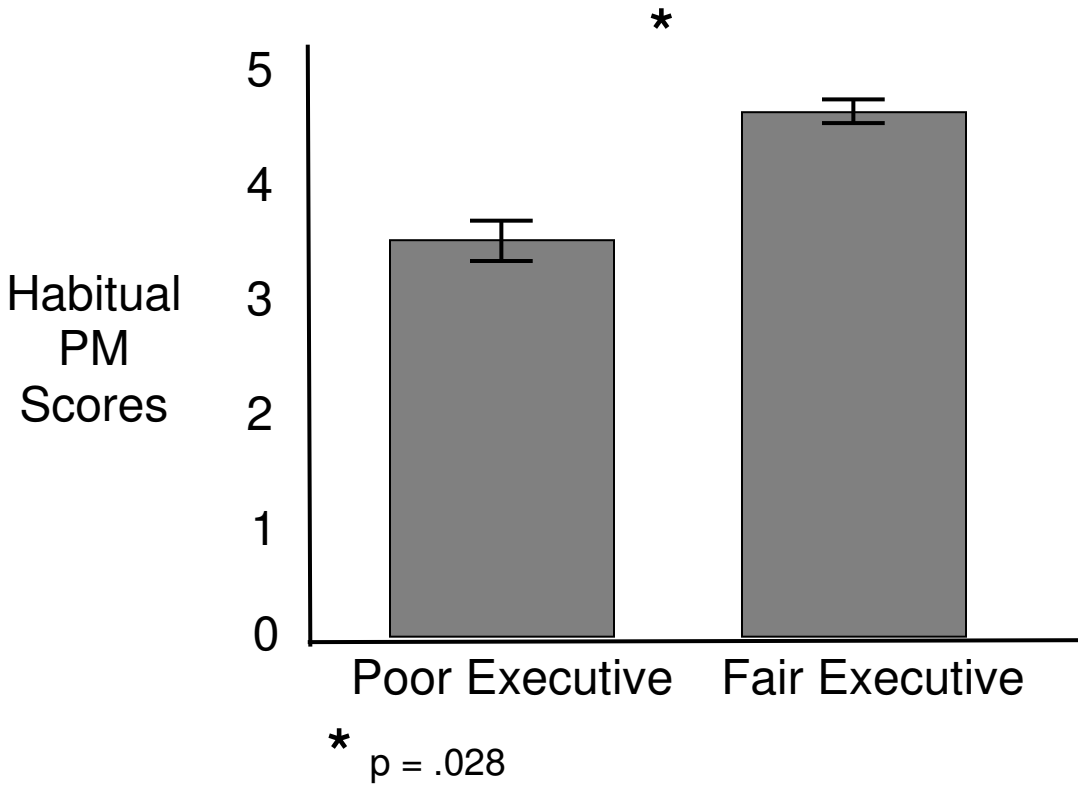
Forty-four participants received the instruction set and completed the habitual PM task. Of the 15 who did not complete the task, 10 participants dropped out of the study prior to receiving the instructions for the task, and five were still completing the task at the time of data analyses. Overall task performance was measured by the number of days the task was completed. Response time variability was determined for each participant completing three or more days of the task. For each of these participants, the mean time of response and standard deviation was calculated. Participant's standard deviation served as the measure of response time variability.

One-way between subjects ANOVAs were calculated to examine the effect of instruction set (general vs. specific) on overall task performance and response time variability. The analyses produced no significant main effect for overall task performance ($F(1,42) = .009$; $p = .923$) or response time variability ($F(1, 37) = .553$; $p = .462$).

As there were no significant main effects for instruction set, groups were collapsed to examine the effect of executive functioning (fair vs. poor) on overall task performance and response time variability. Results from one-way between subjects ANOVAs revealed significant main effects for group for overall task performance ($F(1, 39) = 5.213$; $p = .028$) (Figure 2), but not for response time variability ($F(1, 34) = .866$; $p = .359$). Regardless of instruction set given, participants with fair executive functioning completed significantly more days of the habitual PM task compared to participants with poor executive functioning.

Figure 2

Poor versus Fair Executive Functioning on Habitual PM Task

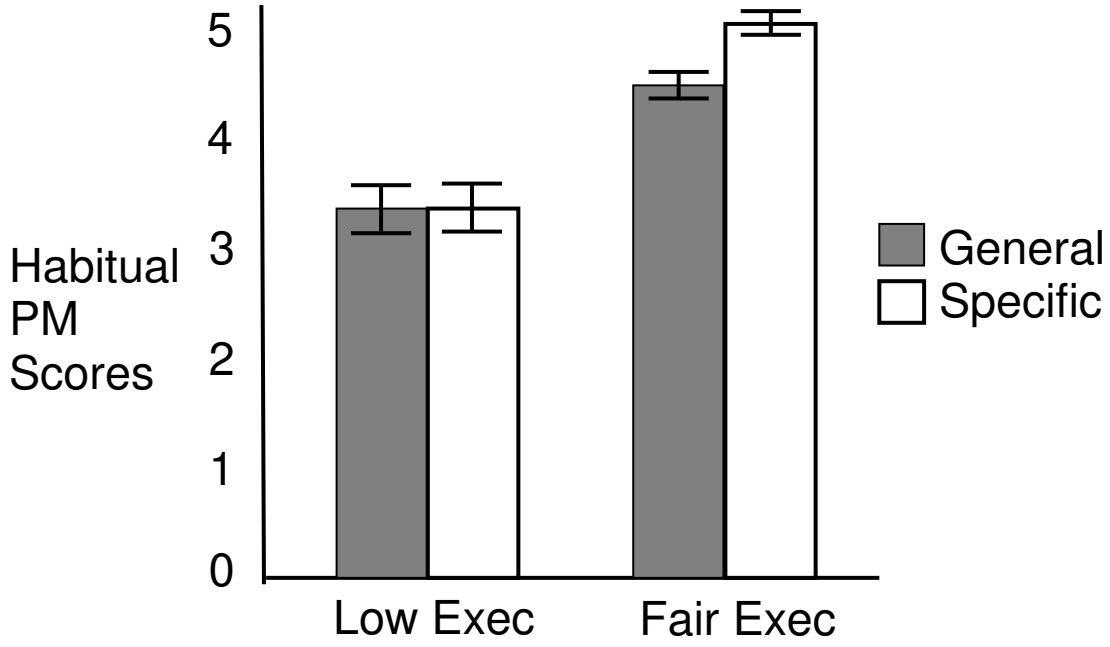


To further explore the effect of task specificity on overall performance and response time variability by level of executive function, the sample was split and the fair and low executive function groups were examined separately with one-way between subjects ANOVAs. For individuals defined to have low executive functions, the analyses produced no significant main effect for response time variability ($F(1, 19) = .343$; $p = .565$), or overall task performance ($F(1,24) = .000$; $p = 1.00$). For individuals defined to have fair executive functions, the analyses produced no significant main effect for response time variability ($F(1, 13) = 2.205$; $p = .161$), but a trend for overall task

performance ($F(1, 13) = 4.129$; $p = .063$) (Figure 3). This indicated a trend for individuals with fair executive functions to demonstrate a benefit in overall performance when provided with a specific retrieval context. However, the possible benefit could not be accounted for by reduced variability of responses across days of the task.

Figure 3

Effect of Retrieval Context Specificity on Overall Habitual PM Task Performance



For Fair Executive Functioning, p = .063

Chapter 8: Discussion

8.1 Medication Adherence and Primary Variables

One of the primary objectives of the current investigation was to examine whether variables shown to predict the completion of delayed intentions or PM tasks in controlled laboratory investigations could be applied to a real world PM task such as medication adherence in patients diagnosed with schizophrenia. Based on the previous literature, variables including PM ability, comprehension of medication instructions, insight into ones mental illness and the benefit of medication, and environmental and social resources supporting medication taking were examined to determine their relationship with medication adherence in this population. The PM literature suggests that real world PM tasks, such as medication-taking, are complex and involve a long chain of cognitive and psychosocial behaviors (Park & Kidder, 1996; Winograd, 1988). Therefore, it can not be thought of as an isolated act of cognition, nor is it likely that any other single factor would account for a large portion of the variance. Therefore, in this investigation, we also examined the 2-way interactive effects of the above variables on adherence to antipsychotic medications and adherence to total psychotropic medication regime.

Though some studies have found relationships between various measures of insight, cognitive abilities, and social and environmental factors with adherence to antipsychotic medications, there was no single variable that was significantly correlated or predicted whether stable outpatients diagnosed with schizophrenia were adherent to their antipsychotic medications. However, it was found that the interaction of raw PM ability and comprehension of medication instructions did predict 10.4% of the variance in

adherence to antipsychotic medications, indicating that neither of the individual variables alone are sufficient in explaining the complexity of antipsychotic medication-taking, but rather the way in which these variables interact with each other to benefit or limit ones ability to adhere with antipsychotic medications. These findings support the hypothesis that both variables are requisite in adherence. Examination of the interaction indicates that at the low end of PM ability, comprehension of medication instructions fails to predict adherence; however, as PM ability increases, the impact of comprehension on medication-taking also increases. Therefore, each variable in isolation fails to capture the complexity of medication adherence. Examining these variables in a multiplicative fashion however, addresses this issue and maximizes our ability to predict a complex real-world PM task.

Similar results were not found for adherence to total psychotropic medication regime. Of the above listed variables, comprehension of medication instructions alone was correlated with total adherence and predicted 7.6% of the variance in adherence ratings. No other hypothesized individual factors were correlated with total psychotropic medication regime and none of the multiplicative factors predicted total medication adherence. It is interesting that comprehension of medication instructions alone was the only predictor of total adherence, but alone failed to explain any of the variance in adherence to antipsychotic medications.

This finding could be related to the fact that more medications, with perhaps greater complexity of instructions, were involved in adherence to total psychotropic medication regime compared to antipsychotic medication regime. This would reasonably

make one's skill in understand medication instructions and solving medication problems more important to successful medication taking. Though the number of medications to be taken offered some indication of complexity of medication regime in the current investigation, it did not account for the complexity represented by multiple dosing times and additional instructions for taking medications (i.e., taken with food, on an empty stomach, not in combination with other medications, etc.). This hypothesis is supported by literature from Morrell, Park, and Poon (1989) who found that comprehension of medication instructions became more important in an elderly population as medication complexity increased.

Based on previous studies examining the factors influencing PM, we expected that our measures of insight and social/environmental factors would have played a role in adherence to medication. The fact that no relationship was found between medication adherence and these variables (or any of our independent variables individually with the exception of comprehension of medication instructions for total psychotropic regime) may be more related to selection bias in the present investigation which reduced our range of scores on both our dependent and independent measures. Participants in the current investigation were stable outpatients recruited from community mental health clinics with a mean age of 44.5 years. Based on the fact that individuals were regularly attending psychiatric outpatient appointments, engaging in medication management with a psychiatrist, had stable living environments, and were likely to have been living with a diagnosis of schizophrenia for many years, they represent a sub-section of patients whose behaviors and demographics would suggest that they have high insight into their illness

and the need for medication and at least sufficient social/environmental resources to support medication taking.

In addition, as participation was voluntary and occurred in the course of a larger psychosocial treatment outcome study aimed at improving medication adherence, the individuals agreeing to participate in such a study are likely to be more compliant than patients who refuse to participate in such investigations (Duncan & Rogers, 1998). As the study had aims related to medication adherence, study personnel demonstrated clear interest in medication-taking and installed a new and novel device in the environment to store medication (the med-Emonitor); therefore, adherence ratings may have been artificially inflated during the baseline period. Extending the baseline period would have allowed patients to habituate to the novelty of the study procedure and would have likely resulted in a broader range of adherence ratings. Recent studies examining rates of adherence among patients with schizophrenia have found that less than 40% of patients adhere to 80% of their prescribed antipsychotic medications (Velligan et al., 2003; Gilmer et al., 2004). However, in the present study, 77% of patients were adherent to at least 80% of their antipsychotic medications with a mean adherence rate of 87.5%. In addition, 73% of patients were adherent to at least 80% of their total psychotropic medication regime with a mean adherence rate of 87.4%. Based on these data, it seems clear that the patients who agreed to participate in the present investigation are not entirely representative of patients with schizophrenia in general and are among some of the most adherent individuals. Due to such a restricted range in scores, a much larger

sample incorporating a more diverse patient population with a longer baseline period would have been necessary to better identify factors predicting medication adherence.

An interesting, though post-hoc, finding was that overall performance on the habitual PM task was actually the best predictor of total psychotropic medication adherence. This particular task was designed to mimic the skills required for medication taking. Specifically, participants were required to comprehend task instructions (comprehension), have some willingness or at least a belief that it was important to complete the task (insight), and the cognitive ability to remember to complete the task on a regular basis (PM ability) or to spontaneously establish a compensatory strategy to remember the task (executive functioning). Habitual PM task performance did correlate significantly with our measures of comprehension of medication instructions ($r = .475$, $p = .001$), insight ($r = -.309$, $p = .041$), and performance-based PM ability ($r = .312$, $p = .039$). Despite the smaller sample size, participants who demonstrated better performance on this task demonstrated better overall medication adherence, accounting for 13.2% of the variance in total adherence ratings. When performance on the habitual PM task and task for comprehension of medication instructions were examined in a step-wise multiple regression analysis predicting total psychotropic medication adherence, only habitual PM task performance entered into the equation. As this brief task attempts to incorporate the specific skills necessary to complete a habitual PM task such as medication-taking, it is not entirely surprising that this relationship would exist. Though performance on the habitual PM task did not significantly predict adherence to antipsychotic medications, again this could be related to a restriction in the range of

adherence ratings, a fairly small sample size, or the relatively reduced complexity of antipsychotic medication regimes (i.e., the modal number of antipsychotic medications prescribed to patients was one). In an effort to identify patients most at risk for having poor medication adherence, it may be important to further investigate the utility of new, brief measures of habitual PM which more closely resemble the skills required for taking medication and reduce the impact of other confounding variables.

8.1.1 Limitations

There were several limitations of the current investigation for predicting medication adherence. Most notably was the small sample size which resulted in low power. As we where attempting to predict a complex task with multiple variables interacting with each other, a larger sample would have offered greater ability to more fully examine the nature of these relationships. Compounding the small sample was the fact that our recruited sample demonstrated considerably higher rates of adherence than would be expected based on recent literature. Regardless of whether this was due to the fact that we used a clinic sample, experienced volunteer bias, or artificial inflation of adherence ratings due to the novelty of study procedures, the result was a restriction in the range of adherence ratings which further reduced our ability to fully examine the relationships that exist between our independent variables and medication adherence. Each of these issues should be carefully considered in future investigations.

8.2 Investigating the Role of Executive Functions in Awareness of PM Deficits and use of Compensatory Strategies

In addition to examining variables which may play a role in predicting medication adherence in individuals diagnosed with schizophrenia and schizoaffective disorder, the present investigation attempted to elucidate the role of executive functions in the awareness of PM deficits and the use of compensatory strategies. Previous research indicates that individuals with frontal lobe dysfunction perform more poorly on measures of PM (Rude, Hertel, Jarrold, Covich, & Hedlund, 1999; Smith, Della Sala, Logie, & Maylor, 2000; Ritch, Tucker, & Vaurio, 2004; Shum, Valentine, & Cutmore, 1999). In addition, awareness of one's PM deficit, or the possibility that one may fail at remembering a PM task, is fundamental to motivate an individual to set up compensatory strategies which may aid in successfully completing the task (Knight et al., 2005; Hannon, 1995). This awareness/judgment of one's abilities is also suggested to be mediated by the frontal lobe (Glisky, 1996). Individuals diagnosed with schizophrenia (a disorder associated with frontal dysfunction) have demonstrated that they often lack the ability to accurately self-report their performance on laboratory and real-world PM tasks (Elvevag, Maylor, & Gilbert, 2003; Velligan et al., 2003).

Consistent with previous literature on PM, the results from the present study demonstrate that individuals exhibiting fair executive functioning significantly outperform individuals with poor executive functioning on a standardized performance-based measure of PM ability. Specifically, the fair executive group mean fell within the average range of PM ability based on normative data (Raskin, 2005); whereas the poor

executive group mean fell in the below average range. However, no difference between the fair and poor executive groups was found on a self-report measure of PM ability. Both groups' pattern of responding indicated that on average, they infrequently failed to perform everyday PM tasks. These finding do appear to support the hypothesis that individuals with poor executive functioning are less reliable in their subjective assessment of PM ability compared to patients with better executive functioning. Should this be the case, these results are particularly important for any research where self-report measures are to be utilized. Though there are a number of patients with fair executive function that may be able to accurately report their daily activities and cognitive abilities, there are at least an equal number of patients who will be unreliable in their self-report.

An alternate hypothesis that could also explain these results is the mismatch between a performance-based measure of raw PM ability and a self-reported measure of real-world PM ability. It is possible that the self-report measure is capturing information beyond one's awareness of abilities. Previous literature has defined level of adaptive functioning by individuals' residential placement (Harvey et al., 1998). If we assume that adaptive functioning would be generally higher for individuals living independently or as heads-of-households in the community rather than under the care of a family member, and take into account that there were no difference between our two living arrangement groups on any of the cognitive measures collected in this investigation, then perhaps raw PM ability in a laboratory measure is not necessarily reflective of achievement in terms of real-world PM ability. Individuals with poorer executive and PM abilities may choose lifestyles that place fewer demands on these skills making them more likely to be

successful in the PM tasks that they do incorporate in their lives. In addition, their view of their ability could be influenced by their successful completion of these tasks through the use of compensatory strategies, which were not allowed in the performance-based PM measure. Also, Conway (1991), Larrabee & Crook (1989) characterize real-world PM ability as intentions that are personally motivating to remember. Individuals with poor executive skills may have failed to be personally motivated to perform well on a laboratory PM task. Poor performance on such a task does not necessarily mean that they would perform poorly on daily PM tasks that would have significant bearing on their lives.

The use of compensatory strategies is one method in which individuals are able to improve performance on PM tasks by setting up prompts in the environment or engaging in mental visualizing or planning activities to aid in remembering. However, one must have some awareness that they have a need to utilize such strategies to motivate them to engage in this process. Data from the present investigation may be suggesting that individuals categorized as having poor executive functioning demonstrate a reduced awareness of their own PM ability. In examining the relationship between executive functions and reported use of compensatory strategies, we found that both fair and poor executive groups reported equal use of compensatory strategies. Based on the previous analyses however, these findings should be interpreted with caution. Our measure for use of compensatory strategies was self-report; there are no standardized objective measures for obtaining this kind of data.

This investigation has shown that individuals with poor executive functioning self-report behaviors and abilities that do not correspond to what would be expected based on a performance-based measure of similar behaviors and abilities. Therefore, we examined the relationship between reported use of strategies and PM ability: both performance-based and self-reported. Pearson correlation coefficients demonstrated a significant relationship between reported use of strategies and both measures of PM ability. However, the direction of the relationships indicated that individuals who *demonstrated better* PM ability and individuals who *reported poorer* PM ability utilized greater levels of compensatory strategies.

Initially, this finding may seem somewhat paradoxical, but not necessarily in light of the previous analyses examining awareness of abilities. Individuals with better executive functioning outperform individuals with poorer executive functioning; however, both groups self-report similar levels of PM ability. Those with better executive skills are likely to be more accurate in their self-reported ability and tend to endorse normal levels of failure in completing day-to-day PM tasks. Individuals with poorer executive skills seem to lack awareness of their reduced ability to perform PM tasks and present themselves more favorably than their performance would suggest. It seems plausible that the same process was at work with reported use of compensatory strategies. Specifically, individuals with better executive skills were likely more aware of their use of strategies and more accurate in reporting them. Individuals with poorer executive skills may have inaccurately reported their use of strategies.

8.2.1 Limitations

There are several limitations to the present study's investigation of the role of executive functions in awareness of PM deficits and use of compensatory strategies. First, it is possible that though we incorporated both a performance-based and self-reported measure of PM ability, the two measures were assessing different abilities as one was laboratory based and the other was based on personally relevant PM tasks. Perhaps future investigations should attempt to gather individuals' self-report of performance on laboratory PM measures to more clearly assess awareness of abilities. Also, the current investigation lacked an objective measure of the use of compensatory strategies. Therefore, based on data that may suggest that individuals with poor executive skills may be inaccurate when self-reporting, few conclusions can be drawn from these data alone. Finally, no data was gathered regarding the complexity of patient's daily lives to assess the type and frequency of one's engagement in everyday PM tasks. Surely, those who engage in more PM tasks will exhibit and report more PM failures than those who engage in fewer PM tasks. This would be an important variable for consideration in interpreting self-report questionnaires of daily performance.

8.3 Investigating the Benefit of Specific Retrieval Contexts in PM

The current study also attempted to explore the benefit of providing a specific retrieval context in PM. Previous literature suggests that such a restriction on the window of opportunity for task completion enhances encoding at the point of forming the intention (McDaniel & Einstein, 2001; Meacham, 1982; Ellis & Shallice, 1996; Ellis, 1988). The authors posit that when the timeframe for completing a PM task is restricted,

the task becomes more salient due to the increased possibility that the window will be missed. Therefore, it is suggested that individuals may rearrange activities in their day to provide cues for remembering the task and devote increased energy visualizing how and when in their schedule they will remember to complete the task. Such activities may be thought of as planning compensatory strategies.

However, the manipulation utilized in the present study failed to find an overall effect for retrieval context specificity. Participants instructed to perform the habitual PM task at a specific time were no more likely to complete the task than individuals who were given a more general timeframe. In addition, the literature would suggest not only that overall performance would be enhanced, but that the time of task completion over several days for a habitual task would be less variable (Meacham, 1982). Again, retrieval context specificity did not have an effect on the variability of task performance in this sample. The factor that did appear to influence performance on the habitual PM task was level of executive functions. Individuals with fair executive skills were able to complete more days of this task than individuals with poor executive skills regardless of the specificity of the instruction set they received. These results might indicate that individuals with higher levels of executive functions may not need or benefit additionally when provided with a specific retrieval context for a fairly simplistic task such as the one used in the present study. Similarly, those with poor executive functioning may not have the ability to make use of cue specificity to spontaneously mobilize additional resources for encoding how they would complete the task.

To further elucidate the relationship between executive functions and retrieval context specificity, we examined the effect of retrieval context specificity on habitual PM task performance separately for fair and low executive function groups. The results indicated that there was no benefit of task specificity for the low executive function group with the group means for both the "general" and "specific" instruction set being identical. However, there was a trend for individuals with fair executive functions to demonstrate a benefit in performance based on retrieval context specificity. Specifically, individuals given a specific timeframe to complete the task performed more days of the task. This appears to suggest that only individuals with at least fair executive functioning are able to recognize the restricted opportunity for task completion and mobilize additional resources to ensure successful task performance. This finding is not contrary to theories based on previous literature using individuals from the normal population for which no systematic executive dysfunction would be expected. However, it does seem to indicate that retrieval context specificity alone is not sufficient to increase overall task performance. Rather, some minimum level of executive functioning appears necessary to alert and enable individuals to employ strategies which would benefit task completion. Future investigations may consider manipulating the subtleness of cue specificity to determine if individuals with executive dysfunction are merely failing to recognize the risk presented by a reduced window of opportunity. In addition, the benefit of a brief intervention to prompt increased encoding (How will you remember to do this? What will you be doing prior to this task? Etc.) with low executive function individuals may be an important area of investigation.

In examining the effect of retrieval context specificity on response time variability, we again separated the fair and low executive functions groups. There was no significant benefit of specificity for any of the groups. Therefore, the results of the present investigation appear to be contrary to Meacham's (1982) theory that the process by which individuals improve their performance on PM tasks with restricted windows of opportunity is through restructuring their daily activities around the task. Should this have happened, individuals more successful at performing a habitual PM task would have demonstrated less variability in the time of task completion on a daily basis. The present investigation did not demonstrate such a finding. However, when considering the executive dysfunction associated with schizophrenia and the poor performance of patients on a modified test of executive skill, it is clear that even our "fair executive" functions group demonstrated below average executive functioning. The modified version of the WCST is not recommended for non-impaired individuals due to an expected ceiling effect. Within the current sample, no patient received the maximum score for categories achieved as would be expected for non-impaired individuals. Therefore, an expectation that the fair executive function group might perform or initiate strategies comparable to non-impaired individuals may be inappropriate.

Results, however, indicate that with at least fair executive functioning, individuals are able to recognize the risk of failure in a task with a restricted window of opportunity; thus increasing task salience and motivating them to employ increased mental energy to determining how they will complete the task. Strategies employed by individuals in this sample may be as variable as the individuals selecting them and do not appear to be

restructuring of daily activities specifically. Perhaps, the reason for this could be that the constrained window of opportunity suggested by the "specific" instruction set was not entirely believable. Participants were not told that they would fail to receive compensation if they did not complete the task within a specific window. They were only requested to complete the task at the specific time and told they would be compensated for each day of task completion. Future investigations may consider manipulations such as this and employ a post-task questionnaire to better elucidate the process by which individuals are able to increase task performance.

8.3.1 Limitations

One limitation in the present study's investigation of the benefit of specific retrieval contexts in PM was the small sample size. Though 59 participants were recruited, only 44 participants were administered the habitual PM task. Of these, only 41 participants had data for the WCST used as our executive functions measure, and only 36 completed three or more days of the habitual PM task to have a measure of response time variability computed. In addition to the reduced sample size, the participants who lacked useable data for the WCST did so due to frustration with the task and poor performance. Therefore, it might be assumed that those with perhaps the poorest executive functions were excluded from the analyses. Based on this information, it is likely that there was insufficient power to detect anything other than very large effects between groups. Future investigations should consider using a larger sample size that would provide sufficient power to detect group differences. In addition, the brevity of the task (5 days) created a somewhat restricted range in performance. A task performed over more days

and yielding a potentially broader range of performance may also increase the power to detect differences between the groups.

8.4 Clinical Implications

Despite the limitations of the current investigation, this is among first studies attempting to apply theory from the newly emerging PM literature to the real-world PM task of medication adherence. Results indicate that medication adherence is, in deed, a complex PM task which likely can only be predicted by examining multiple factors simultaneously; among these factors would be raw PM ability and comprehension of medication instructions. For different populations, factors such as social/environmental resources supporting medication taking and insight into the need for medication may also play a role in adherence. However, this was not found in the current investigation which utilized stable outpatients already regularly engaging in outpatient services. Future investigations should include a sufficient number of participants to fully examine the many complex interactions that exist among these variables and also further explore brief measures which combine the essential skills necessary for taking medication regularly. Such a measure in the current investigation was the best predictor of overall medication adherence.

In addition, the current study has implications for the ways in which adherence should be measured. Findings indicated that individuals diagnosed with schizophrenia and experiencing higher levels of executive dysfunction, self-report task performance that is greater than would be expected based on objective measures. This is problematic as a preponderance of studies have utilized only self-report measures to determine ratings of

medication adherence. It seems clear that for a population in which executive dysfunction is anticipated, objective measures must be utilized to ensure the accuracy of the behavior in question. Self-report measures in these populations appear to be measuring something far different than the behaviors in question. The current investigation suggests that self-report measures may be capturing *awareness* of one's abilities which could vary significantly from one's actual performance.

Finally, there was a trend for individuals with at least fair executive skill to benefit from being offered a specific retrieval context in which to perform a habitual PM task. Though the present study can not explain the process through which this benefit was achieved, the fact that such a trend was found may imply that writing medication instructions to include a specific retrieval context may improve medication adherence for individuals with at least a fair level of executive skill. For individuals with poorer executive skill, it would be important to further investigate additional brief interventions which would bypass deficits in executive functions to achieve similar results.

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