PROSPECTIVE MEMORY DEFICITS IN HUNTINGTON'S DISEASE
AND THE IMPACT ON DAILY LIVING

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Faculty of
San Diego State University

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In Partial Fulfillment
of the Requirements for the Degree
Master of Arts
in
Psychology

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by
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Prospective Memory Deficits in Huntington’s Disease and the Impact on Daily Living

by

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San Diego State University, 2013

Prospective memory (ProM), “remembering to remember,” is a form of memory for future events believed to be necessary for everyday functioning. The frontal lobes, specifically the prefrontal cortex, have been identified as essential to ProM. Huntington’s disease (HD), a neurodegenerative disorder, is associated with frontal lobe dysfunction. Individuals with HD demonstrate impairment on cognitive tasks shown to be dependent on frontal lobe functioning. However, no study to date has examined the effect of HD on ProM.

The current study investigated ProM abilities in HD using the Memory for Intentions Screening Test (MIST), a standardized test of ProM. The study also investigated the relationship between ProM and everyday functioning. Participants included 19 patients diagnosed with mild-moderate HD and 20 matched controls. Participants were administered performance-based and self-report measures of ProM and everyday functioning tasks, in addition to a battery of standardized neuropsychological tests.

The data indicate that HD patients were impaired relative to control participants on a performance-based test of ProM. In addition, HD patients demonstrated significant impairment on a naturalistic test of ProM, which provides an indication that HD patients’ deficits on ProM may affect their ability to perform everyday tasks. HD patients also demonstrated deficits on a performance-based iADL measure compared to control participants. These findings provide the first data to indicate that HD is associated with impairment on a performance-based test of ProM, and provide support for literature on iADL impairment associated with HD. The present findings have important implications for understanding functional independence in this patient population.
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CHAPTER 1

INTRODUCTION

PROSPECTIVE MEMORY

Prospective memory (ProM) is a form of memory for future events, often described as “remembering to remember.” ProM involves remembering to perform an intended action after a delay, in response to a specific cue (Meacham & Singer, 1977). This type of memory is believed to be involved in everyday tasks, such as remembering doctor’s appointments or when to take medications (Kliegel & Martin, 2003). A key aspect of ProM involves a delay between the creation of an intention and performance of the action (Foster, McDaniel, Repovs, & Hershey, 2009).

Tests of ProM are generally either time-based (TB) or event-based (EB). TB tasks require a participant to perform a specified behavior at a designated time, requiring participants to monitor the passage of time. Thus, TB tasks rely on an internal cue based on time perception and monitoring, processes believed to be dependent on the frontal lobes (Harris & Wilkins, 1982; McFarland & Glisky, 2009). EB tasks require a participant to perform a specified behavior in response to a specific event or external cue (Einstein & McDaniel, 1990; Einstein, McDaniel, Richardson, Guynn, & Cunfer, 1995; Henry, MacLeod, Phillips, & Crawford, 2004). Since EB tasks rely on an external cue, they are thought to require less self-initiated monitoring by the participant (McFarland & Glisky, 2009) and may be less sensitive to frontal lobe dysfunction relative to TB ProM tasks (Pirogovsky et al., 2011; Raskin et al., 2011).

The frontal lobes, specifically the prefrontal cortex, have been identified as a primary brain region essential to ProM. Research suggests the rostral (Burgess, Scott, & Frith, 2003; Burgess, Quayle, & Frith, 2001) and anterior (Reynolds, West, & Braver, 2009; Simons, Scholvinck, Gilbert, Frith, & Burgess, 2006) prefrontal cortices play a role in performance on tests of ProM. ProM tasks also may depend on the right dorsolateral, right ventromedial, and left dorsomedial prefrontal cortices (Umeda, Kurosaki, Terasawa, Kato, & Miyahara, 2011).
Research conducted with patient populations known to have frontal lobe dysfunction support the role of the frontal lobe in performing ProM tasks. As discussed below, ProM abilities have been shown to decline in individuals with frontal lobe lesions, healthy older adults, Parkinson’s disease (PD) patients, and persons infected with the human immunodeficiency virus (HIV). Patients with frontal lobe lesions show deficits in tests of ProM. Investigations into individuals with frontal lobe lesions suggests ProM deficits in these individuals may result from deficits in planning, organization, and initiation associated with frontal lobe dysfunction (Shimamura, Janowsky, & Squire, 1991) as well as an inability to retrieve the proper intention after a delayed period (Shallice & Burgess, 1991). Impairment on time- (Volle, Gonen-Yaacovi, Costello Ade, Gilbert, & Burgess, 2011) and event-based (Cheng, Wang, Xi, Niu, & Fu, 2008) ProM tasks have been documented in patients with prefrontal cortex lesions, suggesting lesions in different areas of the prefrontal cortex may cause different deficits in ProM abilities. Declining frontal lobe functioning has been associated with healthy aging (Fuster, 1997). Investigations into this population’s abilities on tests of ProM have resulted in mixed findings; however, studies generally have demonstrated deficits in TB tasks but not in EB tasks, likely due to dependence of TB tasks on the frontal lobes (Harris & Wilkins, 1982; McDaniel, Einstein, Stout, & Morgan, 2003; McFarland & Glisky, 2009). Frontostriatal circuit disruptions have been documented in PD (Zgaljardic, Borod, Foldi, & Mattis, 2003) and HIV infection (Kuper et al., 2011). PD patients show impairments on both TB and EB tests of ProM (Foster et al., 2009; Pirogovsky et al., 2011; Raskin et al., 2011), with poorer performance on TB tasks compared to EB tasks, perhaps suggesting that TB tasks are more dependent on the integrity of the frontal lobes than EB tasks (Pirogovsky et al., 2011; Raskin et al., 2011). HIV patients also demonstrate deficits in tasks of ProM (Carey et al., 2006; Woods et al., 2008; Zogg et al., 2011), likely due to disruption of frontostriatal circuits which may be similar to those documented in HD. As described above, a variety of patient populations who experience frontal lobe dysfunction manifest deficits in tasks of ProM. One population that has not been investigated in terms of ProM abilities is HD. Since HD is associated with frontal lobe impairment and cognitive deficits associated with frontal lobe dysfunction (described in detail below), HD patients are likely to demonstrate impairments on tasks of ProM.
**HUNTINGTON’S DISEASE**

HD is a progressive autosomal dominant inherited neurodegenerative disorder. The disease is caused by expanded cytosine-adenine-guanine (CAG) repeats on chromosome 4 of the huntingtin gene (Huntington’s Disease Collaborative Research Group, 1993). Individuals with CAG lengths greater than 35 repeats are gene carriers and those with greater than 39 CAG repeats will develop the disease (Huntington’s Disease Collaborative Research Group, 1993; Lee et al., 2012). The average age of onset of HD is approximately 35-50 years of age (Farrer & Conneally, 1985; Huntington’s Disease Collaborative Research Group, 1993); longer CAG repeats have been associated with an earlier age of onset (Duyao et al., 1993).

HD is a movement disorder characterized by gradually worsening symptoms. Motor disturbances include chorea, rigidity, hyperkinesia, and oculomotor problems (Berardelli et al., 1999; Rosenblatt, 2007). A clinical diagnosis of HD is based upon the presence of an expansion of CAG repeats and clinical observations of choreic movements (Huntington Study Group, 1996). Research suggests cognitive and psychiatric symptoms are manifest in individuals prior to the onset of motor symptoms, and thus may precede a clinical diagnosis of HD (Beglinger, Duff, et al., 2010; Pirogovsky et al., 2009).

Studies evaluating the neuropathology of HD report impairments consistent with a frontal lobe profile (Beglinger et al., 2005; Snowden, Craufurd, Griffiths, Thompson, & Neary, 2001). Reductions in frontal lobe volume have been documented in moderately to severely affected HD patients (Aylward et al., 1998). Pathology of the striatum—the caudate nucleus and putamen—is the primary pathologic characteristic in this disease (Aylward et al., 1998; Peinemann et al., 2005; Vonsattel, Keller, & Cortez Ramirez, 2011). The presence of striatal atrophy in HD patients (Beglinger, Duff, et al., 2010; Eidelberg & Surmeier, 2011; Reiner et al., 1988; Vonsattel & DiFiglia, 1998; Vonsattel et al., 2011) suggests this disease ultimately leads to disruptions of the frontostriatal circuit (Alexander, Crutcher, & DeLong, 1990; Aylward et al., 1996; De la Monte, Vonsattel, & Richardson, 1988; Fine et al., 2008; Harris et al., 1992).

The frontostriatal circuit is composed of the anterior cingulate cortex, caudate nucleus, dorsolateral prefrontal cortex, medial thalamus, posterior cingulate cortex, and right dentate nucleus (Takare, Minshew, Luna, & Sweeney, 2007). It is comprised of multiple circuits, including motor, oculomotor, dorsolateral prefrontal, lateral orbitofrontal, medial
orbitofrontal, and anterior cingulate circuits (Alexander, & Crutcher, 1990; Alexander, DeLong, & Strick, 1986). The dorsolateral prefrontal circuit has been linked to the regulation of executive functions, attention, and decision-making behaviors (Zgaljardic et al., 2003), all of which are impaired in HD patients.

Frontostriatal circuit disruptions are believed to underlie cognitive impairments in HD, including deficits in executive functioning, working memory, planning, and attention (Beglinger, Duff et al., 2010; Bonelli & Cummings, 2007; Joel, 2001; Lemiere, Decruyenaere, Evers-Kiebooms, Vandenbussche, & Dom, 2004; Peinemann et al., 2005; Thiruvady et al., 2007). Aylward and colleagues (1998) documented the similarity between the cognitive symptoms associated with HD and those of individuals with frontal lobe damage, including difficulty with memory and concentration in both patient populations. Investigations into frontostriatal functions suggest the importance of these circuits to the processes of memory encoding and retrieval (Foster et al., 2009; Kliegel, McDaniel, & Einstein, 2000) and cognitive and behavioral control (Diamond, 1988).

Psychiatric symptoms reported in HD patients include depression, mania, obsessive-compulsive disorder, apathy, irritability, and delirium (Rosenblatt, 2007). Cognitive deficiencies documented in patients with HD tend to be on frontal-lobe dependent tasks, including memory, attention, and executive functioning. HD patients demonstrate deficits in source (Pirogovsky et al., 2007) and temporal order memory (Nicoll et al., in press), likely due to reliance of these forms of memory on the frontal lobes (Janowsky, Shimamura, & Squire, 1989).

As discussed above, pathology of the frontal lobes and frontostriatal circuit disruptions documented in HD likely lead to the cognitive dysfunction evidenced in this disease. Performance on tests of ProM have been demonstrated to be dependent on the integrity of the frontal lobes, thus HD patients would be expected to demonstrate impairments on tasks tapping this type of memory.

**Instrumental Activities of Daily Living**

Instrumental Activities of daily living (iADLs) are daily tasks including housekeeping, managing medication and finances, keeping appointments, and preparing meals (Ahn et al., 2009; Bangen et al., 2010; Cotrell, Wild, & Bader, 2006; Lawton & Brody,
Research suggests the ability to perform iADLs is dependent on the integrity of the frontal lobes (Bottari, Gosselin, Guillemette, Lamoureux, & Ptito, 2011; Goel, Grafman, Tajik, Gana, & Danto, 1997).

Research studies have identified a correlation between performance on ProM tasks and ability to perform iADLs. Woods, Weinborn, Veinoweth, Rooney, and Bucks (2011) demonstrated an association between decreased functioning on EB tasks of prospective memory and impairments with iADLs. Deficits in executive functioning have been shown to relate to decreased iADL abilities in terms of shopping, while problems with episodic memory may lead to difficulties organizing medication routines (Koehler et al., 2011).

Research suggests HD patients suffer from declining abilities to perform iADLs as the disease progresses (Dawson, Kristjanson, Toye, & Flett, 2004). iADL deficits in the early stages of HD have been suggested to indicate that these activities may rely on attention regulation processes as well as psychomotor processing speed (Rothlind, Bylsma, Peyser, Folstein, & Brandt, 1993). Hamilton et al. (2003) suggests there is a correlation between executive functioning abilities of HD patients, level of apathy, and ability to perform iADLs. The motor problems associated with the disease also may be responsible for impairments in iADL abilities (Beglinger, O’Rourke, et al., 2010), as many of these tasks require fine motor skills. In addition to HD, decreased iADL abilities have been shown in many patient populations, including healthy aging (Hill, Mansour, Valentijn, Jolles, & van Boxtel, 2010), individuals with mild cognitive impairment (Jefferson et al., 2008; Teng, Becker, Woo, Cummings, & Lu, 2010), and PD (Pirogovsky, Woods, Filoteo, & Gilbert, 2012; Shulman et al., 2006).

A recent study conducted by Pirogovsky et al. (2012) investigated ProM deficits in PD patients and resulting effects on iADL abilities. PD patients demonstrated deficits on performance-based and self-report measures of ProM and iADLs compared to healthy older adults (Pirogovsky et al., 2012). Performance-based ProM performance was correlated with performance-based iADL performance; however, no correlation was found between performance-based ProM and the self-report iADL measure (Pirogovsky et al., 2012). Given that HD and PD affect the frontostriatal circuit, it was considered likely that individuals with HD also would demonstrate similar ProM deficits to those of individuals with PD.
SUMMARY

ProM, a form of memory for future events, has been shown to depend on the integrity of the frontal lobes and particularly the prefrontal cortex. Due to frontostriatal circuit disruptions associated with HD and the resulting cognitive deficits on frontal lobe dependent tasks, impairments of ProM would be expected in this population. However, no study to date has investigated the effect of HD on ProM. The current study examined ProM abilities in HD using the Memory for Intentions Screening Test (MIST), a standardized test of ProM (Woods et al., 2008). The MIST is composed of TB and EB tasks as well as one naturalistic test of ProM, which allowed for an examination of ProM abilities in HD.

A correlation between performance on ProM tasks and ability to perform iADLs could have implications for understanding functional independence in this patient population. Research suggests HD patients suffer from a decline in the ability to perform iADLs as the disease progresses; therefore, the current study investigated correlations between self-report and performance-based measures of ProM and iADLs. Examining ProM in HD patients will provide new insight into a frontal lobe dependent memory process that may affect iADL dependence. The findings may lead to the use of interventions to teach compensatory cognitive techniques for ProM impairment in order to improve everyday functioning and increase quality of life for HD patients.
CHAPTER 2

METHODS

PARTICIPANTS

Demographic information for study participants is provided in Table 1. Symptomatic HD ($n = 19$) patients with mild-moderate severity as defined by the Unified Huntington’s Disease Rating Scale (UHDRS; Huntington Study Group, 1996) were recruited from the HD Clinical Research Program at the University of California, San Diego. The UHDRS was administered by a senior staff neurologist. The mean total motor score for the HD patients was 26.2 ($SE = 2.7$) out of a possible 124. Based on the UHDRS motor exam, the neurologist assigned a diagnostic confidence rating representing the evaluator’s confidence that the presence of motor abnormalities were a manifestation of HD. Ratings are defined as: 0 = normal (no abnormalities), 1 = non-specific motor abnormalities (<50% confidence that the participant has sufficient motor abnormalities to warrant a diagnosis of HD), 2 = motor abnormalities that may be signs of HD (50–89% confidence), 3 = motor signs that are likely signs of HD (90–98% confidence), 4 = motor abnormalities that are unequivocal signs of HD (>99% confidence). All HD patients received a score of 4; therefore, they met the criteria for a diagnosis of manifest HD. Symptomatic HD patients receive annual neuropsychological testing as part of their participation in the HD Clinical Research Program. Age-matched control ($n = 20$) participants were recruited from San Diego County.

HD participants and controls were matched in terms of age, gender, education, and ethnicity. Controls had no family history of HD. Exclusion criteria for all participants in the study included a history of neurological disorders outside of HD for HD participants, a formal diagnosis of a psychiatric disorder such as major depressive disorder, or a history of traumatic brain injury. All participants were screened for dementia using the Dementia Rating Scale (DRS; Mattis, 1976).

Participants were compensated $10 per hour for participation in this study. All participants gave informed written consent for participation approved by the Institutional Review Boards of San Diego State University and University of California, San Diego.
Table 1. Demographic Characteristics for HD and Control Participants

<table>
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<th>HD (n = 19)</th>
<th>Control (n = 20)</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>59.05 (2.9)</td>
<td>60.9 (3.1)</td>
</tr>
<tr>
<td>Education (years)</td>
<td>15.4 (0.7)</td>
<td>16.5 (0.6)</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>8/11</td>
<td>8/12</td>
</tr>
<tr>
<td>Beck Depression Inventory</td>
<td>12.3 (2.8)</td>
<td>5.3 (1.5)</td>
</tr>
<tr>
<td>Geriatric Depression Scale</td>
<td>1.4 (1.0)</td>
<td>3.1 (.6)</td>
</tr>
<tr>
<td>Dementia Rating Scale</td>
<td>134.3 (1.9)*</td>
<td>141.4 (0.5)*</td>
</tr>
<tr>
<td>CAG repeats</td>
<td>41.6 (0.7)</td>
<td></td>
</tr>
<tr>
<td>Age of Onset</td>
<td>50.4 (2.8)</td>
<td></td>
</tr>
<tr>
<td>UHDRS Total Motor Score</td>
<td>26.2 (2.7)</td>
<td></td>
</tr>
<tr>
<td>UHDRS Functional Assessment</td>
<td>19.9 (0.6)</td>
<td></td>
</tr>
<tr>
<td>UHDRS Independence Scale</td>
<td>75.8 (2.3)</td>
<td></td>
</tr>
<tr>
<td>UHDRS Total Functional Capacity Score</td>
<td>9.5 (0.8)</td>
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Note. Data represent means and standard errors. * Analyses revealed a significant between-groups difference on the DRS $F(1, 36) = 13.48, p < .01.$

MEASURES AND ANALYSES

Each participant individually completed testing during one session. As detailed below, the test battery included measures of performance-based and self-report ProM, performance-based and self-report iADLs, mood and anxiety, and neuropsychological function. The entire testing battery took approximately 2.5 hours for participants to complete. The tasks were presented in the same order to all participants. Of the 19 HD participants, one participant did not complete the Wisconsin Card Sorting Test, one participant did not complete the Advanced Finances Test, and two participants did not complete the self-report questionnaires. Of the 20 control participants, one participant did not complete the Wisconsin Card Sorting Test.
Performance-Based Prospective Memory (ProM)

The Memory for Intentions Screening Test (MIST) was administered as a standardized measure of ProM (Raskin, 2009). The MIST is a 30-minute test consisting of eight ProM tasks and an ongoing word-search puzzle serving as a distractor task. A 24-hour naturalistic task was administered in which participants were instructed to call the test administrator in 24 hours and report the number of hours they slept the night of the testing session. This task served as an assessment of everyday ProM abilities (Raskin, 2009).

Participants were instructed to remove their watch if they were wearing one, as a clock was situated on the wall behind the participant. The placement of the clock required the participant to turn around to check the time during testing. Participants were instructed to complete a word search puzzle by finding words hidden vertically, horizontally, or diagonally and to work as quickly as possible.

The MIST consisted of eight trials including four time-based (TB) tests and four event-based (EB) tests equally divided by delay interval (2-minutes or 15-minutes) and response manner (verbal or physical; Raskin, 2009). The test consisted of verbal instructions, for example, “In 15 minutes, tell me it is time to take a break” (TB test) and “When I show you a red pen, sign your name on your paper” (EB test).

The test was administered and scored as defined by Raskin (2009). Participants could earn a maximum of two points per trial—one point for a correct response and one point for the correct time or event cue. Responses with a time cue were scored as correct if the response was made within one minute before or after the actual cue time for a two-minute delay trial or two minutes before or after the actual cue time for a 15-minute delay trial. Responses with an event cue were scored as correct if the response was made to the correct event cue. One point was assigned for the trial if the participant gave a correct response to an incorrect cue or an incorrect response to a correct cue. Zero points were assigned for the trial if the participant failed to make a response or made an incorrect response to an incorrect cue.

Error types were recorded for all errors committed. A prospective memory or no response error (PM) was committed if the participant did not recognize the cue or the appropriate time at which a response was due. A task substitution error (TS) was committed if a participant provided an incorrect response to a cue. A loss of content error (LC) occurred if the participant recognized the cue or the appropriate time the response was due, but did not
recall the correct response. A loss of time error (LT) was committed when a correct response was performed at an incorrect time.

Detailed scoring guidelines and a scoring rubric (Raskin, 2009) allowed for a MIST summary score ranging from 0 to 48 points. Immediately following the MIST trials, participants completed a retrospective recognition questionnaire to assess recognition memory for the content of the trials. One question was allotted for each trial and each question was worth one point, for a total of eight points. Participants’ MIST performance was compared to their recognition responses to determine their retrieval index scores. Incorrect trials on the MIST that were correctly identified during recognition were given one point on the retrieval index. Incorrect trials on the MIST that were incorrectly identified during recognition were given zero points on the retrieval index. Correct trials on the MIST that were incorrectly identified during recognition were given negative one point on the retrieval index. Correct trials on the MIST that were correctly identified during recognition were given one point on the retrieval index. The total retrieval index score ranged from negative eight points to eight points.

**Self-Report Memory**

Participants completed the Prospective and Retrospective Memory Questionnaire and the Memory Functioning Questionnaire.

**Prospective and Retrospective Memory**

The Prospective and Retrospective Memory Questionnaire (PRMQ) was administered as a self-report measure of prospective and retrospective memory abilities (Smith, Della Sala, Logie, & Maylor, 2000). The 16-item questionnaire consisted of eight items pertaining to prospective memory and eight items pertaining to retrospective memory. Examples of items include, “Do you decide to do something in a few minutes time and then forget to do it?” and “Do you fail to recall things that have happened to you in the last few days?” The prospective memory items were equally divided by cue type (self-cued or environmentally-cued; Smith et al., 2000). The current study focused on the prospective memory self-cued and environmentally-cued scales for its analyses. Items were rated on a 5-point scale from 1 (never) to 5 (very often).
Responses were scored in terms of frequency of forgetting. The PRMQ was administered and scored as defined by Smith et al. (2000). All scores are reported as raw total scores, with higher scores on frequency indicating increased memory problems.

**METAMEMORY**

The Memory Functioning Questionnaire (MFQ) was administered as a self-report measure to evaluate perceived ability to remember information (American Psychological Association, 1990; Gilewski & Zelinski, 1988). The 63-item questionnaire covered general frequency of forgetting, seriousness of forgetting, retrospective functioning, and mnemonics usage. The current study focused on the general frequency of forgetting scale for its analyses. Examples of the questions include, “How would you rate your memory in terms of the kinds of problems that you have?” and “How well do you remember things that occurred last month?” The questionnaire was scored and administered according to Gilewski and Zelinski (1988). Responses were scored on a scale from 1 (major problems) to 7 (no problems). All scores are reported as raw scores, with lower scores indicating poorer memory functioning.

**Performance-Based iADL**

Participants completed the Advanced Finances Test and the Medication Management Ability Assessment.

**MANAGING FINANCES**

The Advanced Finances Test was administered as a performance-based measure of participants’ ability to manage finances (Heaton et al., 2004). Participants were asked to balance a checkbook including paying three bills, depositing one check, and keeping track of their checkbook balance. Participants were informed that if they did not have enough money in their account to pay their entire credit card bill, they were to pay as much of the bill as they could while leaving exactly $100 in their checking account. The assessment was administered and scored according to Heaton et al. (2004). All scores are reported as raw total scores, with lower scores indicating decreased financial management abilities.

**MANAGING MEDICATION**

The Medication Management Ability Assessment (MMAA) was administered as a performance-based measure of the ability to manage a medication regimen (Patterson et al.,
The MMAA is a role-play test in which the investigator played the medication provider and the participant played the patient, simulating a medication management program. Participants were informed about four medications, including the number of pills to take at each dose, the number of doses to take each day, and instructions on taking the medication on an empty stomach or with a meal. Following a 45-minute delay, participants were instructed to describe a typical day, including when and how many of each type of medication they would take. Participants were instructed to report what time they would wake up, the number and type of pills they would take when they wake up, when they would have breakfast, the number and type of pills they would take at breakfast, and so on throughout an entire day. Controls were instructed to hand the investigator the number of pills they would take at each time throughout the day, while the procedure was modified for HD participants to tell the investigator the number of pills they would take at each time throughout the day, to limit the effects of movement problems on task performance. The assessment was administered and scored according to Patterson et al. (2002). All scores are reported as raw total scores, with lower scores indicating decreased medication management abilities.

**Self-Report iADL**

Participants completed the iADL questionnaire and the Mediation Management Efficacy Scale.

**Instrumental Activities of Daily Living (iADLs).**

The iADL questionnaire was administered as a self-report measure of perceived ability to perform daily tasks. A modified version of the Lawton and Brody (1969) iADL scale was used to assess reported iADL abilities (Heaton et al., 2004). The 16-item questionnaire covered degree of independence in the areas of housekeeping, managing finances, buying groceries, cooking, planning social activities, understanding reading materials and television, transportation, using the telephone, home repairs, bathing, dressing, shopping, laundry, taking and keeping track of medication, child care, and work.

Responses were scored twice for each question—once for current ability level and once for highest ability level. The total score was calculated based on the number of activities
in which the participant currently needs assistance, ranging from minimal assistance (a score of zero to one depending on the question) to complete assistance (a score of two or three depending on the question; Heaton et al., 2004). For example, for the item on housekeeping, participants chose a response ranging from “I maintain my house/apartment by myself or only need occasional help for larger jobs” to “I need help with all housekeeping tasks.” The highest possible score on this test coincided with the response that the individual “is fully able to do each of these activities but chooses not to do so,” however, this response did not provide information on how well the participant was able to perform the task independently, thus it was given a score of zero. All scores are reported as difference scores, subtracting the current ability from the best ability for each question, with lower scores indicating decreased abilities to perform iADLs.

**MANAGING MEDICATION**

The Mediation Management Efficacy Scale (MMES), part of the Beliefs Related to Medications Adherence (BERMA) questionnaire, was administered as a self-report measure of perceived medication management abilities (McDonald-Miszczak, Maris, Fitzgibbon, & Ritchie, 2004). The 20-item scale included items such as “I am much worse at remembering new medication information than I used to be” and “I am good at remembering the times to take my medications.” Responses were scored on a scale from 1 (strongly disagree) to 5 (strongly agree). All scores are reported as raw scores, with lower scores indicating poorer medication management abilities.

**Standardized Neuropsychological Tests**

Participants completed the Color-Word Interference Test and the Wisconsin Card Sorting Test.

**COLOR-WORD INTERFERENCE TEST**

The Color-Word Interference Test, part of the Delis Kaplan Executive Function System (D-KEFS), was administered as a test of executive functioning (Delis, Kaplan, & Kramer, 2001). The test is composed of four conditions: (1) color naming, in which participants were instructed to read aloud the color of red, blue, or green blocks, (2) word reading, in which participants were instructed to read aloud the word “red,” “blue,” or
“green,” (3) inhibition, in which participants were instructed to read aloud the color of ink the words “red,” “blue,” or “green” were written in and not to read the word itself, and (4) inhibition and switching in which participants were instructed to read aloud the color of ink the words “red,” “blue,” or “green” were written in and not to read the word itself, however if a word was inside of a box, they were instructed to read the word and not the color of the ink. The time each participant took to complete each condition was recorded in addition to the number of uncorrected and corrected errors that were made. All scores are reported as raw time scores to complete each condition, with lower scores indicating increased speed of completion.

**WISCONSIN CARD SORTING TEST**

The Wisconsin Card Sorting Test (WCST) was administered as a second test of executive functioning ability. The WCST taps the integrity of frontal lobe functioning by requiring participants to determine the principle of sorting a deck of cards (Dehaene & Changeux, 1991; Grant & Berg, 1948; Heaton, Chelune, Talley, Kay, & Curtiss, 1993). The test was administered in its computerized Version 4 format (Heaton & Psychological Assessment Resources, 2003) in which participants must match stimulus cards to the target cards by inferring the sorting rule from the response of “correct” or “incorrect” for each attempt given by the computer (Amos, 2000; Dehaene & Changeux, 1991; Grant & Berg, 1948; Heaton et al., 1993). The test was scored as defined by the WCST manual (Heaton et al., 1993). Total scores, total errors, and perseverative responses are reported for the WCST. All scores are reported as raw scores, with lower scores indicating poorer frontal lobe functioning.

**Mood and Anxiety**

Due to the occurrence of depression, mood fluctuations, and anxiety in HD patients (Roos, 2010; Rosenblatt, 2007) and the negative impact of these symptoms on performance on neuropsychological tests, a self-report measure of depressive, mood, and anxiety symptoms was given to all study participants. Participants younger than 65 years of age were administered the Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996); participants 65 years and older were administered the Geriatric Depression Scale (GDS) in its short form (Yesavage et al., 1983). The BDI-II covered symptoms of depression, changing
mood, and anxiety, with items on sadness, pessimism, past failure, loss of pleasure, feelings involving guilt and punishment, self-dislike, self-criticalness, suicidal thoughts, crying, agitation, loss of interest, indecisiveness, worthlessness, loss of energy, changes in sleep, irritability, changes in appetite, difficulty concentrating, fatigue, and loss of interest in sex (Beck et al., 1996). For example, for the item on sadness, participants chose from responses ranging from “I do not feel sad” to “I am so sad or unhappy that I can’t stand it.” The GDS covered depressive feelings, mood disturbances, and anxiety, with items on life satisfaction, activities and interests, boredom, helplessness, and worthlessness (Yesavage et al., 1983). For example, participants answered questions such as “Are you in good spirits most of the time?” and “Do you think that most people are better off than you are?”

The BDI-II was administered and scored as defined by Beck et al. (1996). The GDS was administered and scored as defined by Yesavage et al. (1983). All scores are reported as raw total scores with higher scores indicating increased mood fluctuations and feelings of anxiety and depression.

**Statistical Analysis**

Data were checked for normality using the Shapiro-Wilk test of normality \( (p < .05) \) and appropriate non-parametric statistics were used for non-normally distributed data. Mann-Whitney \( U \) tests were used to examine group differences on the following non-normal measures: MIST, MMAA, Advanced Finances Test, PRMQ, MFQ, MMES, iADL questionnaire, WCST, and D-KEFS Color-Word Interference Test. Spearman rank correlational analyses were used to examine the relationships between variables of interest. Cohen’s d effect size estimates were examined for dichotomous variables. The critical alpha level in the current study was set at .05 and trend level findings \( (p < .08) \) are reported.
CHAPTER 3

PREDICTED OUTCOMES AND HYPOTHESIS

AIM 1: EXAMINE THE NATURE AND EXTENT OF PROM IMPAIRMENT IN HD

Rationale:

- This study provides the first investigation of ProM impairment in HD through the use of a standardized measure of ProM.

Hypotheses:

1. HD participants were hypothesized to demonstrate deficits on a performance-based test of ProM. HD patients were hypothesized to show a lower MIST summary score and commit more errors on the MIST compared to controls.

2. Available literature on ProM suggests TB tasks are more sensitive to frontal lobe dysfunction than EB tasks. Since HD results in frontostriatal circuit disruptions, it was hypothesized that HD patients would show greater impairment on performance-based tests of ProM that were TB relative to EB.

3. Self-report measures are sometimes considered a less accurate assessment of actual abilities than are performance-based measures. It was hypothesized that a performance-based measure of ProM would correlate poorly with self-report measures of ProM (PRMQ and MFQ) as participants were expected to overestimate their ProM abilities in a self-report measure.

AIM 2: INVESTIGATE THE ASSOCIATION BETWEEN PROM AND EVERYDAY FUNCTIONING IN HD

Rationale:

- Research suggests ProM performance is correlated with iADL abilities. The current study investigated the relationship between performance-based and self-report measures of ProM and performance-based and self-report measures of iADLs.

Hypotheses:

1. HD participants were hypothesized to demonstrate deficits on performance-based tests of iADLs (Advanced Finances Test and MMAA). HD participants were hypothesized to self-report greater difficulties with iADLs (iADL questionnaire and MMES).

2. It was hypothesized that performance-based measures of iADLs would correlate poorly with self-report measures of iADLs as participants were expected to overestimate their iADL abilities in a self-report measure. HD participants were
expected to overestimate their iADL abilities, but still self-report more iADL problems compared to controls.

3. It was hypothesized that a performance-based measure of ProM would be correlated with performance-based measures of iADL.

4. It was hypothesized that self-report measures of ProM would be correlated with self-report iADL measures, as participants were expected to overestimate both their ProM and iADL abilities.

**AIM 3: INVESTIGATE THE RELATIONSHIP BETWEEN PROM AND NEUROPSYCHOLOGICAL FUNCTION**

Rationale:

- Research suggests ProM performance is correlated with neuropsychological performance on tests of executive functioning. The current study investigated the relationship between performance-based and self-report measures of ProM and standardized measures of neuropsychological functioning.

Hypotheses:

1. HD participants were hypothesized to demonstrate deficits on the D-KEFS Color-Word Interference Test and the WCST. HD participants were hypothesized to exhibit perseverative behavior and commit more errors on the WCST compared to controls.

2. It was hypothesized that a performance-based ProM measure would be correlated with neuropsychological measures.

3. It was hypothesized that self-report measures of ProM would correlate poorly with neuropsychological measures.

4. with neuropsychological measures.
CHAPTER 4

RESULTS

PROSPECTIVE MEMORY

As shown in Table 2 and Figure 1, HD participants demonstrated significantly lower scores on the MIST summary score compared to controls \((p < .001)\). In addition, as shown in Figures 2 and 3, HD participants demonstrated significantly lower scores on the TB trial \((p < .001)\) and 24-hour task \((p < .01)\) compared to controls. HD participants exhibited trend level lower scores on the EB trial \((p = .075)\) compared to controls; however, performance was not significantly different between groups \((p > .05)\; \text{see Table 2}\). HD participants committed significantly more errors on the MIST \((M = 3.68, SE = .33)\) compared to controls \((M = 2.15, SE = .32; p < .01)\). Analyses revealed significant differences between HD and control participants in the number of prospective memory errors \((M = 1.89, SE = .41\) and \(M = .45, SE = .17, \text{respectively}; p < .001)\) and loss of content errors committed \((M = .95, SE = .20\) and \(M = .60, SE = .15, \text{respectively}; p < .05)\). However, there were no significant differences between groups in the number of task substitution errors and loss of time errors committed \((p > .05)\).

Analyses revealed no significant differences between HD and control participants on the PRMQ scales or the MFQ \((p > .05)\; \text{see Table 2}\). There were no significant correlations between any of the MIST variables and the PRMQ scales in the HD group \((p > .05)\). Analyses revealed a significant correlation between the MIST EB trial and the PRMQ environmentally-cued scale in the control group \((\rho = -.889, p < .05)\). There were no significant correlations between any of the MIST variables and the MFQ in the HD group \((p > .05)\). Analyses revealed a significant correlation between the MIST EB trial and the MFQ in the control group \((\rho = .889, p < .05)\). In summary, the HD participants demonstrate impairment on the performance-based test of ProM compared to controls; however, the self-report measures of ProM did not differ between the groups. Therefore, it appears the HD participants overestimated their ProM abilities in the self-report measures.
### Table 2. Performance on Prospective Memory Measures for HD and Control Participants

<table>
<thead>
<tr>
<th>Prospective memory</th>
<th>HD (n = 19)</th>
<th>Control (n = 20)</th>
<th>p</th>
<th>d</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIST Summary Score</td>
<td>30.5 (2.0)</td>
<td>39.8 (1.2)</td>
<td>&lt;.001</td>
<td>1.24</td>
</tr>
<tr>
<td>MIST Time-based Scale</td>
<td>4.3 (0.5)</td>
<td>6.5 (0.3)</td>
<td>&lt;.001</td>
<td>1.33</td>
</tr>
<tr>
<td>MIST Event-based Scale</td>
<td>5.8 (0.4)</td>
<td>6.8 (0.3)</td>
<td>.075</td>
<td>0.64</td>
</tr>
<tr>
<td>MIST 24-hour Task</td>
<td>0.3 (0.2)</td>
<td>1.1 (0.2)</td>
<td>&lt;.01</td>
<td>0.97</td>
</tr>
<tr>
<td>PRMQ Self-cued Scale</td>
<td>10.8 (1.1)^a</td>
<td>10.0 (0.4)</td>
<td>.91</td>
<td>0.36</td>
</tr>
<tr>
<td>PRMQ Environmentally-cued Scale</td>
<td>10.3 (0.9)^a</td>
<td>9.3 (0.5)</td>
<td>.84</td>
<td>0.23</td>
</tr>
<tr>
<td>MFQ Frequency of Forgetting Scale</td>
<td>4.5 (0.3)^a</td>
<td>5.3 (0.2)</td>
<td>.28</td>
<td>0.74</td>
</tr>
</tbody>
</table>

*Note.* Data represent means and standard errors. MIST = Memory for Intentions Screening Test; PRMQ = Prospective and Retrospective Memory Questionnaire; MFQ = Memory Functioning Questionnaire; *d* = Cohen’s *d* effect size estimate.

^a 17 HD participants completed the PRMQ and MFQ.

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**Figure 1.** Total MIST summary score for HD and control participants.
As shown in Table 3, analyses revealed significant differences between HD and control participants on the Advanced Finances Test ($p < .01$). HD participants performed significantly worse on the Advanced Finances Test compared to controls. There were no significant differences between groups on the MMAA ($p > .05$). Analyses revealed
significant differences between HD and control participants on the iADL questionnaire ($p < .001$; see Table 3). HD participants self-reported significantly more difficulty with the items on the iADL questionnaire compared to controls. There were no significant differences between groups on the MMES ($p > .05$). There were no significant correlations between the performance-based measures of iADLs and self-report measures of iADLs in the HD group ($p > .05$). Analyses revealed a significant correlation between the MMAA and the MMES in the control group ($\rho = .618, p < .01$). The MMAA did not significantly correlate with the iADL questionnaire in the control group ($\rho = .256, p > .05$). The Advanced Finances Test did not significantly correlate with the self-report measures of iADLs in the control group ($p > .05$).

### Table 3. Performance on iADL Measures for HD and Control Participants

<table>
<thead>
<tr>
<th>iADLs</th>
<th>HD ($n = 19$)</th>
<th>Control ($n = 20$)</th>
<th>$p$</th>
<th>$d$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Performance-based Measures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMAA</td>
<td>30.4 (1.0)$^a$</td>
<td>31.1 (0.7)</td>
<td>.92</td>
<td>0.18</td>
</tr>
<tr>
<td>Advanced Finances Test</td>
<td>9.2 (1.0)</td>
<td>12.9 (0.5)</td>
<td>&lt;.01</td>
<td>1.04</td>
</tr>
<tr>
<td>Self-report Measures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>iADL Questionnaire</td>
<td>-6.4 (1.4)$^b$</td>
<td>-0.5 (0.5)</td>
<td>&lt;.001</td>
<td>1.53</td>
</tr>
<tr>
<td>MMES</td>
<td>75.5 (3.9)$^b$</td>
<td>83.6 (3.0)</td>
<td>.09</td>
<td>0.54</td>
</tr>
</tbody>
</table>

Note. Data represent means and standard errors. MMAA = Medication Management Ability Assessment; iADL = modified version of the Lawton & Brody Instrumental Activities of Daily Living Scale; MMES = Medication Management Efficacy Scale; $d =$ Cohen’s d effect size estimate.

$^a$ 18 HD participants completed the MMAA.

$^b$ 17 HD participants completed the iADL questionnaire and MMES.

### Relationship Between Prospective Memory and iADLs

The MIST summary score was not significantly correlated with the Advanced Finances Test ($\rho = .125, p = .61$) or the MMAA ($\rho = -.002, p = .99$) for the HD patients. Similarly, the MIST TB trial and EB trial were not significantly correlated with the Advanced Finances Test ($\rho = .175, p = .47$ and $\rho = .188, p = .44$, respectively) or the MMAA ($\rho = -.084, p = .74$ and $\rho = .325, p = .19$, respectively), for the HD patients. Analyses revealed a significant correlation between the MIST summary score and the Advanced Finances Test.
in the control group ($\rho = .482, p < .05$). However, the MIST summary score did not significantly correlate with the MMAA ($\rho = .098, p = .68$) for the control participants. The MIST TB trial and EB trial were not significantly correlated with the Advanced Finances Test ($\rho = .387, p = .09$ and $\rho = .370, p = .11$, respectively) or the MMAA ($\rho = -.054, p = .82$ and $\rho = .306, p = .19$, respectively) in the control group. Analyses revealed a significant correlation between the PRMQ self-cued scale and the iADL questionnaire in the HD group ($\rho = -.543, p < .05$). However, there were no significant correlations between the PRMQ scales and the MMES or between the MFQ and the self-report measures of iADLs in the HD group ($p > .05$). There were no significant correlations between the self-report measures of ProM and the self-report measures of iADLs in the control group ($p > .05$). In summary, the results indicate there is not a relationship between the performance-based measure of ProM and the performance-based measures of iADLs for the HD group in the present sample.

**Neuropsychological Functioning**

As shown in Table 4, HD participants demonstrated significantly lower scores on the WCST compared to controls ($p < .05$). In addition, HD participants demonstrated significantly lower scores on the inhibition scale of the D-KEFS Color-Word Interference Test ($p < .05$) compared to controls. However, there were no significant differences between groups on the inhibition contrast score of the D-KEFS Color-Word Interference Test ($p > .05$; see Table 4). HD participants committed significantly more total errors ($M = 32.11, SE \pm 2.70$) and perseverative errors on the WCST ($M = 18.44, SE \pm 2.51$) compared to controls ($M = 15.38, SE \pm 4.30; p < .001$ and $M = 13.44, SE \pm 3.23; p < .05$, respectively).

There were no significant correlations between any of the MIST variables and the neuropsychological measures in either group ($p > .05$). Additionally, there were no significant correlations between the self-report measures of ProM and the neuropsychological measures in either group ($p > .05$).
### Table 4. Performance on Neuropsychological Measures for HD and Control Participants

<table>
<thead>
<tr>
<th>Neuropsychological Functioning</th>
<th>HD (n = 19)</th>
<th>Control (n = 20)</th>
<th>p</th>
<th>d</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WCST</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Errors</td>
<td>32.11 (2.7)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>15.38 (4.3)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt; .001</td>
<td>1.23</td>
</tr>
<tr>
<td>Perseverative Errors</td>
<td>18.44 (2.5)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>13.44 (3.3)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt; .05</td>
<td>0.40</td>
</tr>
<tr>
<td><strong>D-KEFS Color-Word Interference Test</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhibition Scale</td>
<td>7.68 (1.0)</td>
<td>10.45 (0.7)</td>
<td>&lt; .05</td>
<td>0.71</td>
</tr>
<tr>
<td>Inhibition vs. Color Naming&lt;sup&gt;c&lt;/sup&gt;</td>
<td>11.74 (0.8)</td>
<td>11.00 (1.1)</td>
<td>= .35</td>
<td>0.21</td>
</tr>
</tbody>
</table>

*Note.* Data represent means and standard errors. WCST = Wisconsin Card Sorting Test; <sup>d</sup> = Cohen’s d effect size estimate.

<sup>a</sup> 18 HD participants completed the WCST.

<sup>b</sup> 19 control participants completed the WCST.

<sup>c</sup> D-KEFS primary contrast measure for inhibition vs. color naming.
CHAPTER 5

DISCUSSION

The objective of the current study was to conduct a preliminary examination of ProM abilities in HD patients and investigate the relationship between ProM and iADLs in this population. Research suggests a variety of patient populations who experience frontal lobe dysfunction demonstrate deficits in ProM (e.g., Pirogovsky et al., 2012; Raskin et al., 2011; Woods et al., 2008). Since HD is associated with frontal lobe related cognitive deficits (Aylward et al., 1998; Beglinger et al., 2005; Beglinger, Duff, et al., 2010; Bonelli & Cummings, 2007; Joel, 2001; Lemiere et al., 2004; Peinemann et al., 2005; Snowden et al., 2001; Thiruvady et al., 2007), it was hypothesized that HD patients would demonstrate impairments on a performance-based test of ProM (MIST). In support of the hypothesis, HD patients demonstrated significantly lower MIST summary scores compared to control participants and the effect size for group differences was large ($d = 1.24$). The findings provide the first data to indicate that HD is associated with impairment on a performance-based test of ProM. The current data also add to the existing literature on the relationship between frontal lobe dysfunction and ProM impairment.

Research on ProM suggests that TB tasks are self-cued and thus may be more sensitive to frontal lobe dysfunction than EB tasks, which are event-cued (Harris & Wilkins, 1982; McFarland & Glisky, 2009; Pirogovsky et al., 2012; Raskin et al., 2011). Therefore, it was hypothesized that HD patients would show greater impairment on the TB trials of the MIST than on the EB trials. The results of the present study are consistent with this hypothesis as HD patients demonstrated significantly lower scores on the TB trial (large effect size, $d = 1.33$), and trend level lower scores on the EB trial (medium effect size, $d = .64$) of the MIST compared to controls. The current study provides the first data to indicate that HD patients are impaired on a performance-based test of ProM. These findings are consistent with a recent study that found PD patients demonstrated significant impairment on the MIST summary score and TB trial and trend level lower scores on the EB trial compared
to controls (Pirogovsky et al., 2012) and provide further evidence to suggest TB tasks of ProM may be more sensitive to frontal lobe dysfunction than are EB tasks.

It was hypothesized that HD patients would commit more errors on the performance-based test of ProM compared to controls due to frontal lobe impairment and cognitive deficits associated with the disease (Aylward et al., 1998; Beglinger et al., 2005; Beglinger, Duff et al., 2010; Bonelli & Cummings, 2007; Joel, 2001; Lemiere et al., 2004; Peinemann et al., 2005; Snowden et al., 2001; Thiruvady et al., 2007). HD patients committed significantly more total errors (large effect size, $d = 1.06$) on the MIST compared to control participants. Of the error types recorded on the MIST, HD patients committed significantly more ProM errors compared to controls and the effect size for group differences was large ($d = 1.05$). In addition, HD patients committed significantly more loss of content errors (small effect size, $d = .46$) compared to controls. There were no significant differences between groups on the number of loss of time and task substitution errors committed. HD patients performed significantly worse on the 24-hour naturalistic test of ProM compared to control participants and the effect size for group differences was large ($d = .97$). This finding demonstrates the ProM deficits observed in the laboratory-based test of ProM also are observed in a more naturalistic ProM measure, and provides an indication that HD patients’ deficits on ProM may affect their ability to perform everyday tasks.

Participants were expected to overestimate their ProM abilities in self-report measures; therefore, it was hypothesized that the MIST would correlate poorly with self-report measures of ProM. The results indicate that for the HD patients, the MIST was not correlated with the self-report measures of ProM (PRMQ scales and MFQ). Within the control participants, however, the results indicate a negative relationship between the MIST EB trial and the PRMQ environmentally-cued scale and a positive relationship between the MIST EB trial and MFQ. Although the negative relationship between the MIST EB trial and the PRMQ environmentally-cued scale were not expected for the control participants, there is a possible explanation for this finding. The control participants appear to have provided an underestimation of their prospective and retrospective memory abilities on the PRMQ, as their self-report abilities on the PRMQ environmentally-cued scale are lower than their performance on the MIST EB trial would indicate. The positive relationship between the
MIST EB trial and the MFQ may indicate the control participants have provided an accurate estimation of their memory abilities on the MFQ.

Research suggests the ability to perform iADLs is dependent on the integrity of the frontal lobes (Bottari et al., 2011; Goel et al., 1997) and HD patients’ abilities to perform iADLs decline as the disease progresses (Dawson et al., 2004). It was hypothesized that HD patients would demonstrate deficits on performance-based tests of iADLs. In support of the hypothesis, HD patients demonstrated significant deficits on the Advanced Finances Test (large effect size, $d = 1.04$). The HD patients demonstrated lower scores on the MMAA; however, this between-group difference was not significant (small effect size, $d = .18$). The current findings suggest there are not differences between groups on the performance-based measure of medication management abilities in this sample. This result is in contrast to the finding that PD patients demonstrated trend level lower scores on the MMAA compared to control participants (Pirogovsky et al., 2012). As discussed above, a modification was made to the MMAA in the present study to limit the effect of motor problems on HD patients’ task performance. Although the modification was not expected to have a significant effect on the task, it is possible that this modification reduced our ability to detect between-group differences on this measure.

Additionally, it was hypothesized that HD patients would self-report greater difficulty with iADLs compared to control participants. In support of this hypothesis, HD patients self-reported significantly greater difficulty with items on the iADL questionnaire compared to controls (large effect size, $d = 1.53$); however, no significant differences between groups were found on the MMES. This finding supports our results that there were no significant differences between groups on a performance-based measure of medication management; therefore, it may reflect similar medication management abilities between groups in addition to an accurate estimation of medication management abilities by participants in the HD and control groups.

It was hypothesized that the performance-based measures of iADLs would correlate poorly with self-report measures of iADLs, as participants were expected to overestimate their iADL abilities in a self-report measure. The results indicate that for the HD patients, the performance-based measures of iADLs (Advanced Finances Test and MMAA) were not correlated with the self-report measures of iADLs (iADL questionnaire and MMES). These
findings are consistent with the hypothesis, as although HD patients reported greater impairment on the self-report measures of iADLs compared to controls, HD patients were expected to overestimate their iADL abilities in a self-report measure. Within the control participants, the Advanced Finances Test was not correlated with the self-report measures of iADLs. The MMAA was not correlated with the iADL questionnaire in this group; however, the results indicate a positive relationship between the MMAA and the MMES in the control participants. As discussed above, the findings may reflect accurate self-report of medication management abilities by control participants that reflect their abilities on a performance-based measure of medication management.

Research evidence suggests ProM performance is correlated with the ability to perform iADLs (Woods et al., 2011). Therefore, it was hypothesized that the MIST would be correlated with the performance-based measures of iADLs. Contrary to the hypothesis, the present study did not find correlations between the MIST and the performance-based measures of iADLs (Advanced Finances Test and MMAA) in the HD patients. The findings are surprising given the results that the HD patients demonstrated significant deficits on the MIST and the Advanced Finances Test compared to controls, and may be the result of homogeneity of HD patients’ performance in terms of disease severity. Therefore, the current findings may not provide an accurate indication of the relationship between ProM and iADLs in HD. The present study also may lack sufficient power to detect a significant correlation between ProM performance and iADL ability in HD. A significant positive relationship was observed between the MIST summary score and the Advanced Finances Test in the control participants; however, the results indicate the MIST variables were not correlated with the MMAA in the control group.

It was hypothesized that the self-report measures of ProM would be correlated with the self-report measures of iADLs, due to the expectation that participants would overestimate their ProM and iADL abilities in self-report measures. The present study found a significant negative relationship between the PRMQ self-cued scale and the iADL questionnaire within the HD patients. The results indicated there was not a correlation between the PRMQ scales and the MMES for the HD patients, nor was there a correlation between the MFQ and the self-report measures of iADLs for the HD patients. Within the control group, there were no correlations between the self-report measures of ProM and the
self-report measures of iADLs. The findings suggest the participants may not have overestimated their ProM and iADL abilities to the same extent in the self-report measures. Neuropsychological tests of executive functioning have been demonstrated to be dependent on the frontal lobes (Bonelli & Cummings, 2007; Joel, 2001; Lemiere et al., 2004; Thiruvady et al., 2007). Deficits in executive functioning have been documented in HD (Beglinger, Duff et al., 2010; Peinemann et al., 2005). Therefore, it was hypothesized that HD patients would demonstrate deficits on the WCST and the D-KEFS Color-Word Interference Test compared to controls. In support of the hypothesis, HD patients exhibited significantly poorer performance on the WCST compared to controls (large effect size, $d = 2.34$). In addition, HD patients demonstrated significantly lower scores on the inhibition scale of the D-KEFS Color-Word Interference Test compared to controls (medium effect size, $d = .71$). These results are consistent with literature suggesting HD negatively affects executive functioning abilities. However, when color naming was factored into a primary contrast measure by calculating a contrast scaled score for inhibition versus color naming, the groups did not significantly differ, which suggests that the HD patients may have a speed of processing deficit rather than an inhibition deficit.

It was hypothesized that HD patients would exhibit perseverative behavior and commit more errors on the WCST compared to controls. Consistent with this hypothesis, HD patients committed significantly more total errors (large effects size, $d = 1.23$) on the WCST compared to control participants. Of the total number of errors committed on the WCST, HD patients committed significantly more perseverative errors (small effect size, $d = .40$), compared to control participants. The results are consistent with previous research suggesting HD is associated with perseverative behavior on the WCST (Josiassen, Curry, & Mancall, 1983; Lawrence et al., 1996).

It was hypothesized that a performance-based test of ProM would be correlated with measures of neuropsychological functioning. Contrary to the hypothesis, the results suggest there is not a correlation between the MIST and the WCST or between the MIST and the D-KEFS Color-Word Interference Test in either group. A possible explanation for the current finding is the theory that ProM and neuropsychological functioning may reflect different frontal lobe processes, which may be affected to different degrees in HD (Baddeley, Della Sala, Papagno, & Spinnler, 1997; Katai, Maruyama, Hashimoto, & Ikeda, 2003). It is
possible that ProM abilities may rely on different aspects of executive functioning, and thus
different frontal lobe mechanisms, compared to the aspects of executive functioning the
WCST or D-KEFS Color-Word Interference Test are dependent on.

It was hypothesized that self-report measures of ProM would correlate poorly with
measures of neuropsychological functioning. In support of this hypothesis, the results
indicate there were no correlations between the self-report measures of ProM (PRMQ scales
and MFQ) and the measures of neuropsychological functioning (WCST and D-KEFS Color-
Word Interference Test) in either group.
CHAPTER 6

LIMITATIONS

A primary limitation of the present study was the relatively small sample size. HD is a relatively rare disease and studies investigating HD generally include sample sizes comparable to the sample included in the present study. However, the sample was not large enough to examine the incremental value of ProM in relation to other predictors of functional impairment in HD. Therefore, future studies with larger sample sizes are needed to continue to investigate ProM impairment as well as predictors of functional impairment in HD. The unequal sample sizes between HD and control groups will be resolved as one additional HD patient is currently being recruited to participate in this study. Another limitation of the current study is the homogeneity of HD patients in terms of disease severity. Recruiting HD patients within the mild-moderate stage of the disease increased our understanding of the effects of HD on ProM, iADLs, and executive functioning. However, including a homogeneous sample of HD patients in terms of disease severity likely led to a reduction in the range of performance within the HD group, resulting in insufficient statistical power to identify significant relationships. Another limitation of this study is the use of a cross-sectional design. A longitudinal design would have allowed for an investigation of changes in performance in participants over time, while the present study examined current performance of HD and control participants. A final limitation of the present study is the modification made to the MMAA to limit the effect of motor problems on HD patients’ task performance. The test was modified with the expectation that it would not significantly affect the ability of the test to assess medication management abilities; however, it is possible the modification did have an effect on the current findings.
CHAPTER 7

IMPLICATIONS AND FUTURE DIRECTIONS

Examining ProM in HD patients provides new insight into a frontal lobe dependent memory process. The deficits observed in this study on a performance-based test of ProM and ability to perform iADLs in HD patients could have implications for understanding functional independence in this patient population. The current findings highlight the need to assess ProM abilities as part of routine neuropsychological testing.

Future studies with larger sample sizes should continue to investigate ProM abilities in HD across the progression of the disease. For example, this study could be replicated with pre-manifest gene carriers for HD in addition to later stages of HD to assess cognitive changes relating to ProM throughout the course of the disease. Future studies with larger sample sizes also should continue to investigate the relationship between ProM and iADLs in HD. If a relationship between ProM performance and iADL abilities is identified in HD, the findings could lead to the use of interventions to teach compensatory cognitive techniques for ProM impairment in order to improve everyday functioning and increase quality of life for HD patients. Additionally, the findings could result in behavioral interventions for HD patients that structure daily living tasks in a way that reduces demand on the frontal lobes. Future studies could include additional predictors of iADL abilities that were not assessed in the current study, such as mnemonic usage and compensatory cognitive strategies. Additionally, future studies could use more naturalistic tests to assess performance-based ProM and iADL abilities in the laboratory.

Future research should continue with the goal of developing performance-based tests to assess ProM. The findings from the current study, and others that utilize such measures, have important implications for the development and evaluation of standardized neuropsychological tests used to assess memory function.
CHAPTER 8

CONCLUSION

ProM is a form of memory for future events and is believed to be involved in memory for everyday tasks. The current study revealed impairment in HD patients relative to control participants on a performance-based test of ProM. In addition, HD patients demonstrated significant impairment on a more naturalistic test of ProM compared to control participants, which provides an indication that HD patients’ deficits on ProM may affect their ability to perform everyday tasks. HD patients also demonstrated deficits on a performance-based measure of iADLs compared to control participants. These findings provide the first data to indicate that HD is associated with impairment on a performance-based test of ProM, and provide support for existing literature on iADL impairments associated with HD.

The deficits observed in this study on a performance-based and naturalistic test of ProM as well as ability to perform iADLs in HD patients could have implications for understanding functional independence in this patient population. Future research may identify a relationship between ProM performance and iADL abilities in HD, and the findings from such a study could lead to the use of interventions to teach compensatory cognitive techniques for ProM impairment in order to improve everyday functioning and increase quality of life for HD patients. Additionally, the findings could result in behavioral interventions for HD patients that structure daily living tasks in a way that reduces demand on the frontal lobes. Future research should continue to investigate ProM abilities in HD across the progression of the disease and continue to investigate the relationship between ProM and iADLs in HD.
REFERENCES


