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Effects of Motivation on Prospective Memory Performance in Huntington's Disease

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by

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Table of Contents

List of Tables

List of Figures

Abstract

Prospective memory (PM) refers to memory for future intentions and involves several cognitive processes including memory, executive functions, and attention. PM has been studied extensively in clinical populations in which these cognitive processes are impaired but has only recently been studied in Huntington's disease (HD), a neurodegenerative disease of the basal ganglia that is associated with neuropsychiatric, movement, and cognitive changes. The purpose of the present study was to further examine PM in HD, as well as investigate the influence of impulsivity on PM performance and whether a monetary incentive (either reward or loss) would improve PM performance. Results of the current study indicated that overall individuals with HD performed worse on a PM task compared to Controls. Control participants evidenced significantly better PM performance when they could have potentially lost money compared to a Neutral PM task. HD participants demonstrated a similar pattern of findings at a trending significance level. Impulsivity, as measured by the total score on the BIS-11, was not related to PM performance in either group. Controls scored significantly higher on a self-reported measure of prospective and retrospective memory (PRMQ) relative to HD participants with a trending association between the PRMQ and PM performance in Controls, but no association in HD participants. While there was a significant difference between groups on a recognition test of PM cues, there was no difference between groups on a free recall test of PM task instructions. These results build upon previous research that has found PM deficits in HD by investigating possible factors that may improve PM performance in this clinical population. Future research should investigate other motivational factors that may further increase PM performance in HD.

Introduction

Prospective Memory (PM) is colloquially known as "remembering to remember". This type of memory process is ubiquitous to our everyday lives. We use prospective memory to remember to do things such as attending appointments, taking cookies out of the oven, putting gas in the car, and phoning a friend on their birthday. Researchers have been interested in PM for many years because it is an important function for daily life. As such, PM has been associated with the ability to perform activities of daily living such as managing finances, medication adherence, and cooking (Woods, Weinborn, Velnoweth, Rooney, & Bucks, 2012; Zogg, Woods, Sauceda, Wiebe, & Simoni, 2012). Furthermore, as those activities are important for independent living, researchers have investigated PM ability in different populations where successful management of daily activities is of concern (Woods et al., 2008). Researchers want to better understand the PM process to help identify factors and develop strategies that may improve PM performance (Fish, Wilson, & Manly, 2010; Kliegel, Altgassen, Hering, & Rose, 2011).

In order to form an intention, and at a later point recognize and successfully act on that intention, the PM process has been conceptualized to involve many cognitive processes including retrospective memory, working memory, attention, and executive functions such as planning (Harrison, Mullet, Whiffen, Ousterhout, & Einstein, 2014; Rose, Rendell, McDaniel, Aberle, & Kliegel, 2010; Schnitzspahn, Stahl, Zeintl, Kaller, & Kliegel, 2013). Therefore, to better understand these cognitive processes, researchers have studied the neurobiology of PM. Researchers have found that successful PM ability relies heavily on the prefrontal cortex due to

the need to plan how and when a future intention will be accomplished (Burgess, Gonen-Yaacovi, & Volle, 2011). Since researchers have found associations between prefrontal processes and PM function, there have been numerous studies looking at PM performance in populations with prefrontal cognitive deficits, since that area is associated with planning, behavioral regulation, and monitoring (Costa et al., 2015; Terrett et al., 2014).

When studying PM in clinical populations, researchers are also interested in factors which both positively and negatively influence PM performance. A behavior that may decrease PM performance is impulsivity. Impulsivity has been studied due to associated factors such as poor planning, lack of perseverance to see a task through, sensation seeking, and risk taking (Cuttler, Relkov, & Taylor, 2014). Likewise, researchers have sought to understand factors that may support or enhance PM (McDaniel & Einstein, 2000). Some of those factors include how visible or salient the PM target is (Scullin, McDaniel, Shelton, & Lee, 2010) and the motivation behind successfully fulfilling the PM task (Penningroth & Scott, 2007). One way researchers have studied motivation is by offering a monetary incentive, which has shown to increase PM performance in certain populations (Cook, Rummel, & Dummel, 2015; McCauley, McDaniel, Pedroza, Chapman, & Levin, 2009). However, different populations react differently to monetary incentives. Populations that may be more reward seeking are individuals with impulsive behaviors such as substance users and gambling addicts (Balodis et al., 2012; Balodis & Potenza, 2015). Some populations with neurodegenerative disorders also show evidence of impulsive behaviors and increased motivation towards receiving rewards (Czernecki et al., 2002; Perry, Sturm, Wood, Miller, & Kramer, 2015).

In particular, Huntington's disease is one such population that has evidence of impulsivity and disinhibition, as well as cognitive decline, particularly in the prefrontal cortical

regions (Paulsen, 2011; Paulsen, Ready, Hamilton, Mega, & Cummings, 2001). As described earlier, PM performance is associated with cognitive ability and may be impacted by impulsive behaviors. As such, researchers have begun to study PM ability in the HD population. Early studies have shown that HD individuals perform worse on PM tasks as compared to healthy controls (Nicoll et al., 2014).

However, what has not been investigated yet is how adding incentives to improve motivation toward completing a PM task may improve PM performance in the HD population. The following review will first discuss the concept of PM and common paradigms to study the memory process. The neuroanatomy of PM will also be reviewed as well as how the neuroanatomy impacts clinical populations including populations with neurodegenerative diseases and impulsive behaviors. In addition, factors that are associated with successful PM will be discussed including motivation and earning potential rewards. Finally, an overview of HD and how this particular population's PM ability may be uniquely impacted by impulsivity and cognitive decline will be reviewed. Likewise, their responsiveness to reward and the potential for improved PM ability will be discussed. This study seeks to further the understanding of PM in HD as well as investigate factors that may improve PM performance in this population.

Prospective Memory

Prospective Memory (PM) refers to the act of forming an intention to complete at a future point in time (McDaniel & Einstein, 2000). Over the past several years, researchers have become increasingly interested in factors that help facilitate successful completion of a PM task (Graf & Uttl, 2001; Ihle, Schnitzspahn, Rendell, Luong, & Kliegel, 2012; McDaniel & Einstein, 2000). First, In order to study PM, researchers typically investigate either event-based or time-

based PM cues. Event-based cues are found in the environment and require external monitoring of surroundings. For example, if one wants to remember to mail a letter in the morning they may place the letter by the door where it can be seen on the way out. The intention is to mail the letter the next morning, and that intention is paired with an external cue, i.e., the letter by the door. When one sees the letter, he or she will be cued to perform the intended action of mailing the letter. Time-based cues require internal-monitoring of time passing rather than the external monitoring for event-based cues (for a review: Gonen-Yaacovi & Burgess, 2012). Again using the example of mailing a letter, if someone wanted to hand the letter directly to the mailman at 2:00 PM, then the person would internally monitor the passing of time throughout the day in order to meet the mailman at 2:00 PM. An important distinction though, is that if the person set an alarm for 2:00 PM, then the task would shift to primarily an event-based task due to the external cue of the alarm.

Researchers have investigated the difference in performance between event-based and time-based PM cues. Studies have found that relative to event-based cues, time-based cues require more effortful internal monitoring and thus rely more on the executive functions and frontal lobes in order to successfully recognize and carryout a PM intention (McDaniel & Einstein, 2000; Mioni, Stablum, McClintock, & Cantagallo, 2012). As such, studies have investigated the difference in performance between time-based and event-based PM cues in populations such as Parkinson's disease, Huntington's disease, and HIV, with known executive function deficits due to frontal lobe impairments and have found that generally these populations perform worse on the time-based tasks compared to the event-based tasks (Carey, Woods, Rippeth, Heaton, & Grant, 2006; Costa, Peppe, Caltagirone, & Carlesimo, 2008; Nicoll et al., 2014; Raskin et al., 2011).

In addition, two different types of event-based cues are studied: focal or non-focal. Focal cues are directly related to the intention, where as non-focal cues do not share similar qualities with the intention (McDaniel & Einstein, 2000). In the above example of mailing the letter, the letter cue would be considered a focal cue because the letter is inherent to the intention. However, if the person were to pair the intention of mailing the letter with picking up the car keys, then the car keys would be considered a non-focal cue because the keys are not directly related to the intention of mailing the letter. It is hypothesized that focal cues rather than non-focal are easier to identify when an individual is engaged in an ongoing task (i.e., a type of distractor task that is meant to divide attention) and thus successful completion of a PM intention is more likely. Non-focal cues require more strategic monitoring of the environment and subsequently require more cognitive effort which may lead to fewer successful executions of intentions (McDaniel & Einstein, 2000).

There are several ways in which researchers investigate PM performance. A very common measure of PM includes instructing a participant to press a special key whenever they see a particular target cue (i.e., the word tree) while engaging in a lexical decision making task (i.e., deciding whether a string of letters is either a word or non-word) (e.g., Bugg, Scullin, & McDaniel, 2013; Cook et al., 2015; Costa et al., 2015; R. E. Smith, 2003). Researchers vary whether the cue is focal (e.g., a specific word) or non-focal (e.g., a word with two syllables) depending on the research question or desired level of difficulty.

Besides studying PM in the laboratory and using behavioral outcomes to assess performance, researchers have also used neuroimaging in conjunction with laboratory measures to better understand the neurological basis of PM. Imaging has not only helped to bring new

insights regarding which brain areas are activated during PM, but has also identified areas activated during more specific processes such as recognition of focal and non-focal cues.

Neurobiology of Prospective Memory

Although conceptualized as a memory process, PM has been studied within the context of executive functions and there is much support regarding associations between PM and prefrontal processes (Burgess et al., 2011; Glisky, 1996; Martin, Kliegel, & McDaniel, 2003; Neulinger, Oram, Tinson, O'Gorman, & Shum, 2015). For example, the ability to plan (a component of executive functioning) has been shown to be associated with the process of forming the initial PM intention and that the greater the plan elaboration, the more successful the individual is at fulfilling the PM intention at a later point (Kliegel, McDaniel, & Einstein, 2000; McDaniel & Einstein, 2011; McDaniel, Howard, & Butler, 2008).

Neuroimaging studies have supported the role of prefrontal processes in prospective memory (PM). The primary area thought to be most associated with prospective memory is the anterior prefrontal cortex or Brodmann's area 10 (BA 10), but also associated are the precuneus and parietal lobes (Burgess et al., 2011). BA 10 is a large area that occupies the most frontal portion of the human brain and then continues through to the rostal portion of the frontal cortex. In addition, BA 10 has connections with the anterior temporal cortex and the cingulate. Among many other functions, it is suggested that BA 10 is active during memory retrieval and may help to coordinate cognitive operations when more than one cognitive process is required to fulfill a behavioral goal (Ramnani & Owen, 2004). Neuroimaging has also indicated that different neuroanatomical regions are activated depending on whether the cue is focal or non-focal as well as the different phases of PM, i.e., plan formation, retention, initiation, and execution (Kliegel et

al., 2000; McDaniel, LaMontagne, Beck, Scullin, & Braver, 2013). Cona, Scarpazza, Sartori, Moscovitch, and Bisiacchi (2015) summarized that for highly salient or focal cues, the medial anterior prefrontal cortex was activated, but for cues that require a high memory component such as the non-focal cues, researchers see greater activation of the lateral anterior prefrontal cortex.

The prefrontal cortex is associated with the cognitive process of executive functioning, which refers to "…those capacities that enable a person to engage successfully in independent, purposive, self-directed, and self-serving behavior" (Lezak, Howieson, & Loring, 2012, p. 37). By extending PM research to clinical populations, especially in populations with executive function deficits, additional insights can be made regarding PM abilities. Populations that are of particular interest due to the degeneration of the frontal-striatal circuitry are Parkinson's and Huntington's disease.

Prospective Memory in Clinical Populations

Prospective memory (PM) is relevant in clinical populations for several reasons. First, as mentioned before, PM relies on many executive functions such as planning, cognitive flexibility, and monitoring. Furthermore, executive functions, which may be conceptualized as such processes that support goal driven behavior, planning, inhibition, cognitive flexibility, and monitoring (for a review: Jurado & Rosselli, 2007), have also been associated with activities of daily living (Cahn-Weiner, Boyle, & Malloy, 2002; Jefferson, Paul, Ozonoff, & Cohen, 2006). The association between independent living and functional abilities are important areas of study within clinical populations. As such, PM has been studied within the context of functional abilities and activities of daily living in clinical populations such as older adults, Parkinson's disease, HIV, and populations with impulsive behaviors such as ADHD (e.g. Altgassen, Koch, &

Kliegel, 2014; Henry, MacLeod, Phillips, & Crawford, 2004; Kliegel, Jäger, Altgassen, & Shum, 2008; Woods et al., 2012).

Older Adults

As people age, cognitive deficits gradually occur in areas such as episodic memory, working memory, inhibition, attention, and executive functioning (Braver et al., 2001). Based on these cognitive declines and their association with PM, several researchers have investigated PM performance in older adults (McDaniel & Einstein, 2011). In one PM study, participants were divided into four groups: high and low functioning prefrontal processes and high and low functioning hippocampal processes. Researchers found that high functioning prefrontal adults significantly outperformed low functioning prefrontal adults on PM tasks suggesting that intact prefrontal processes are needed for successful PM performance. Furthermore, the same study found that individuals with high hippocampal functioning also evidence more successful PM performance than the low hippocampal functioning group (McDaniel & Einstein, 2011; McDaniel, Glisky, Guynn, & Routhieaux, 1999). However, there is evidence that suggests that older adults are aware of their PM deficits and employ compensatory strategies to mitigate those deficits. For example, numerous studies have shown what is referred to as the age paradox between older and younger adults (e.g., Schnitzspahn, Ihle, Henry, Rendell, & Kliegel, 2011; Weber et al., 2011). The age paradox refers to the finding that older adults perform better on naturalistic PM tasks (i.e., outside of the laboratory) than younger adults, whereas, within the laboratory setting, younger adults demonstrate better performance than older adults on PM tasks. These findings suggest that older adults have worse prospective memory than younger adults, however, they are more aware of their memory deficits. As such, they have developed

compensatory strategies (e.g., writing notes, using alarms) to use in real world environments and are more used to using those strategies (Glisky, Polster, & Routhieaux, 1995).

Parkinson's Disease

Parkinson's disease (PD) is a neurodegenerative disorder characterized by akinesia, bradykinesia, and tremor. The disease is a result of is degeneration of the caudate nucleus, a structure within the functional system of the basal ganglia, among other areas (Nelson & Kreitzer, 2014). The degeneration of the caudate nucleus results in dopamine depletion of the caudate and putamen in the basal ganglia which in turn affects the fronto-striatal circuits to the prefrontal cortex (Redgrave et al., 2010). The fronto-striatal circuit which has been shown to be associated with executive functions such as planning and task shifting includes projections that connect the prefrontal cortex, the striatum, the globus pallidus, substantia nigra, and the thalamus (Tekin & Cummings, 2002). In that Parkinson's disease negatively affects the fronto-striatal circuit and in turn executive functioning which is one of the cognitive components of prospective memory (PM), several empirical studies have investigated PM within the PD population (Costa et al., 2015; Katai, Maruyama, Hashimoto, & Ikeda, 2003; Kliegel et al., 2011). A recent review suggests that impairment on time-based and event-based cues are relatively similar in PD; however, time-based tasks may be slightly more impaired, but this may be due to the association between time-based cues and the cognitive demands on prefrontal processes (Ramanan & Kumar, 2013).

Investigating different cue types, Foster and colleagues (2013) compared healthy controls to cognitively intact (as assessed by a screening measure of global cognition) PD patients on a PM task which manipulated whether the PM cue (both focal and non-focal) arrived at regular intervals (e.g., taking medication at the same time each day) or irregular intervals (e.g.,

remembering to pick up dry-cleaning). The researchers found PM performance improved with focal cues rather than non-focal cues during regular PM tasks. However, PM performance was impaired for both focal and non-focal cues when presented with an irregular PM task. These findings suggest that PM performance for tasks such as taking medication that occur at regular intervals can improve with the use of focal cues.

Costa et al. (2015) investigated the differences in PM abilities between healthy controls, individuals with PD, and individuals with PD who have mild cognitive impairment (MCI). In broad terms, MCI refers to individuals who evidence some cognitive deficits, but are still able to manage activities of daily living reasonably well. The study found that individuals with PD without MCI demonstrated similar PM performance to healthy controls when asked to remember to respond to a focal, event-based cue. However, individuals with PD and with MCI performed significantly worse than both PD without MCI and healthy controls. Importantly, decreased executive function ability rather than memory was found to predict worse PM performance. These findings suggest that executive functions may be more related to successful PM performance than memory.

Populations with Impulsive Behaviors

Impulsivity can be defined as "... actions that appear poorly conceived, prematurely expressed, unduly risky, or inappropriate to the situation and that often results in undesirable consequences (Daruna & Barnes, 1993). Impulsivity is often studied within the context of clinical populations such as Attention Deficit Hyperactivity Disorder (ADHD), alcohol and substance use, gambling disorders, and bipolar disorder. Furthermore, impulsivity has been suggested to be associated with the prefrontal cortical processes of executive function (e.g., behavioral control vs. disinhibition, planning vs. non-planning) (Bickel, Jarmolowicz, Mueller,

Gatchalian, & McClure, 2012). Studies have found that greater impulsivity is associated with worse executive functions (Bari & Robbins, 2013; Sjöwall, Roth, Lindqvist, & Thorell, 2013; Verdejo-García et al., 2010). Relatedly, PM has also been studied within the context of executive functions (Glisky, 1996; Kliegel et al., 2000; West, Scolaro, & Bailey, 2011) and studies have shown that individuals with deficits of executive functioning such as inhibition, task switching, and working memory evidence worse PM performance (Schnitzspahn et al., 2013; West et al., 2011). In that impulsivity has been associated with worse performance on measures of executive function and that worse executive functioning has been associated with worse PM performance, researchers have investigated PM in individuals with increased impulsivity. In a sample of healthy college undergraduates, Cuttler et al. (2014) found the Non-Planning subscale of the Barrett Impulsivity Scale -11 (BIS-11: (Patton & Stanford, 1995) was negatively associated with behavioral measures of PM. Furthermore, worse performance on measures of PM have also been found in populations who use substances such as methamphetamine and ecstasy as compared to healthy adults (Rendell, Gray, Henry, & Tolan, 2007; Rendell, Mazur, & Henry, 2009). In adult ADHD populations, worse performance on an event-based PM task using non-focal cues was observed when compared to healthy adults (Altgassen, Koch, et al., 2014).

As has been described, PM has been studied in many different clinical populations including older adults, PD, and individuals with impulsive behaviors. These studies have shown that generally these populations perform worse on measures of PM compared to healthy individuals. Kliegel et al. (2011) suggests that once PM deficits have been understood in the clinical population, researchers should investigate interventions to improve PM performance. The importance of increasing PM performance in clinical populations is linked with facilitating

independent living. One way in which researchers have improved PM performance is by manipulating the motivation towards completing the PM task.

Motivation

Motivation and Prospective Memory

Motivation has been investigated as an important contributor to PM (McDaniel & Einstein, 2000). The Motivational-Cognitive Model of PM (Penningroth & Scott, 2007) proposes that individuals who view PM tasks as more important or more goal related will use both more effortful and automatic processing while maintaining the PM intention over time until it can be fulfilled. Specifically, Penningroth and Scott theorize that for tasks that have higher perceived importance, individuals will employ greater use of strategies (e.g., setting an alarm, noting the intention in a calendar, mental rehearsal) during the initial formation of the intention in order to increase automatic retrieval at the appropriate time to initiate the task. The perceived importance of the PM task also theoretically increases the accessibility of intentions during the time between when the initiation was formed and when it is completed leading to increased automatic retrieval of the PM task.

Many studies have used motivating factors to increase PM performance such as stressing the importance of PM performance during task administration (Kliegel, Martin, McDaniel, & Einstein, 2004), using pro-social motivation (Brandimonte, Ferrante, Bianco, & Villani, 2010), and offering rewards such as extra class credit (Jeong & Cranney, 2009) or money (Cook et al., 2015; McCauley et al., 2009; McCauley et al., 2011). Altgassen and colleagues (2007) found that PM performance improved when the importance of the PM task was stressed relative to the ongoing task. Alternatively, when the ongoing task was implied to be more important, PM performance was worse. Pro-social incentives have also been used. Brandimonte et al. (2010)

found increased performance on a PM task when participants felt that they were helping another individual (i.e., helping a graduate student obtain data for their Master's thesis).

Another way in which researchers have increased motivation toward the PM task is by adding an incentive such as a monetary reward. Some studies have used a monetary incentive task to investigate whether participants respond differentially to either a loss or a reward condition (Bugg et al., 2013). In a between subjects study, Cook et al. (2015) found that participants had a significantly greater percentage of correctly identified PM cues embedded within a lexical decision making task when they were presented with either a monetary loss or monetary gain incentive as compared to a neutral condition (no monetary loss or gain). Similarly, in studies involving children with TBI, researchers found that the children with a history of moderate TBI had a higher PM response rate when offered larger monetary rewards than when offered smaller monetary rewards (i.e., dollars vs. pennies) (McCauley et al., 2009; McCauley et al., 2011).

Studies have shown that PM performance is improved by increasing motivation towards completing a PM task. How motivation and reward can improve PM performance can be further understood by studying the neural underpinnings of motivation and reward in both healthy adults and in clinical populations.

Motivation and Reward

Research has shown that different populations may react differently to incentives. The neurobiology of reward processing may explain why clinical populations evidence different reactions to rewards or losses than a healthy adult. Studies have shown that reward processing is associated with areas such as the basal ganglia, specifically the caudate nucleus (Hikosaka, Kim, Yasuda, & Yamamoto, 2014) and the nucleus accumbens (Knutson, Adams, Fong, & Hommer,

2001). The dorsolateral and the orbital frontal cortex also show activation for reward processing (Thut et al., 1997). Furthermore, research shows that individuals with lower dopamine synthesis in the putamen show a greater "Now" bias (preferring immediate rewards rather than waiting for larger reward) (Smith et al., 2016). Populations who have shown disruption of this area include substance users, Parkinson's disease, and Huntington's disease (Bonelli & Cummings, 2008; Nelson & Kreitzer, 2014; Volkow et al., 2014).

Conversely, researchers have found that healthy adults demonstrate loss aversion when faced with risky choices meaning that adults may be averse to losing what they have already perceived to gain (Tversky & Kahneman, 1991). Developmental studies have shown that while risk taking for gains decreases across the life span, risk taking to avoid losses develops throughout childhood and into adulthood and then remains stable through later life (Weller, Levin, & Denburg, 2011). Neuroanatomy studies have also found evidence that healthy adults demonstrate loss aversion. For example, an event-related brain potential (ERP) study found evidence that individuals had a greater reaction in the medial prefrontal cortex area to loss situations than gains (Gehring & Willoughby, 2002). Furthermore, a case study in which an individual with bilateral amygdala lesions demonstrated decreased sensitivity to losses as compared to healthy individuals (Paulsen et al., 2001) indicating that the amygdala is an important brain structure for influencing loss aversion.

There is an extensive literature linking impulsivity and reward seeking behaviors such that impulsive populations (e.g., compulsive gamblers, eating disordered, substance abusers, ADHD) have demonstrated increased activity towards rewarding stimuli, particularly for rewards that are immediate rather than delayed (Beck et al., 2009; de Wit & Richards, 2004; C. T. Smith et al., 2016). Huntington's disease (HD) is another clinical population with reported impulsive

behaviors (Paulsen, Smith, Long, investigators, & Group, 2013; Rao et al., 2014). However, there are no studies to date, which have investigated how impulsive traits may effect motivation towards earning a potential reward or avoiding a potential loss in HD patients. By investigating the effects of impulsivity and motivation towards earning a reward (or avoiding a loss) on PM performance in HD individuals, greater insight into how impulsive behaviors may impact PM as well as potential intervention strategies may be found.

Huntington's Disease

Overview

Huntington's disease (HD) is a progressive autosomal dominant neurodegenerative disorder that is caused by a gene mutation on chromosome 4 that results in an expanded cytosine-adenine-guanine (CAG) repeat (MacDonald et al., 1993). Disease onset typically occurs around 35 to 45 years of age and is diagnosed at the onset of the motor symptoms (for a review: Dumas, van den Bogaard, Middelkoop, & Roos, 2013). Before the onset of motor symptoms, HD gene positive individuals are considered to be in the prodromal or presymptomatic phase of the disease.

HD is classified as a frontal-subcortical dementia due to the disruption between the striatum and the frontal lobes (Bonelli & Cummings, 2008). The first major neurological changes in HD occur in the basal ganglia and are specifically seen as atrophy of the striatum, which is comprised of the caudate nucleus and putamen. Typically changes are first seen in the tail and body of the caudate and then progress through to the head of the caudate (Papoutsi, Labuschagne, Tabrizi, & Stout, 2014). Furthermore, the striatum is one of the primary locations for medium spiny neurons, which are associated with the neurotransmitter GABA and the

primary location for dopamine D1 and D2 receptors (Hall et al., 1994; Ito, Takahashi, Arakawa, Takano, & Suhara, 2008). The loss of medium spiny neurons results in lower levels of dopamine. Furthermore, the dopamine transporter (DAT), which is a protein located on the dopamine terminals presynaptically, has been shown to be reduced in the brains of individuals with HD. It is suggested that both the presynaptic and postsynaptic dopamine systems are disrupted in HD due to both the degradation of the D1 and D2 receptors as well as DAT (Cepeda, Murphy, Parent, & Levine, 2014). Outside of the basal ganglia, neuronal loss is also found in the cerebral cortex, thalamus, hippocampus, and hypothalamus (Bäckman & Farde, 2001; Cepeda et al., 2014). Decreased volume of the amygdala has also been found in HD (Pavese et al., 2003). The losses in the prefrontal and temporal cortices, thalamus, and striatum affect the normal functioning of the cortico-striato-thalamocortical circuitry (Cepeda et al., 2014).

HD is associated with motor abnormalities, neuropsychiatric symptoms (e.g., depression and anxiety), and changes in cognitive abilities (Cepeda et al., 2014; Paulsen et al., 2001). While the most prominent feature of HD is typically motor abnormalities, changes in emotional well-being and cognitive abilities may be seen well before the motor manifestations (e.g. Harrington et al., 2012; Julien et al., 2007).

Reviews of the HD literature report a high prevalence of irritability, aggression, apathy (i.e., decreased motivation), depression and anxiety (Anderson & Marder, 2001; Paulsen et al., 2001; Van Duijn, Kingma, & Van der Mast, 2007). One of the most reported neuropsychiatric symptoms among HD individuals and their family is increased irritability (60%) and aggression (40-60%) (Anderson & Marder, 2001; Paulsen et al., 2001). Apathy, which is conceptualized as "…a diminished motivation not attributable to diminished level of consciousness, cognitive

impairment, or emotional distress (Marin, 1990)" is also highly prevalent in the HD population, with studies citing that roughly 55% of patients reported loss of interest and motivation (Anderson & Marder, 2001; Paulsen et al., 2001). Slightly less prevalent than apathy is depression with prevalence being reported at around 30% (Slaughter, Martens, & Slaughter, 2001). Finally, one study found that 52% of HD individuals reported experiencing anxiety (Paulsen et al., 2001).

In one study, prevalence of disinhibition in HD was found to be about 35% in a sample of 52 gene positive individuals (Paulsen et al., 2001). Other studies have also found evidence for increased rates of disinhibition. For example, on a measure of frontal systems and behaviors (Frontal System Behavioral Scale: FrSBe), companions of gene positive participants reported higher rates of disinhibition than the gene positive participants themselves. Furthermore, companion ratings of FrSBe total score, apathy, and disinhibition significantly predicted smaller striatal volume in a subset of gene positive participants (Duff et al., 2010). In behavioral studies, researchers have found that during Go/No-Go tasks that have been modified to measure divided attention, response inhibition, vigilance, and response flexibility, HD participants had significantly longer reaction times, committed more errors, and had greater numbers of omissions than control participants (Sprengelmeyer, Lange, & Hömberg, 1995). In addition, HD patients who were in the early stages of the disease as assessed by the Unified Huntington's Disease Rating Scale Total Functional Capacity (UHDRS TFC: (Kremer & Group, 1996; Shoulson & Fahn, 1979) were found to take significantly longer to complete the Stroop test which is a measure of inhibition, cognitive flexibility, and task switching (Delis, Kaplan, & Kramer, 2001; Lippa & Davis, 2010) indicating that HD participants have greater difficulty in these areas than healthy controls.

Regarding changes in cognition, memory studies have found that delayed recall is significantly impaired in HD individuals; however, recognition memory has shown more variable results (For a review: Montoya et al., 2006). A meta-analysis found that in HD participants with mild to moderate cognitive impairment (as assessed by the Mini-Mental State Examination: MMSE) recall and recognition memory were both significantly impaired as compared to healthy controls. However, the HD participants with mild cognitive impairment had significantly better recall and recognition than the moderate to severely impaired HD participants. Furthermore, in the mildly cognitive impaired group, there was a significant difference between effect sizes of recall (d = 1.80) and recognition memory (d = 1.38) compared to healthy controls indicating that recognition memory was significantly better than free recall in mildly affected HD participants (Montoya et al., 2006). In comparison to other clinical populations with known memory deficits such as Alzheimer's disease and Korsakoff Syndrome, HD participants have demonstrated significantly better recognition memory (Delis et al., 1991). Furthermore, other studies have not found a significant difference in recognition memory between HD participants and healthy controls (Nicoll et al., 2014).

Several studies have examined memory in HD throughout the different stages of disease (Dumas et al., 2013; Paulsen, 2011). However, until recently, there has been a dearth of PM research in the HD population. Researchers are becoming more interested in PM abilities in HD due to the disease negatively affecting the fronto-striatal circuit which affects executive functioning (Tekin & Cummings, 2002) and documented memory deficits, particularly with encoding and retrieval (Lemiere, Decruyenaere, Evers-Kiebooms, Vandenbussche, & Dom, 2004).

Huntington's Disease and Prospective Memory

As mentioned above, PM has recently been studied in the HD population. Nicoll et al. (2014) investigated event- and time-based PM as well as a naturalistic PM task with 20 participants with a confirmed HD diagnosis and 20 community controls. As expected, HD participants performed significantly worse when presented with time-based cues after both a short delay (2 minutes) and longer delay (15 minutes). Interestingly, HD participants performed worse than controls when presented with an event-based cue after 2 minutes, but did not differ from controls when presented with an event-based cue after 15 minutes. There was no significant difference in post-test recognition scores between groups suggesting that the HD group successfully encoded the PM cues, but demonstrated difficulty retrieving the intention at the appropriate time. Significantly more HD participants failed the naturalistic PM task in which they were instructed to call the examiner within 24 hours and report on their sleep. Also of interest, there were no significant differences between HD participants and controls on their self-reported PM abilities. However, this finding may not be surprising due to numerous studies reporting lack of awareness regarding symptoms in HD (Nicoll et al., 2014). This study furthered the understanding of PM performance in a symptomatic HD population; however, investigation is needed regarding factors that may impact PM performance in HD.

Awareness in Huntington's Disease

As prevalent and pronounced as the motor, cognitive, and neuropsychiatric changes have been reported in HD, there has much research into the awareness of these changes in HD individuals (Duff et al., 2010; Hoth et al., 2007; Vitale et al., 2001). For example, research has shown that symptomatic HD individuals report experiencing motor symptoms such as twitching or jerking far less than they report consequences of their motor symptoms such as dropping or

spilling items (Snowden, Craufurd, Griffiths, & Neary, 1998). HD individuals are also more likely to disagree with informants regarding their abilities to complete activities of daily living, behavioral control, and emotional control in that HD individuals will rate their abilities in these areas as significantly higher than their informant's ratings on their abilities. Interestingly though, when asked to rate the abilities of their informants, ratings between HD individuals and informants were more similar indicating that the lack of awareness regarding abilities is unique to the HD individual (Duff et al., 2010; Hoth et al., 2007). It is suggested that the lack of symptom awareness in HD is due to the disruption of the frontal-subcortical connections (Duff et al., 2010; Hoth et al., 2007; Zamboni & Wilcock, 2011). This theory is supported by several studies which have found associations between decreased awareness of symptoms to disruptions of the frontal lobes and frontal circuitry (e.g., Vitale et al., 2001; Zamboni & Wilcock, 2011).

Reward and Huntington's Disease

There has been much research investigating reward pathways in patients with basal ganglia disorders (Sesack & Grace, 2010). Studies have found that in these populations there is greater sensitivity to reward than to loss (Harsay, Buitenweg, Wijnen, Guerreiro, & Ridderinkhof, 2010). Furthermore, there is evidence that HD individuals prefer immediate larger rewards with reduced loss sensitivity (Czernecki et al., 2002; Hikosaka et al., 2014). In addition, research has demonstrated differential response between reward and neutral conditions, but no differential response between loss and neutral conditions in HD (Campbell, Stout, & Finn, 2004). Since researchers have already shown that PM performance can be improved by offering incentives such as monetary reward, and that populations with decreased dopamine synthesis are more reward sensitive, it is reasonable to investigate the effect of reward on PM performance in the HD population.

Purpose

The purpose of the present study is to expand on the current understanding of prospective memory (PM) abilities in the HD population by investigating the influence of motivation (e.g., sensitivity to reward) on PM in patients with Huntington's Disease (HD) when compared to healthy controls. In addition, this study will also examine the influence of impulsivity on the potential to earn (or lose) a potential reward in these patients. Specifically, it is predicted that HD participants will demonstrate better performance on a PM task (i.e., greater response accuracy to PM targets) when presented with a reward condition relative to either a loss or neutral (no reward or loss) condition unlike controls who generally, as a group, demonstrate most accurate performance in loss conditions. Furthermore, in that previous research with impulsive populations have shown increased sensitivity to reward (Duff et al., 2010; Novak & Tabrizi, 2010; Stout, Rodawalt, & Siemers, 2001), participants' level of impulsivity is also predicted to be associated with their PM performance when presented in a reward condition. In particular, higher impulsivity will be associated with worse performance on a PM test. However, impulsivity will be associated with a greater response rate to PM target cues during the reward condition relative to either the loss or neutral condition.

Although seemingly important, there is a dearth of research on PM ability in HD. This study will add a valuable contribution to the literature regarding PM abilities in the HD population and the influence of motivation on those abilities. PM has been shown to be associated with laboratory measures of functional ability (Buckholtz et al., 2010; Patel et al., 2013), declines in activities of daily living (e.g. Pirogovsky, Woods, Filoteo, & Gilbert, 2012; Woods et al., 2012),

and lower health-related quality of life (e.g. Woods et al., 2008) all of which are relevant to clinical populations including HD. Furthermore, research has shown that individuals with HD may lack awareness regarding their cognitive difficulties (e.g.Doyle et al., 2012). In particular, studies have shown that HD individuals overestimate their PM abilities as evidenced by discrepant results between a self-report PM questionnaire and a behavioral measure of PM abilities (de Langavant et al., 2013). As such, self-reported PM ability will be compared to performance on a behavioral measure of PM in both HD participants and healthy controls.

Hypotheses

1. Huntington's disease participants will perform worse on the Neutral (i.e., no loss or gain) condition of a PM task than healthy control participants as evidenced by fewer correct responses to PM cues.
2. The pattern of performance will differ across the three PM conditions for HD and Controls participants.
    a. Huntington's disease participants will demonstrate better performance on a PM task, (i.e., higher rate of correctly responding to a PM cue), during the monetary Reward condition compared to a monetary Loss condition or a Neutral condition.
    b. Healthy control participants will demonstrate increased PM performance when presented with a monetary Loss PM condition relative to a monetary Reward or Neutral PM condition.
3. Impulsivity as reported on the BIS-11 will be strongly related to PM performance.
    a. Higher endorsements of impulsive traits, as reported on the BIS-11, will be associated with worse overall performance on the Neutral PM conditions for all participants.
    b. Higher endorsements of impulsive traits, as reported on the BIS-11, will be associated with a higher percentage of accurate responses to monetary Reward PM cues
4. The PRMQ will be differentially associated with performance on the behavioral measure of PM for HD and Controls.

a. There will be a positive relationship between Control participants' total score on the PRMQ and overall PM performance, in that higher scores on the PRMQ will correlate with greater accuracy to PM cues.

b. In HD participants, a significant relationship would not be expected between the PRMQ and accuracy measures of PM.

5. Retrospective recognition memory performance will not differ between HD and Controls but will be differentially associated to PM performance for these groups.

   a. There will be no difference in retrospective recognition memory performance between HD and Controls.

   b. Retrospective recognition memory performance will be associated with PM performance for Control participants

   c. Retrospective recognition memory performance will not be associated with PM performance for HD patients.

Method

Participants

Potential participant identification was comprised of 1) consulting the medical staff at the Huntington's disease (HD) Center of Excellence at the University of South Florida and 2) patient medical record review. From this process, a total of 117 participants were contacted from the HD Center of Excellence and agreed to participate. Of the 117 participants, a total of 87 participants were consented to participate in the study. The other 30 participants (18 HD, 12 Control) did not participate due to the following reasons: misunderstood the location for study (1 HD, 1 Control), unable to make their appointment time (12 HD, 6 Control), declined at appointment due to either the time commitment or feeling ill (3 HD, 3 Control), lived too far away (control), or after reconsideration determined ineligible due to having the Westphal variant of HD (HD), with significant psychiatric issues (HD), and diagnosis of ALS (Control) (see Figure 1).

Participants with HD were included in the study if they had been diagnosed with HD as assessed by the Motor Scale of the Unified Huntington's Disease Rating Scale (UHDRS) and were in the mild to moderate disease stage per the Total Functional Capacity scale (TFC) (Kieburtz et al., 2001; Shoulson & Fahn, 1979). A neurologist, who specializes in movement disorders, administered the UHDRS. The TFC was verbally administered to participants.

The Motor Scale of the UHDRS evaluates the motor manifestations of HD such as dystonia, chorea, oculomotor function, gait, and postural stability. Higher scores on the UHDS indicate greater disease severity. An individual is considered to have clinically manifested HD

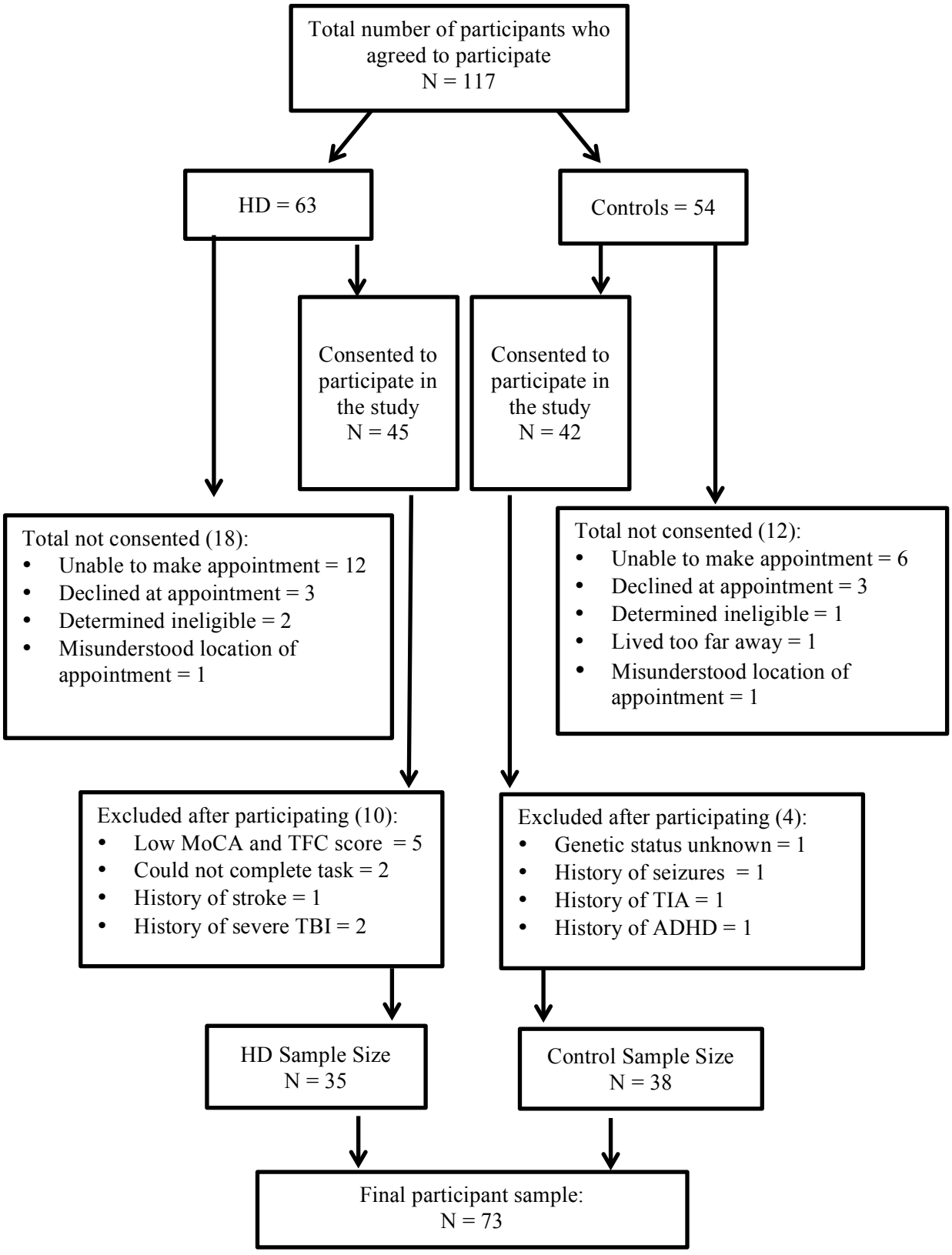

Figure 1. Participant recruitment flow chart

if the clinician indicates a score of 4 (unequivocal motor signs, ≥99% confidence) on the diagnostic confidence level question.

The Motor Scale has been found to have good internal consistency and good interrater reliability (Cronbach's alpha = 0.95, intraclass correlation coefficient = 0.94 respectively) (Huntington study group, 1996).

The TFC assesses ability to perform activities of daily living (ADLs) as well as instrumental activities of daily living (IADLs) such as engaging in productive work, managing finances, completing household chores, and ability to live at home. Higher scores indicate greater independence and less disease severity. Staging of disease progression can be determined from the TFC using the following cut scores: Stage I: 13-11, Stage II: 10-7, Stage III: 6-3, and Stage IV: 2-1, and Stage V: 0. Disease severity is considered to be mild if the individual with HD is in either Stage I or Stage II. Moderate severity is considered Stage III. Stage IV and V indicate severe disease pathology (Shoulson & Fahn, 1979). In the current study, 8 participants were considered to be in Stage I, 24 participants were in stage II, and 3 participants were in Stage III of the disease process.

Due to the difficulty of recruiting participants with HD and their spouses, control participants were included if they were ever married to, were currently married to, or have had a significant relationship with an individual with HD and were not at risk for developing the disease. Spouses or other individuals with significant relationships with a person with HD were recruited due to the increased likelihood of having similar social economic status, education, and home environment. This provided an advantage over community controls whose social factors may be very disparate from that of the participants with HD. Of the 38 control participants, 28

participants were married to someone with HD, 4 participants were a significant other of someone with HD, 4 participants were the unaffected parent of someone with HD, 1 participant was a gene negative child of an HD participant, and 1 participant was a gene negative niece of an HD participant.

After consenting to participate in the study, participants were administered a semi-structured interview (see Appendix A) in order to gather pertinent demographic information as well as identify potential medical or mental health diagnosis which may preclude their participation in the study and which may not have been included in their medical record. As such, exclusionary criteria for both the HD and control groups, included evidence of neurological disorders (other than Huntington's disease) such as stroke or a confirmed diagnosis of dementia and significant mental health disorders such as bipolar affective disorder or schizophrenia. Participant's cognitive ability was assessed prior to enrollment with the Montreal Cognitive Assessment (MoCA: Nareddine et al., 2005). A cutoff score of 21 or below was used to determine whether administration of a capacity to consent questionnaire was needed (Dalrymple-Alford et al., 2010); however, a cutoff score to determine eligibility to participate in the study was not predetermined. Of the total participants consented, 13 individuals (11 HD, 2 Controls) were administered the capacity to consent questionnaire to gauge their level of understanding of the consent form.

From the total of 87 subjects who participated in the study, an additional 14 (10 HD, 4 control) were excluded from the analyses. Ten participants with HD were excluded due to either very low MoCA and TFC scores (n = 5) or inability to complete the study task (n = 2). Two participants were excluded due to history of stroke (n = 1), or history of severe TBI (n = 2) which were not documented in medical record but were identified in interview. A total of four

control participants were excluded due to unknown genetic risk status (1), history of seizures (1), history of TIA (1), and history of ADHD (1).

Seventy-three participants were included in the final analyses, 35 individuals with HD and 38 controls. Participant demographics and clinical characteristics can be seen in Table 1. Of the HD participants, 42.86% were male. The control group was comprised of 52.63% male. The two groups did not differ in age or education. HD and control participants differed significantly on total MoCA score with participants with HD performing significantly worse than controls (HD: M = 23.34, SD = 3.12; control: M = 26.13, SD = 2.38; p = <0.001).

Table 1. Mean (Standard Deviation) of Group Demographics

	Huntington's disease (n = 35)		**Controls (n = 38)**		
	M (SD)	**Range**	**M (SD)**	**Range**	***p***
Gender (% male)	42.86		52.63		.48
Age (years)	52.06 (10.99)	27 - 71	54.7 (13.6)	19 - 73	.36
Education (years)	14.23 (2.09)	12 - 19	14.05 (2.51)	11 - 20	.75
MoCA	23.34 (3.12)	18 - 29	26.13 (2.68)	21 - 30	< .001
Race/Ethnicity (%)					
White	97.14	-	97.37	-	-
Hispanic	2.86	-	2.63	-	-
Self-Reported Mental Health Diagnoses					
Depression (%)	48.57	-	21.05	-	
Anxiety (%)	25.71	-	18.42	-	
Clinical Characteristics					
CAG repeat length (n = 24)	43.71 (2.91)	39 - 52	-	-	-
Total Functional Capacity	9.17 (2.04)	5 - 13	-	-	-
UHDRS (n = 33)	28.45 (15.45)	2 - 60	-	-	-

Notes: MoCA = Montreal Cognitive Assessment, UHDRS = Unified Huntington's disease Rating Scale

Measures

Cognitive Screening Measure

Montreal Cognitive Assessment *(MoCA: (Nasreddine et al., 2005))*: The MoCA is a cognitive screening tool that was originally developed to identify individuals with Mild Cognitive Impairment (MCI). The screening measure is designed to quickly assess the cognitive domains of short-term memory, visuospatial abilities, executive functions, attention, working memory, and language abilities. In addition, orientation to time and place is assessed. Administration of the MoCA takes approximately 10 minutes and the final score is based on total points attained out of a maximum of 30 points. A score of 26 (25 or below) has been reported in the literature as a cutoff score to indicate cognitive impairment. The MoCA has been shown to have good sensitivity (90%) and specificity (87%) in detecting MCI (Nasreddine et al., 2005). Studies have also shown that the MoCA is an adequate and may even be a more sensitive screening tool for cognitive impairment in HD compared to the MMSE (Videnovic et al., 2010; Gluhm et al, 2013).

Prospective Memory Task

PM Lexical Decision Making Task: The PM Lexical decision (PMLD) task was administered on a MacBook laptop using the computer program, SuperLab (Abboud, 1999). Three separate PM motivational blocks were administered to all participants. All participants received each of the three motivational blocks. Separate instructions were provided for each of the motivational blocks. Instructions for these blocks are provided below. The three motivational blocks were Neutral (i.e., no loss or gain), Monetary Reward, and Monetary Loss. All participants received the Neutral block first followed by either the Monetary Reward or Monetary Loss block which were presented to subsequent participants in a counterbalanced order. Each PM motivational

block included 70 items: 30 words, 30 non-words, and 10 PM cues of one of three semantic categories (i.e. animals, clothing, and food). The three PM semantic category targets were counterbalanced across the three PM motivational blocks so that no one semantic category cue was always associated with any one of the motivational blocks (e.g. animal PM targets were not consistently associated with the Neutral block). The words and non-words were randomly distributed in each list; however, word list order was consistent across participants. The words or non-words appeared one at a time on the screen separated by a "plus" symbol. The 10 PM cues (17% of total items) appeared in a pseudorandom order, with PM cues never appearing as the first item and never appearing as consecutive items. In order to adjust for level of difficulty, the next word did not appear until the participant made a response. Accuracy and reaction times were collected for each item.

To create the three 70 item motivational blocks comprised of 30 words, 30 nonwords, and 10 PM semantic target words, 90 common one to two syllable words were selected from the Affective Norms for English Words (ANEW) (Bradley & Lang, 1999) word list. Words were either one to two syllables and between five and seven letters in length. The final three word lists were equated regarding frequency and valance. Ninety orthographically regular non-words were created from the selected words. The thirty prospective memory (PM) target words were also one to two syllables and five to seven letters in length and were derived from one of three semantic themes: animals, clothing, and food.

Instructions for the Prospective Memory Task, Neutral Condition:

> "Later you are going to see a string of letters presented one at a time. Your task is to decide as quickly and accurately as possible whether the string of letters represents a word or a non-word.

If the string of letters is a word, you are to press the "Green" key, if it is a non-word, you are to press the "Red" key. Once you press a key, the word or non-word will disappear and a new string of letters will appear.

However, if you see a word that refers to an Animal such as cat or bird, you should press the "Yellow" key. It is important to remember that every time you see an Animal word, you have to press the "Yellow" key.

Do you have any questions? I will not be able to remind you which key to press later."

Instructions for the Prospective Memory Task, Reward Condition:

"Later, you will see another block of items and will continue to press either the "Green" key if you see a word or the "Red" key if you see a non-word as quickly and accurately as possible.

However, if you see a word that refers to Clothing such as hat or boots, you should press the "Yellow" key.

During this task, you have the opportunity to earn up to $5 if you remember to press the "Yellow" key every time you see a Clothing word.

For every Clothing word that you respond correctly to, you will *earn* a percentage of the $5. If you respond correctly to all the Clothing words, then you will receive the full $5."

Instructions for the Prospective Memory Task, Loss Condition:

"Later, you will see another block of items and will continue to press either the "Green" key if you see a word or the "Red" key if you see a non-word as quickly and accurately as possible.

However, this time, if you see a word that refers to Food such as cheese or peach, you should press the "Yellow" key.

During this task, you are being given $5 to remember to press the "Yellow" key every time you see a word that describes Food.

For every Food word you do not respond correctly to, you will *lose* a percentage of the $5. If you respond correctly to all Food words, then you will get to keep the full $5.

Do you have any questions? I will not be able to remind you which key to press later."

Self-Report Questionnaires

Barrett Impulsivity Scale-11 (BIS-11: (Patton & Stanford, 1995; Stanford et al., 2009)): The BIS-11 is a self-report measure of impulsivity. Self-report was obtained for all participants. For HD participants, informant-report was also obtained. The BIS-11 questionnaire has 30 statements that are responded to on a four-point scale with response types: "Rarely/Never", "Occasionally", "Often", and "Almost Always/Always." Scores range from 30 – 120. A score of 72 or above is considered to reflect a highly impulsive individual, whereas scores between 52 and 71 are considered to be within normal limits (Stanford et al., 2009). The BIS-11 is comprised of three secondary factors: motor, attentional, and non-planning. The reliability of the factors has been shown to be mostly acceptable, .59, .74, and .72 respectively (Patton & Stanford, 1995).

Prospective Retrospective Memory Questionnaire (PRMQ*:* (G. Smith, Del Sala, Logie, & Maylor, 2000): The PRMQ is a self-report questionnaire designed to assess common every day memory problems. The questionnaire is composed of 16 questions that are rated on a 5-point scale of: Very Often = 5, Quite Often = 4, Sometimes = 3, Rarely = 2, and Never = 1. The 16 questions address four different aspects of memory: prospective self-cued, prospective environmentally cued, retrospective self-cued, and retrospective environmentally cued. Higher scores on the questionnaire represent better-perceived prospective and retrospective memory. The PRMQ total score, the Prospective scale, and the Retrospective scale have been shown to have adequate reliability, 0.89, 0.84, and 0.80 respectively; however, a deviation in scoring (response scores were reversed from the original version) may have affected the reliability and

validity of the study. The PRMQ has been used before in a study investigating PM ability in HD (Nicoll et al., 2014).

Piloted Procedure

The study was administered to two healthy adults for the primary purposes of assessing the total time of the study, clarity of instructions, and proper order of measures. The volunteer's performance on the PM task evidenced limited variability in PM responses such that pilot participant 1 (male, 33 years old) scored 10, 9, and 9, on the Neutral, Reward, and Loss blocks respectively. Pilot participant 2 (female, 29 years old) scored 10, 10, and 8 on the Neutral, Reward, and Loss blocks respectively. However, based on these preliminary results, the task difficulty was not increased as there was concern that doing so might create possible floor effects for HD participants since even young normal participants made some errors on the task. Moreover, HD and Control participants for the study would likely be much older than piloted participants. Overall time of the task was also an important consideration in making the study feasible and being mindful of participant's time since many HD individuals travel a significant distance to USF and have other obligations on the study date (e.g., clinic appointment). Piloting indicated that the study could be completed within a reasonable amount of time (45 – 60 minutes) thus reducing participant burden.

Procedure

Participants were administered the MoCA cognitive screening tool. Capacity to consent was assessed if their score was 21 or below (Karlawish et al., 2013). The consent form was then reviewed with the participants and they were given the opportunity to read the consent form and

ask any questions they may have had prior to providing informed consent. After signing the consent form, participants were administered the practice lexical decision task which consisted of 20 items (10 words, 10 non-words) randomly presented. Following the practice administration, they were given the instructions for the Neutral PM block. They were then asked to rate their confidence on a scale of 1 – 10 of being able to remember those instructions later. Following completion of the Neutral block, participants then completed the BIS-11, a self-report questionnaire, to serve as a distractor task. Following completion of these tasks, the participants were then administered the task instructions for either the Monetary Reward or Monetary Loss block which was counterbalanced across participants. Again, the participants were asked to rate their confidence level in remembering the instructions. They were then administered another self-report questionnaire as a distractor task. When finished, the participants were administered the PM task (either the Reward or Loss block). This same process was then repeated for the last PM task block: administer the task instructions, rate confidence level, complete a self-report questionnaire, and complete PM task.

Following the third and last PM task, participant's recognition of the instructions was assessed. Participants were asked to freely recall which key they were supposed to hit if they saw a word, a non-word, and a word pertaining to a specific category. Participants were then administered the last self-report questionnaire, the PRMQ to complete. Following completion of the PRMQ, participants completed a "yes/no" recognition test to measure recall of the PM target cues (see Figure 2 below for diagram of procedure). Due to a computer entry error, the recognition test included 29 of the 30 PM cues (combined from all three conditions) as well as 30 foils. Foils were concrete words, 1 – 2 syllables, and 5 – 7 letters in length. Participants were then provided the full $10 regardless of performance for their participation in the study and

debriefed as to the nature of the study. Participants were then given the opportunity to ask questions and provide their impression of the task. Five participants opted to donate their compensation to the HD Research Fund at USF.

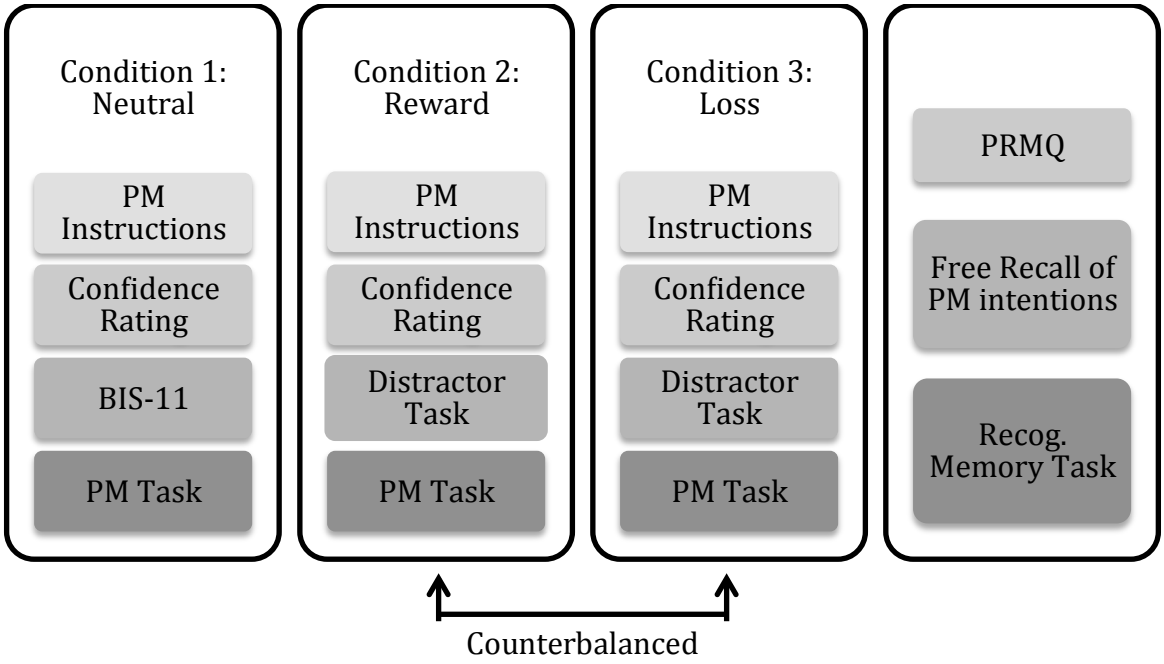

Figure 2. Diagram of study procedure

Analyses and Results

The Reward / Loss counterbalance was checked to see if there was a significant difference in performance between participants who were administered the Reward or Loss block first. A Mann-Whitney U test, did not find a significant difference in PM performance in either the Reward (p = .882) or Loss (p = .984) block between counterbalance groups (i.e., R/L, L/R).

Before performing analyses, the primary variables (i.e., number of correctly identified PM targets and questionnaire data) were reviewed for accuracy and significant outliers were identified (i.e., greater than 2 standard deviations). Variables of interest were next analyzed for normality. Acceptable levels of normality were found for all questionnaire data. However, for the primary variable of correctly identified PM targets, ceiling effects were observed and normality did not improve after removing significant outliers and transforming the variables. Outliers were replaced into the dataset to improve power and non-parametric analyses were then used for all analyses utilizing this variable as non-parametric analyses are less influenced by both outliers and non-normally distributed data. See Table 2 for descriptive statistics on correctly identified PM targets for each block and Table 3 for the number of participants per correctly identified PM targets. Frequency charts depicting number of correct PM responses by group and PM block can be found in Appendices B, C, and D.

In order to obtain an accurate reaction time per PM task per participate, reaction times for non-accurate responses were first excluded from the initial descriptive analysis in order to generate only the reaction time mean and standard deviations for accurate responses. Next,

reaction times above or below 3 standard deviations from the mean were excluded from each cell for each participant. Descriptive analyses were then rerun to find the median reaction time for each PM task per participant.

Table 2. Descriptive and Normality Statistics of PM Performance for each Block

	Huntington's Disease (n=35)			Control (n=38)		
	Median (IQ Range)	**S**	**K**	**Median (IQ Range)**	**S**	**K**
PM Target Correct						
Neutral	9 (8 – 10)	-2.04	4.61	10 (9 – 10)	-1.72	2.34
Reward	10 (8 – 10)	-1.98	2.96	10 (10 – 10)	-3.49	13.30
Loss	10 (9 – 10)	-2.71	7.98	10 (10 – 10)	-3.94	14.87
Total	28 (24 – 29)	-2.22	4.79	29 (27 – 30)	-2.01	4.02
PM Target Correct RT (msec)						
Neutral	1565.28 (1386.19 – 1994.91)	1.96	4.40	1207.62 (1081.85 – 1374.95)	3.80	19.14
Reward	1545.40 (1381.02 – 1856.27)	3.52	13.21	1179.50 (1078.95 – 1405.50)	4.48	24.14
Loss	1545.44 (1403.67 – 1898.41)	2.20	6.51	1202.70 (1069.98 – 1394.94)	4.62	25.01

Notes: PM = Prospective Memory, RT = reaction time, IQ = Interquartile; S = Skewness, K = Kurtosis

Table 3. Number of participants per correctly identified PM target cues

	Neutral		**Reward**		**Loss**	
Identified PM Cues	**HD**	**Control**	**HD**	**Control**	**HD**	**Control**
10	10	20	22	31	18	31
9	11	12	3	4	10	4
8	6	2	3	1	1	1
7	2	1	1	1	3	0
6	2	3	1	0	0	0
5	2	0	1	1	1	0
4	0	0	0	0	0	0
3	0	0	1	0	1	0
2	1	0	1	0	0	0
1	0	0	0	0	0	0
0	1	0	2	0	1	2
Total	35	38	35	38	35	38

Notes: PM = prospective memory, HD = Huntington's disease

The hypotheses were initially conceptualized using the performance on the three blocks of the PM task (Neutral, Reward, and Loss) as assessed by total number of correctly identified

PM targets as the primary dependent variable. As noted above, although multiple attempts at data transformation were attempted, none resulted in a distribution of PM task scores approaching normal and therefore, nonparametric statistics were used to test hypotheses with the number of correctly identified PM items as a variable. In addition, due to ceiling effects, additional analyses were run using the reaction time (RT) data as the primary dependent variable in applicable analyses. It was reasoned that RT may provide a more sensitive index of performance in the PM task. RT data were used only for hypotheses in which predictions were made for within group effects only rather than any between group effects as HD participants would likely be expected to have much slower motor responses than Control participants. See Table 2 above for descriptive statistics on RTs to the three blocks of the PM task.

The total score on the BIS-11 was calculated for self-reported ratings for all participants and informant-reported ratings for HD participants. The total score of the PRMQ as well as the two primary subscales: Prospective Memory and Retrospective Memory were also calculated for all participants. Tables 4 and 5 present the descriptive and normality statistics of the questionnaire data for the total sample and separately for each group.

Table 4. Descriptive and Normality Statistics of Questionnaires for Total Sample

Questionnaires	Mean (SD)	Range	Skewness	Kurtosis
BIS – 11: Total Score				
BIS-11 Self-Reported	62.38 (9.93)	39 – 87	0.15	-0.12
BIS-11 Informant-Reported	73.60 (8.87)	56 – 90	-0.29	-0.44
PRMQ				
PRMQ	55.94 (10.19)	32 – 74	-0.49	-0.06
Prospective Memory	26.87 (5.45)	14 – 37	-0.34	-0.35
Retrospective Memory	29.44 (5.08)	17 – 40	-0.48	0.19

Note: BIS-11 = Barrett Impulsivity Scale-11; PRMQ = Prospective Retrospective Memory Questionnaire

Table 5. Descriptive and Normality Statistics of Questionnaires by Participant Group

	Huntington's Disease Participants				Control Participants			
	Mean (SD)	**Range**	**S**	**K**	**Mean (SD)**	**Range**	**S**	**K**
BIS-11								
BIS-11 Self-Reported	65.74 (11.63)	44–93	0.32	-0.27	60.08 (8.60)	39–77	-0.26	-0.11
BIS-11 Informant	73.60 (8.87)	56–90	-0.29	-0.44	-	-	-	-
PRMQ								
Total PRMQ	51.00 (13.69)	22–80	-0.22	-0.17	59.37 (7.90)	41–74	-0.26	0.05
PM	24.29 (7.41)	9–40	-0.14	-0.37	23.32 (4.66)	18–37	-0.27	-0.16
RM	26.71 (6.65)	12–40	-0.37	-0.19	31.05 (3.73)	22–38	-0.11	0.06

Note: PM = Prospective Memory, BIS-11 = Barrett Impulsivity Scale-11, RM = Retrospective Memory, S = Skewness, K = Kurtosis

Main Analyses

Hypothesis 1: Huntington's disease participants will perform worse on the Neutral (i.e., no loss or gain) block of a PM task than healthy control participants as evidenced by fewer correct responses to PM cues.

A Mann-Whitney U Test revealed a significant difference in the PM performance between groups on the Neutral block indicating that participants with HD (*mean rank* = 30.91, *n* = 35) performed significantly worse than the Control participants (*mean rank* = 42.61, *n* = 38), *U* = 452, *z* = -2.48, *p* = .013, *r* = -.29.

Hypothesis 2: PM performance will differ across participants.

a. *Huntington's disease participants will demonstrate better performance on a PM task during the Monetary Reward block compared to a Monetary Loss block or a Neutral block.*
b. *Healthy control participants will demonstrate increased PM performance when presented with a Monetary Loss PM block relative to a Monetary Reward or Neutral PM block.*

The variables representing the correctly identified PM cues for the Neutral, Reward, and Loss blocks were non-normally distributed despite multiple attempts at data transformation. As such the Friedman Test, a non-parametric analysis, was used to assess the PM performance within groups. Within the HD participant group, the results of the Friedman Test indicated that there was a statistically significant difference in correctly identified PM cues across the three blocks χ^2 (2, n = 35) = 7.43, p = .024. Planned follow-up analyses using the Wilcoxon Signed Rank test did not reveal a significant difference between the Neutral (*mean rank* = 13.00) and Reward (*mean rank* = 17.67) block, z = -1.02, p = .308, r = -.17 or between the Loss (*mean rank* = 7.85) and Reward (*mean rank* = 11.56) block, z = -0.31, p = .756, r = -.05. However, the Wilcoxon Signed Rank revealed a trending significance difference between the Neutral (*mean rank* = 10.94) and Loss (*mean rank* = 13.40) blocks, z = -1.95, p = .051, r = -.33 suggesting that there was possibly better performance on the Loss block than the Neutral block.

The results of the Friedman Test indicated that within the Control group there was a statistically significant difference in correctly identified PM cues across the three blocks, Neutral, Reward, and Loss, χ^2 (2, n = 38) = 10.667, p = .005. Planned follow-up analyses using the Wilcoxon Signed Rank test indicated that the Control group performed significantly better on the Loss (*mean rank* = 13.10) block than on the Neutral (*mean rank* = 11.03) block, z = -2.04, p = .041, r = -.33. Also, the Wilcoxon Signed Rank revealed a trending difference between the Neutral (*mean rank* = 9.69) and Reward (*mean rank* = 13.75) blocks, z = -1.92, p = .055, r = -.31 suggesting that the Control group performed nonsignificantly better on the Reward block than the Neutral block. There was not a significant difference between the Reward (*mean rank* = 7.21) and Loss (*mean rank* = 7.79) block, z = .13, p = .898, r = -.02. See Table 6 below for a table of all comparisons with corresponding mean ranks and significance values.

Additional Analyses: Reaction Time

As mentioned earlier, reaction time (RT) data was also used as a dependent variable in applicable analyses due to potential ceiling effects in the PM task performance data. The variables representing the RT for correctly identified PM cues during the Neutral, Reward, and Loss blocks were broadly non-normally distributed despite using a log transformation. As such, the Friedman Test was again used to assess RT for correctly identified PM cues within groups. The results of the Friedman Test indicated that within the Control group there was not a statistically significant difference in RT across the three blocks, Neutral, Reward, and Loss blocks, χ^2 (2, n = 36) = .72, p = .697. Similarly, within the HD participant group, the results of the Friedman Test again did not indicate a statistically significant difference in reaction times across the three blocks χ^2 (2, n = 31) = .58, p = .748.

Table 6. Prospective memory (PM) block comparisons by group

	PM Blocks	**Mean Ranks**	*z*	*p*
Huntington's disease	Control	13.00	-1.02	.308
	Reward	17.67		
	Control	10.94	-1.95	.051
	Loss	13.40		
	Reward	11.56	-.31	.756
	Loss	7.85		
Controls	Control	9.69	-1.02	.055
	Reward	13.75		
	Control	11.03	-1.95	.041
	Loss	13.10		
	Reward	7.21	-.31	.898
	Loss	7.79		

Note: PM = prospective memory

Hypothesis 3: Impulsivity as reported on the BIS-11 will be strongly related to PM performance.

a. *Higher endorsements of impulsive traits, as reported on the BIS-11, will be associated with worse performance on the Neutral PM block for all participants.*
b. *Higher endorsements of impulsive traits, as reported on the BIS-11, will be associated with a higher number of accurate responses to monetary Reward PM cues.*

The relationship between BIS-11 total score for each of the PM blocks: Neutral, Reward, and Loss was investigated using Spearman Rank Order Correlations for the total sample of combined HD and Control participants as well as for each group separately. Results of the analyses did not reveal a significant correlation between any of the variables. See Table 7 for results.

Additional Analyses: Correlations between BIS-11 and PM performance by group and between the BIS-11 informant report and total PM performance.

Given that informant report on the BIS-11 was obtained for HD participants, the relationship between BIS-11 total score and each of the PM blocks was again investigated for HD participants only. However, no significant correlations were found between the BIS-11 informant report and total PM performance in the HD group.

Table 7. Spearman Rank Order Correlations between BIS-11 Self-Report and PM performance

	Neutral PM	Reward PM	Loss PM
Total Sample (N=73)			
BIS-11 Total	-.09	.06	.03
Huntington's disease (N=35)			
BIS-11 Total	-.10	.17	.17
BIS-11 Informant Report (N=25)	.34	-.11	-.17
Controls (N=38)			
BIS-11 Total	.14	.14	-.04

Notes: Prospective memory (PM), BIS-11 = Barrett Impulsivity Scale-11

Hypothesis 4: The PRMQ will be differentially associated with performance on the behavioral measure of PM for HD and Controls.

a. *There will be a positive relationship between Control participants' total score on the PRMQ and overall PM performance, in that higher scores on the PRMQ will correlate with greater accuracy to PM cues.*

b. *In HD participants, a significant relationship would not be expected between the PRMQ and accuracy measures of PM.*

The relationship between total PM performance across the three conditions and self-reported prospective and retrospective memory as measured by the PRMQ was investigated using Spearman rank order correlation analysis due to the non-normally distributed total PM performance variable. Results of the analysis revealed a trending, positive correlation between total PM performance and total PRMQ in the Control participants, $r_s = .30$, $n = 38$, $p = .072$. Within the HD participant group, no significant relationships were found between total PM performance and the PRMQ. See Table 8 for correlation results.

Table 8. Spearman Rank Order Correlations between PM total score and PRMQ for Control and HD participants

	Total Prospective Memory Performance
Control Participants	
PRMQ Total	.30^
PM Total[E]	.28^
RM Total[E]	.33*
HD Participants	
PRMQ Total	.02
PM Total[E]	-.05
RM Total[E]	<.01

Notes: HD = Huntington's disease; PRMQ = Prospective Retrospective Memory Questionnaire, PM = Prospective memory, RM = Retrospective memory, ^ trending significance level, * $p < .05$, [E] Exploratory analyses

Hypothesis 5: Retrospective recognition memory performance will not differ between HD and Controls, but will be differentially associated with PM performance for these groups.

a. *There will be no difference in retrospective recognition memory performance between HD and Controls.*
b. *Retrospective recognition memory performance will be associated with PM performance for Control participants.*
c. *Retrospective recognition memory performance will not be associated with PM performance for HD patients.*

On a recognition task in which the participants were instructed to press either a "Yes" or "No" button to indicate whether the word presented was a PM target word, a Mann-Whitney U Test revealed a significant difference between groups indicating that the Control group (*mean rank* = 41.47, $n = 37$) recognized significantly more PM target words than individuals with HD (*mean rank* = 31.24, $n = 35$), $U = 463.50$, $z = -2.34$, $p = .019$, $r = -.28$.

The relationship between total PM performance across the three conditions and the number of correct responses to PM target cues on a "yes / no" recognition task was investigated using two separate Spearman rank order correlation analysis due to both variables beings non-normally distributed. Results of the first analysis revealed a strong, positive correlation between total PM performance and percentage of correct responses to PM cues in the Control participants, $r = .41$, $n = 37$, $p = .011$. Within the HD participant group, a strong, positive correlation was also found between total PM performance and the percentage of correct responses to PM cues, $r = .54$, $n = 35$, $p = .001$.

Additional Analyses: Free recall of Response Keys and Confidence Ratings for PM Conditions

On a free recall task asking the participant what each of the response keys (i.e., green, red, and yellow) were associated with (i.e., words, non-words, or PM targets), there was a 100% accuracy in response in both the Control group and in the HD participant group. Therefore, both groups clearly understood the task and were able to retain the instructions for the task throughout.

Participants were also asked to rate their confidence on a scale of 1 – 10 of their ability to remember instructions for each of the three PM blocks immediately after instructions were administered for each block. Total confidence ratings in the ability to recall PM task instructions were compared between the two participant groups. A Mann-Whitney U Test revealed a significant difference in total confidence ratings between HD (*mean ranking* = 27.70, $n = 35$) and control participants (*mean ranking* = 45.57, $n = 38$), $U = 339.50$, $z = -3.71$, $p < .001$, $r = -.43$.

Discussion

The purpose of the present study was to build upon previous research and further investigate prospective memory (PM) ability in a sample of individuals with Huntington's disease (HD) as compared to healthy Controls. In addition, since impulsive behaviors have been reported in individuals with HD (Paulsen et al., 2001) and impulsive behaviors have also been associated with poorer PM performance (Chang & Carlson, 2014; Cuttler, O'Connell, & Marcus, 2016) this study also sought to examine the influence of self-reported impulsivity on a PM task in this population. Lastly, since PM ability has been demonstrated to be worse in individuals with HD compared to healthy Controls (Nicoll et al., 2014), this study investigated whether incentives, either monetary reward or avoidance of a monetary loss, would significantly alter PM performance.

Prospective Memory Performance in Huntington's Disease

Several studies have found significant differences in PM between clinical populations such as Parkinson's disease and healthy Control populations (Costa et al., 2008; Costa et al., 2015; Katai et al., 2003); however, only one study, to this author's knowledge, has specifically investigated PM in the HD population (Nicoll et al., 2014). Nicoll and colleagues found that the HD participants performed significantly worse than healthy Controls on a time-based PM task and were at a trend level difference on an event-based PM task. Consistent with Nicoll and colleagues' findings, HD participants in the present study performed significantly worse on the Neutral (i.e., no reward or loss incentive) block than the healthy Control participants. However,

the data indicates that the majority of both groups were able to correctly identify all, or nearly all, PM target cues (> 9 correctly identified PM cues: HD = 21, Control = 32). This suggests that individuals with HD may be more successful at completing PM tasks in their daily lives if the tasks are simple and have an easily identifiable PM cue as opposed to PM tasks that may require greater recruitment of executive functions, i.e., a time-based PM task.

Effects of Motivation on Prospective Memory

A unique aspect of the current study, which has not been investigated to date, sought to further investigate PM in Huntington's disease participants by examining the influence of motivation (e.g., sensitivity to reward) on PM when compared to healthy controls. This hypothesis was driven by the Motivational-Cognitive Model of PM proposed by Penningroth and Scott (2007) which suggested that individuals who viewed a PM intention as having more importance (e.g., potential monetary gain or lose) will use both more effortful and automatic processing while maintaining the PM intention over time until it can be fulfilled. Studies investigating this model found that participants evidenced better PM performance for both conditions of monetary loss and gain in PM tasks relative to a neutral PM task (e.g. Cook et al., 2015). Furthermore, in normal adults, there is a large body of research in decision-making that supports the theory that adults tend to be more loss averse than reward driven (Anbarci, Arin, Kuhlenkasper, & Zenker, 2017; Tversky & Kahneman, 1991; Wu, Van Dijk, Aitken, & Clark, 2016).

Following this research, it was hypothesized that the healthy Controls in this study would evidence better PM performance on the Loss block relative to the Neutral block. Consistent with the previously reviewed studies, Control participants evidenced better PM performance on the

monetary Loss block compared to the Neutral block. However, while the Control participants were predicted to have better performance on the Loss block, the participants with HD were predicted to perform better on the Reward block relative to the Neutral block. Recent research has found that individuals with disorders of the basal ganglia and the frontal-striatal circuitry are more reward sensitive (Balconi, Angioletti, Siri, Meucci, & Pezzoli, 2018; Balodis et al., 2012; Hikosaka et al., 2014; Wang et al., 2017). Furthermore, it is widely viewed that the neurotransmitter, dopamine, is a primary component of learning and reward processing (e.g. Caravaggio et al., 2018) and studies have reported on the increased release of dopamine in individuals with HD (Cepeda et al., 2014). However, the results of the current study did not find that the participants with HD evidenced better PM performance on the Reward block compared to the Neutral block. In fact, there was a trending difference between the Loss block and the Neutral block within the HD group, which was similar to the significant findings within the Control group who had better performance on the Loss block relative to Neutral block.

While this finding does not follow the original hypothesis of the current study, the results are in line with research by Minati et al. (2011) who found that both PD and HD patients performed similarly to controls on a mixed gambling decision task. Specifically, all participants weighed potential losses more than potential gains, and overall, participants ended with a positive amount of money. This finding highlighted the role of the ventral striatum during anticipation of rewards (Hikosaka et al., 2014; Knutson et al., 2001). The striatum, and in particular the caudate, is the primary area of the basal ganglia that is initially affected in HD. As such, individuals with HD may not be receiving the same increase in striatal activation when anticipating rewards. Furthermore, previous study paradigms often provided feedback on losses or gains after each trial. However, in the current study, feedback was not provided during the

PM task as to whether the participant correctly identified a PM target cue. The decision to exclude immediate feedback during the task was made in order to limit the amount of external cues that may have impacted the participant's ability to spontaneously recognize and respond appropriately to a PM cue.

Prospective Memory and Impulsivity

While the literature suggests that individuals may have increased motivation to complete prospective memory (PM) intentions associated with a monetary incentive (either reward or loss), research has also found an association between impulsivity and reward seeking behavior (Clark & Dagher, 2014; Dissabandara et al., 2014), and therefore, it was hypothesized that higher rates of impulsivity would be associated with better PM performance on the Reward PM block. However, the literature also suggests that there is a negative relationship between impulsivity and PM. This has been found with both self- reported impulsivity and PM ability (e.g., Cuttler et al., 2016; Cuttler et al., 2014) as well as with worse performance on aspects of PM (e.g., planning phase, time-based cues) in individuals with disorders associated with impulsivity such as ADHD (Altgassen, Kretschmer, & Kliegel, 2014; Fuermaier et al., 2013). As such, self-reported rates of impulsivity were predicted to be negatively associated with the Neutral PM block for all participants. However, no significant relationships were found between self-reported impulsivity and PM performance. This non-finding may be attributed to the lack of high impulsivity reported by participants. A score of 72 or higher on the BIS-11 is considered to reflect a highly impulsive individual (Stanford et al., 2009); however, the mean score of self-reported impulsivity for the entire study sample ($M = 62.38$) reflected a level of impulsivity that was within normal limits. Furthermore, each group's self-reported impulsivity was also

considered within normal limits (HD: *M* = 65.74, Control: *M* = 60.08) and when analyzed separately, impulsivity was again not significantly correlated with PM performance. It is possible that a lack of high impulsivity in the study sample, made it difficult to detect a significant relationship between impulsivity and PM performance.

In that research has found that some individuals with HD lack awareness of their symptoms (Hoth et al., 2007; Sitek et al., 2012) and thus may underreport behaviors, an additional correlational analysis was run to investigate the relationship between the informants' ratings on the BIS-11, which was indicative of high impulsivity (*M* = 73.60) per Stanford et al. (2009), and PM performance. However, despite reflecting high impulsivity, the informants' report did not correlate with the HD participants PM performance. In addition, the type of PM cue (i.e., event-based, focal) used in the current study also required far less monitoring of the environment and attentional resources, which are more impaired in individuals with higher levels of impulsivity (Dickman, 1993; Evenden, 1999). As such the attentional demands may not have reached a level at which they would have been negatively impacted by impulsive traits in the participants with HD.

Awareness of Prospective Memory Ability

The relationship between self-reported prospective and retrospective memory, as measured by the PRMQ, and total PM performance was also investigated. Specifically, the healthy control group was hypothesized to have a positive relationship between the PRMQ and total PM performance, whereas a relationship between the PRMQ and PM performance was not expected in the HD group. This hypothesis was driven by previous research that has found that some individuals with HD lack awareness of their symptoms including motor (Vitale et al.,

2001) and functional abilities (Hoth et al., 2007). These research findings have significant implications for the ability of individuals with advancing disease to safely live independently. Furthermore, recent research has found that the self-reported PM ability of participants in clinical populations (e.g., HD and PD) is not correlated with their performance on a behavioral task (Nicoll et al., 2014; Pirogovsky et al., 2012) lending further support that individuals with some neurodegenerative disorders may lack awareness of their deficits.

As such, the current study hypothesized that individuals with HD would also lack awareness of their PM abilities and thus their self-reported PM abilities would not be correlated with their PM performance. As expected, the HD participants' self-report of prospective and retrospective memory was not significantly correlated with their performance on the PM task. However, there was a trend level finding of a positive association between the healthy controls' self-reported PM ability and their performance on the PM task. This suggests that relative to participants with HD, the healthy controls may have better awareness of their PM abilities.

In an effort to get an in-the-moment assessment of participant's confidence in their ability to correctly recall the PM intentions at a later point in time, participants were asked to rate their confidence level on a scale of 1-10 after receiving each PM task instruction. Interestingly, a Mann-Whitney U Test revealed a significant difference between the total confidence ratings between HD (*mean rank* = 27.70, $n = 35$) and control participants (*mean rank* = 45.57, $n = 38$), $U = 339.50$, $z = -3.71$, $p < .001$, $r = -.43$ indicating that the healthy controls participants were much more confident in their ability to remember task instructions than the participants with HD.

Recognition of the Prospective Memory Intentions

While PM performance was predicted to be worse in the participants with HD than in the control participants, their recognition memory for the PM task was predicted to be the same for both groups. Studies have demonstrated that recognition memory remains relatively preserved in HD particularly when compared to individuals with amnestic disorders (Butters, Sax, Montgomery, & Tarlow, 1978) or cortical neurodegenerative diseases (Kamminga, O'Callaghan, Hodges, & Irish, 2014). Furthermore, some studies investigating PM ability in neurodegenerative disorders involving the basal ganglia such as PD and HD have found that recognition memory of the PM task intentions is relatively similar to that of the control participants particularly for tasks that may be less cognitively demanding (e.g. Erin R Foster et al., 2013; Katai et al., 2003; Nicoll et al., 2014). Conversely, some studies have found the recognition of the PM task to be significantly worse than the control participants (Costa et al., 2008; Raskin et al., 2011). In the present study, participant groups differed significantly in a "Yes/No" recognition test of the PM target words with the HD participant group correctly identifying fewer PM target words than the control group. However, this recognition task assumed that participants would be able to recognize the PM target words by applying the knowledge of the three categories of the PM targets: food, clothing, and animals. As such, this task may have required higher order cognitive abilities in order to perform well. Conversely, on a simple free recall task of study intentions (e.g., "When were you supposed to press the yellow key?"), there was a 100% response accuracy rate for all participants. This suggests that participants retained the PM intention and task instructions; however, other factors such as divided attention between the ongoing task and monitoring for PM target cues may have impacted PM performance in the HD participant group.

In addition, it was hypothesized that the healthy controls' performance on the recognition task would be positively correlated with their PM performance. A significant relationship between the recognition task and PM performance was not expected in the HD group. However, a significant, positive relationship was also found between performance on the recognition task and PM task performance for both the healthy controls and the HD participants.

Limitations

This study is not without its limitations. First, the sample size was limited due to various challenges in recruiting participants in the study, and as such, the analyses may be underpowered. In addition, the individuals who participated in the study may have been a unique sample in that not at all individuals with HD seek medical treatment or are motivated to come to their appointments. For example, the individuals who had initially agreed to participate in the study, but did not show for the appointment may have differed from the study participants in a meaningful way (e.g., possibly worse prospective memory). Also, the individuals who participated in the study may have had higher levels of motivation than other individuals with HD which may have contributed to their PM task performance. Furthermore, the healthy control participants were recruited due to their relationship with an HD participant. Spouses or significant others of the HD individuals were recruited in an effort to compare individuals with similar characteristics such as social environment, social economic status, and education. While in this study, the control participants, who were a spouse, significant other, or a gene negative family member, allow for better comparisons to be made between gene positive and gene negative individuals, they may not be truly representative of a healthy control population.

In regard to participant characteristics, another potential limitation of the study was the relatively normal rates of self-reported impulsivity on the BIS-11. However, impulsivity is also considered a complex construct that is often considered to be comprised of several components such as lack of planning (or acting without thinking), lack of persistence, sensation seeking, and urgency (G. T. Smith et al., 2007; Stanford et al., 2009). In fact, previous studies have found that subscales of the BIS-11, such as the motor and nonplanning, were negatively correlated with PM performance (Cuttler et al., 2016; Cuttler et al., 2014). However, in the present study, to reduce Type I error, correlations among the BIS-11 subscales and PM performance were not investigated. Future studies, with an increased sample size, might investigate these relationships between the components of impulsivity and PM. The relatively normal rates of self-reported impulsivity may also have contributed to the nonsignificant relationships and it may be that a wider range including more extreme levels of high impulsivity are needed to influence PM performance. Without this, it may not have been possible to adequately investigate whether impulsivity was associated with PM performance.

Although the informants' report on the BIS-11 reflected high levels of impulsivity, this particular sample of individuals with HD may have had better insight into their personal characteristics thus suggesting that the informants may have over reported impulsive characteristics. In support of this, the HD group consistently reported lower confidence in their ability to recall the PM instructions at a later time compared to the Control group. The HD group also reported more prospective and retrospective memory failures on the PRMQ during their daily lives than the Control participants. Even though self-reported prospective and retrospective memory failures in the HD group was not significantly correlated with their PM performance, they still performed worse on the Neutral PM block than the Control participants

suggesting that the HD participants had a degree of insight into their abilities. In order to further investigate the effects of impulsivity on PM performance in HD, future studies may consider pre-selecting participants with higher self-or informant-reported rates of impulsivity.

The lexical decision task has been used in several studies to assess PM performance (Bugg et al., 2013; Cook et al., 2015; Marsh, Hicks, & Cook, 2005; Scullin et al., 2010). However, the study paradigm may have contributed to another limitation of the study such that the PM task produced ceiling effects and was non-normally distributed in both the HD and control participants (see Appendices C – E for frequency data). Although there was generally more variability in the number of correctly identified PM cues in the HD group than in the Control group, both participant groups evidenced a large number of participants who correctly identified 7 or greater PM cues out of a possible 10. The high rate of correct responding may be due to the type of PM cue chosen for this study. In order to reduce the cognitive burden on participants, focal, event based PM cues (versus non-focal, event based cues) were used. Focal, event-based cues do not require the same effort processing as non-focal cues that rely more on the prefrontal cortex to monitor the environment (McDaniel et al., 2013). Instead, increased activation of the medial temporal gyrus has been observed during recognition of focal cues (McDaniel et al., 2013). In HD, the striatum and thus the fronto-striatal circuit is the primary area of neuronal loss with the temporal lobes being relatively spared (Walker, 2007). Based on the neuropathology of HD, research would suggest that individuals with HD should have an easier time identifying focal cues rather than non-focal cues. Furthermore, research has shown that while speech production may be impacted as Huntington's disease progresses, other language abilities such as recognizing word associations remain intact (Paulsen, 2011). As such, the sematic nature of the PM target cue may have played to the cognitive strengths of the

participants with HD. Future studies may want to investigate whether increasing the cognitive challenge using non-focal PM cues (e.g., identifying certain phonemes or number of syllables) rather than focal cues (e.g., words that are animals) may result in more variability in the PM performance and thus potentially more robust motivation effects from incentives.

Furthermore, future studies may want to formally assess whether the monetary incentive truly motivated performance on the PM tasks. Qualitatively, during debriefing, 5 participants verbally indicated that they were not motivated by the money and as such, chose to donate their money to the HD Research Fund at USF. Additionally, other participants stated that they did not believe they were going to be receiving actual money while other participants stated that $10 was not enough money to feel motivated. In order to increase the salience of the incentive, future studies may consider possibly showing the participants the money first, so that they know that it is a true incentive. Studies might also purchase gift cards with higher monetary value and use a raffle ticket system (e.g., 1 raffle ticket per correct PM response).

Future Directions

There is a large body of research that has established PM deficits in individuals with neurodegenerative diseases as well as growing evidence of PM deficits specifically within the HD population. Despite the study's limitations, it replicates previous research showing that individuals with HD evidence worse PM performance than healthy controls. Furthermore, as expected, the Control group evidenced better PM performance on the Loss block relative to the Neutral block indicating that the Control group was more motivated to avoid losses than earn rewards, which is consistent with previous research. While the participants with HD did not

perform better on the Reward PM block relative to the Neutral block as expected, their performance on the Loss block relative to the Neutral block was trending towards significance.

While offering incentives may increase motivation towards completing the PM intention, it is important to understand what type of incentive is important to the individual. In the present study, some individuals indicated that they might have been more motivated by a food incentive rather than a monetary incentive. Furthermore, research has shown that motivational factors that are meaningful to the participant can improve PM performance (Walter & Meier, 2014). As such, a future area of study should investigate whether self-selected reward or incentive in an HD population may further improve PM memory.

Avenues of future research should investigate specific strategies that will help support successful PM ability in the daily lives of individuals with PM. Other researchers have successfully improved PM ability in everyday life by using various interventions such as aerobic and resistance training (Cuttler, Connolly, LaFrance, & Lowry, 2018), mental or verbal rehearsal of the PM intention encoding strategy (Erin R. Foster, McDaniel, & Rendell, 2017), and technology aids such as electronic calendars and cell phones (Cruz, Petrie, Goudie, Kersel, & Evans, 2016; El Haj, Gallouj, & Antoine, 2017; Ferguson, Friedland, & Woodberry, 2015). Likewise, a logical next step in PM research in HD should generalize results found in the laboratory to real life situations. In particular, investigating whether an exercise routine may be an effective way to boost PM performance may be relevant due to the potential for secondary gains such as improved balance, muscle tone, and emotion regulation.

Another avenue of research may include a cognitive training program to help individuals with HD learn how to better monitor the environment for PM cues. As mentioned earlier in the discussion, one of the differences in this study relative to other incentive studies was that

performance feedback during the PM tasks was not utilized. However, providing feedback to participants may assist in error monitoring and fostering the learning of new strategies to better recognize PM cues in the environment. Future studies might look at administering multiple PM trials with providing feedback after each one as well as offering an incentive to improve their PM performance.

Continuing to look at ways to improve PM ability in individuals with HD is an important avenue of research. PM memory is associated with many activities of daily living such as remembering to pay bills, take medication at the appropriate time, and recalling day-to-day intentions such as remembering to do laundry or remembering that one needs to make a doctor's appointment. In that HD is a unique neurodegenerative disease that tends to negatively affect individuals in the prime years of their life, studying ways to improve their ability to remain independent is crucial. In fact, the fear of losing one's independence due to worsening disease symptoms has been associated with thoughts of suicide in individuals with HD (Novak & Tabrizi, 2010; Paulsen, Hoth, Nehl, Stierman, & Group, 2005). Researching ways to help support PM ability in individuals with HD is important to helping them remain independent for as long as possible.

References

Abboud, H. (1999). SuperLab Pro: User manual (version 2.0)[computer software]. *San Pedro: Cedrus Corporation*.

Altgassen, M., Koch, A., & Kliegel, M. (2014). Do inhibitory control demands affect event-based prospective memory performance in ADHD? *Journal of attention disorders*, 1087054713518236.

Altgassen, M., Kretschmer, A., & Kliegel, M. (2014). Task dissociation in prospective memory performance in individuals with ADHD. *Journal of attention disorders, 18*(7), 617-624.

Anbarci, N., Arin, K. P., Kuhlenkasper, T., & Zenker, C. (2017). Revisiting loss aversion: Evidence from Professional Tennis. *Journal of Economic Behavior & Organization*. doi:https://doi.org/10.1016/j.jebo.2017.10.014

Anderson, K. E., & Marder, K. S. (2001). An overview of psychiatric symptoms in Huntington's disease. *Current psychiatry reports, 3*(5), 379-388.

Bäckman, L., & Farde, L. (2001). Dopamine and cognitive functioning: brain imaging findings in Huntington's disease and normal aging. *Scandinavian journal of psychology, 42*(3), 287-296.

Balconi, M., Angioletti, L., Siri, C., Meucci, N., & Pezzoli, G. (2018). Gambling behavior in parkinson's disease: Impulsivity, reward mechanism and cortical brain oscillations. *Psychiatry research*. doi:10.1016/j.psychres.2018.03.041

Balodis, I. M., Kober, H., Worhunsky, P. D., Stevens, M. C., Pearlson, G. D., & Potenza, M. N. (2012). Diminished frontostriatal activity during processing of monetary rewards and losses in pathological gambling. *Biological psychiatry, 71*(8), 749-757.

Balodis, I. M., & Potenza, M. N. (2015). Anticipatory reward processing in addicted populations: a focus on the monetary incentive delay task. *Biological psychiatry, 77*(5), 434-444.

Bari, A., & Robbins, T. W. (2013). Inhibition and impulsivity: behavioral and neural basis of response control. *Progress in neurobiology, 108*, 44-79.

Beck, A., Schlagenhauf, F., Wüstenberg, T., Hein, J., Kienast, T., Kahnt, T., . . . Heinz, A. (2009). Ventral striatal activation during reward anticipation correlates with impulsivity in alcoholics. *Biological psychiatry, 66*(8), 734-742.

Bickel, W. K., Jarmolowicz, D. P., Mueller, E. T., Gatchalian, K. M., & McClure, S. M. (2012). Are executive function and impulsivity antipodes? A conceptual reconstruction with special reference to addiction. *Psychopharmacology, 221*(3), 361-387.

Bonelli, R. M., & Cummings, J. L. (2008). Frontal-subcortical dementias. *The neurologist, 14*(2), 100-107.

Bradley, M. M., & Lang, P. J. (1999). *Affective norms for English words (ANEW): Instruction manual and affective ratings*. Retrieved from

Brandimonte, M. A., Ferrante, D., Bianco, C., & Villani, M. G. (2010). Memory for pro-social intentions: When competing motives collide. *Cognition, 114*(3), 436-441.

Braver, T. S., Barch, D. M., Keys, B. A., Carter, C. S., Cohen, J. D., Kaye, J. A., . . . Mumenthaler, M. S. (2001). Context processing in older adults: evidence for a theory relating cognitive control to neurobiology in healthy aging. *Journal of Experimental Psychology: General, 130*(4), 746.

Buckholtz, J. W., Treadway, M. T., Cowan, R. L., Woodward, N. D., Benning, S. D., Li, R., . . . Shelby, E. S. (2010). Mesolimbic dopamine reward system hypersensitivity in individuals with psychopathic traits. *Nature neuroscience, 13*(4), 419-421.

Bugg, J. M., Scullin, M. K., & McDaniel, M. A. (2013). Strengthening encoding via implementation intention formation increases prospective memory commission errors. *Psychonomic bulletin & review, 20*(3), 522-527.

Burgess, P. W., Gonen-Yaacovi, G., & Volle, E. (2011). Functional neuroimaging studies of prospective memory: what have we learnt so far? *Neuropsychologia, 49*(8), 2246-2257.

Butters, N., Sax, D., Montgomery, K., & Tarlow, S. (1978). Comparison of the neuropsychological deficits associated with early and advanced Huntington's disease. *Archives of neurology, 35*(9), 585-589.

Cahn-Weiner, D. A., Boyle, P. A., & Malloy, P. F. (2002). Tests of executive function predict instrumental activities of daily living in community-dwelling older individuals. *Applied neuropsychology, 9*(3), 187-191.

Campbell, M. C., Stout, J. C., & Finn, P. R. (2004). Reduced autonomic responsiveness to gambling task losses in Huntington's disease. *Journal of the International Neuropsychological Society, 10*(02), 239-245.

Caravaggio, F., Fervaha, G., Browne, C. J., Gerretsen, P., Remington, G., & Graff-Guerrero, A. (2018). Reward motivation in humans and its relationship to dopamine D2/3 receptor availability: A pilot study with dual [^{11}C]-raclopride and [^{11}C]-(+)-PHNO imaging. *Journal of Psychopharmacology, 32*(3), 357-366. doi:10.1177/0269881118756059

Carey, C. L., Woods, S. P., Rippeth, J. D., Heaton, R. K., & Grant, I. (2006). Prospective Memory in HIV-1 Infection. *Journal of Clinical and Experimental Neuropsychology, 28*(4), 536-548. doi:10.1080/13803390590949494

Cepeda, C., Murphy, K. P., Parent, M., & Levine, M. S. (2014). The role of dopamine in Huntington's disease. *Progress in brain research, 211*, 235.

Chang, J., & Carlson, S. R. (2014). Trait impulsivity and prospective memory abilities: An exploratory study. *Personality and Individual Differences, 56*, 40-44.

Clark, C. A., & Dagher, A. (2014). The role of dopamine in risk taking: A specific look at Parkinson's disease and gambling. *Frontiers in behavioral neuroscience, 8*.

Cona, G., Scarpazza, C., Sartori, G., Moscovitch, M., & Bisiacchi, P. S. (2015). Neural bases of prospective memory: a meta-analysis and the "Attention to Delayed Intention"(AtoDI) model. *Neuroscience & Biobehavioral Reviews, 52*, 21-37.

Cook, G. I., Rummel, J., & Dummel, S. (2015). Toward an understanding of motivational influences on prospective memory using value-added intentions. *Frontiers in human neuroscience, 9*.

Costa, A., Peppe, A., Caltagirone, C., & Carlesimo, G. A. (2008). Prospective memory impairment in individuals with Parkinson's disease. *Neuropsychology, 22*(3), 283.

Costa, A., Peppe, A., Zabberoni, S., Serafini, F., Barban, F., Scalici, F., . . . Carlesimo, G. A. (2015). Prospective memory performance in individuals with Parkinson's disease who have mild cognitive impairment. *Neuropsychology, 29*(5), 782.

Cruz, G., Petrie, S., Goudie, N., Kersel, D., & Evans, J. (2016). Text messages reduce memory failures in adults with brain injury: A single-case experimental design. *The British Journal of Occupational Therapy, 79*(10), 598-606. doi:10.1177/0308022616640299

Cuttler, C., Connolly, C. P., LaFrance, E. M., & Lowry, T. M. (2018). Resist forgetting: Effects of aerobic and resistance exercise on prospective and retrospective memory. *Sport, Exercise, and Performance Psychology, 7*(2), 205-217. doi:10.1037/spy0000112

Cuttler, C., O'Connell, D., & Marcus, D. K. (2016). Relationships between dimensions of impulsivity and prospective memory. *European Journal of Personality, 30*(1), 83-91. doi:10.1002/per.2038

Cuttler, C., Relkov, T., & Taylor, S. (2014). Quick to act, quick to forget: The link between impulsiveness and prospective memory. *European Journal of Personality, 28*(6), 560-568.

Czernecki, V., Pillon, B., Houeto, J., Pochon, J., Levy, R., & Dubois, B. (2002). Motivation, reward, and Parkinson's disease: influence of dopatherapy. *Neuropsychologia, 40*(13), 2257-2267.

Dalrymple-Alford, J., MacAskill, M., Nakas, C., Livingston, L., Graham, C., Crucian, G., . . . Wells, S. (2010). The MoCA well-suited screen for cognitive impairment in Parkinson disease. *Neurology, 75*(19), 1717-1725.

Daruna, J. H., & Barnes, P. A. (1993). A neurodevelopmental view of impulsivity.

de Langavant, L. C., Fenelon, G., Benisty, S., Boisse, M.-F., Jacquemot, C., & Bachoud-Levi, A.-C. (2013). Awareness of memory deficits in early stage Huntington's disease. *PloS one, 8*(4), e61676.

de Wit, H., & Richards, J. B. (2004). *Dual determinants of drug use in humans: reward and impulsivity.* Paper presented at the 50th Nebraska Symposium on Motivation, Mar, 2002, University of Nebraska, Lincoln, NE, US; Presented at the aforementioned symposium.

Delis, D. C., Kaplan, E., & Kramer, J. H. (2001). *Delis-Kaplan executive function system: Technical manual*: Psychological Corporation.

Delis, D. C., Massman, P. J., Butters, N., Salmon, D. P., Cermak, L. S., & Kramer, J. H. (1991). Profiles of demented and amnesic patients on the California Verbal Learning Test: Implications for the assessment of memory disorders. *Psychological Assessment: A Journal of Consulting and Clinical Psychology, 3*(1), 19.

Dickman, S. J. (1993). Impulsivity and information processing.

Dissabandara, L. O., Loxton, N. J., Dias, S. R., Dodd, P. R., Daglish, M., & Stadlin, A. (2014). Dependent heroin use and associated risky behaviour: The role of rash impulsiveness and reward sensitivity. *Addictive Behaviors, 39*(1), 71-76. doi:10.1016/j.addbeh.2013.06.009

Doyle, K., Weber, E., Atkinson, J. H., Grant, I., Woods, S. P., & Group, H. N. R. P. (2012). Aging, prospective memory, and health-related quality of life in HIV infection. *AIDS and Behavior, 16*(8), 2309-2318.

Duff, K., Paulsen, J. S., Beglinger, L. J., Langbehn, D. R., Wang, C., Stout, J. C., . . . Queller, S. (2010). "Frontal" behaviors before the diagnosis of Huntington's disease and their

relationship to markers of disease progression: evidence of early lack of awareness. *The Journal of neuropsychiatry and clinical neurosciences, 22*(2), 196-207.
Dumas, E. M., van den Bogaard, S., Middelkoop, H., & Roos, R. (2013). A review of cognition in Huntington's disease. *Front Biosci (Schol Ed), 5*, 1-18.
El Haj, M., Gallouj, K., & Antoine, P. (2017). Google Calendar enhances prospective memory in Alzheimer's disease: A case report. *Journal of Alzheimer's disease, 57*(1), 285-291. doi:10.3233/JAD-161283
Evenden, J. L. (1999). Varieties of impulsivity. *Psychopharmacology, 146*(4), 348-361.
Ferguson, S., Friedland, D., & Woodberry, E. (2015). Smartphone technology: Gentle reminders of everyday tasks for those with prospective memory difficulties post-brain injury. *Brain Injury, 29*(5), 583-591. doi:10.3109/02699052.2014.1002109
Fish, J., Wilson, B. A., & Manly, T. (2010). The assessment and rehabilitation of prospective memory problems in people with neurological disorders: A review. *Neuropsychological rehabilitation, 20*(2), 161-179.
Foster, E. R., McDaniel, M. A., & Rendell, P. G. (2017). Improving prospective memory in persons with Parkinson disease: A randomized controlled trial. *Neurorehabilitation and Neural Repair, 31*(5), 451-461. doi:10.1177/1545968317690832
Foster, E. R., Rose, N. S., McDaniel, M. A., & Rendell, P. G. (2013). Prospective memory in Parkinson disease during a virtual week: effects of both prospective and retrospective demands. *Neuropsychology, 27*(2), 170.
Fuermaier, A. B., Tucha, L., Koerts, J., Aschenbrenner, S., Westermann, C., Weisbrod, M., . . . Tucha, O. (2013). Complex prospective memory in adults with attention deficit hyperactivity disorder. *PloS one, 8*(3), e58338.
Gehring, W. J., & Willoughby, A. R. (2002). The medial frontal cortex and the rapid processing of monetary gains and losses. *Science, 295*(5563), 2279-2282.
Glisky, E. L. (1996). Prospective memory and the frontal lobes. *Prospective memory: Theory and applications*, 249-266.
Glisky, E. L., Polster, M. R., & Routhieaux, B. C. (1995). Double dissociation between item and source memory. *Neuropsychology, 9*(2), 229.
Gonen-Yaacovi, G., & Burgess, P. W. (2012). Prospective memory: The future for future intentions. *Psychologica Belgica, 52*(2), 173.
Graf, P., & Uttl, B. (2001). Prospective memory: A new focus for research. *Consciousness and cognition, 10*(4), 437-450.
Hall, H., Sedvall, G., Magnusson, O., Kopp, J., Halldin, C., & Farde, L. (1994). Distribution of D1-and D2-dopamine receptors, and dopamine and its metabolites in the human brain.
Harrington, D. L., Smith, M. M., Zhang, Y., Carlozzi, N. E., Paulsen, J. S., & Group, P.-H. I. o. t. H. S. (2012). Cognitive domains that predict time to diagnosis in prodromal Huntington disease. *Journal of Neurology, Neurosurgery & Psychiatry, 83*(6), 612-619.
Harrison, T. L., Mullet, H. G., Whiffen, K. N., Ousterhout, H., & Einstein, G. O. (2014). Prospective memory: Effects of divided attention on spontaneous retrieval. *Memory & Cognition, 42*(2), 212-224.
Harsay, H. A., Buitenweg, J. I., Wijnen, J. G., Guerreiro, M. J., & Ridderinkhof, K. R. (2010). Remedial effects of motivational incentive on declining cognitive control in healthy aging and Parkinson's disease. *Frontiers in aging neuroscience, 2*, 144.

Henry, J. D., MacLeod, M. S., Phillips, L. H., & Crawford, J. R. (2004). A meta-analytic review of prospective memory and aging. *Psychology and aging, 19*(1), 27.
Hikosaka, O., Kim, H. F., Yasuda, M., & Yamamoto, S. (2014). Basal ganglia circuits for reward value-guided behavior. *Annual review of neuroscience, 37*, 289.
Hoth, K. F., Paulsen, J. S., Moser, D. J., Tranel, D., Clark, L. A., & Bechara, A. (2007). Patients with Huntington's disease have impaired awareness of cognitive, emotional, and functional abilities. *Journal of Clinical and Experimental Neuropsychology, 29*(4), 365-376.
Ihle, A., Schnitzspahn, K., Rendell, P. G., Luong, C., & Kliegel, M. (2012). Age benefits in everyday prospective memory: The influence of personal task importance, use of reminders and everyday stress. *Aging, Neuropsychology, and Cognition, 19*(1-2), 84-101.
Ito, H., Takahashi, H., Arakawa, R., Takano, H., & Suhara, T. (2008). Normal database of dopaminergic neurotransmission system in human brain measured by positron emission tomography. *Neuroimage, 39*(2), 555-565.
Jefferson, A. L., Paul, R. H., Ozonoff, A., & Cohen, R. A. (2006). Evaluating elements of executive functioning as predictors of instrumental activities of daily living (IADLs). *Archives of Clinical Neuropsychology, 21*(4), 311-320.
Jeong, J. M., & Cranney, J. (2009). Motivation, depression, and naturalistic time-based prospective remembering. *Memory, 17*(7), 732-741.
Julien, C. L., Thompson, J. C., Wild, S., Yardumian, P., Snowden, J. S., Turner, G., & Craufurd, D. (2007). Psychiatric disorders in preclinical Huntington's disease. *Journal of Neurology, Neurosurgery & Psychiatry, 78*(9), 939-943.
Jurado, M. B., & Rosselli, M. (2007). The elusive nature of executive functions: a review of our current understanding. *Neuropsychology review, 17*(3), 213-233.
Kamminga, J., O'Callaghan, C., Hodges, J. R., & Irish, M. (2014). Differential prospective memory profiles in frontotemporal dementia syndromes. *Journal of Alzheimer's disease, 38*(3), 669-679.
Karlawish, J., Cary, M., Moelter, S. T., Siderowf, A., Sullo, E., Xie, S., & Weintraub, D. (2013). Cognitive impairment and PD patients' capacity to consent to research. *Neurology, 81*(9), 801-807. doi:10.1212/WNL.0b013e3182a05ba5
Katai, S., Maruyama, T., Hashimoto, T., & Ikeda, S. (2003). Event based and time based prospective memory in Parkinson's disease. *Journal of Neurology, Neurosurgery & Psychiatry, 74*(6), 704-709.
Kieburtz, K., Penney, J. B., Corno, P., Ranen, N., Shoulson, I., Feigin, A., . . . Marshall, F. J. (2001). Unified Huntington's disease rating scale: reliability and consistency. *Neurology, 11*(2), 136-142.
Kliegel, M., Altgassen, M., Hering, A., & Rose, N. S. (2011). A process-model based approach to prospective memory impairment in Parkinson's disease. *Neuropsychologia, 49*(8), 2166-2177.
Kliegel, M., Jäger, T., Altgassen, M., & Shum, D. (2008). Clinical neuropsychology of prospective memory.
Kliegel, M., Martin, M., McDaniel, M., & Einstein, G. (2004). Importance effects on performance in event‐based prospective memory tasks. *Memory, 12*(5), 553-561.

Kliegel, M., McDaniel, M. A., & Einstein, G. O. (2000). Plan formation, retention, and execution in prospective memory: A new approach and age-related effects. *Memory & Cognition, 28*(6), 1041-1049.
Knutson, B., Adams, C. M., Fong, G. W., & Hommer, D. (2001). Anticipation of increasing monetary reward selectively recruits nucleus accumbens. *J Neurosci, 21*(16), RC159.
Kremer, H., & Group, H. S. (1996). Unified Huntington's disease rating scale: reliability and consistency.
Lemiere, J., Decruyenaere, M., Evers-Kiebooms, G., Vandenbussche, E., & Dom, R. (2004). Cognitive changes in patients with Huntington's disease (HD) and asymptomatic carriers of the HD mutation. *Journal of neurology, 251*(8), 935-942.
Lezak, M., Howieson, D., & Loring, D. (2012). Neuropsychological assessment. 5th edn Oxford University Press. *Oxford, New York, ISBN, 10*, 9780195395525.
Lippa, S. M., & Davis, R. N. (2010). Inhibition/switching is not necessarily harder than inhibition: An analysis of the D-KEFS color-word interference test. *Archives of Clinical Neuropsychology*, acq001.
MacDonald, M. E., Ambrose, C. M., Duyao, M. P., Myers, R. H., Lin, C., Srinidhi, L., . . . Groot, N. (1993). A novel gene containing a trinucleotide repeat that is expanded and unstable on Huntington's disease chromosomes. *Cell, 72*(6), 971-983.
Marin, R. S. (1990). Differential diagnosis and classification of apathy. *Am J Psychiatry, 147*(1), 22-30.
Marsh, R. L., Hicks, J. L., & Cook, G. I. (2005). On the relationship between effort toward an ongoing task and cue detection in event-based prospective memory. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 31*(1), 68.
Martin, M., Kliegel, M., & McDaniel, M. A. (2003). The involvement of executive functions in prospective memory performance of adults. *International Journal of Psychology, 38*(4), 195-206.
McCauley, S. R., McDaniel, M. A., Pedroza, C., Chapman, S. B., & Levin, H. S. (2009). Incentive effects on event-based prospective memory performance in children and adolescents with traumatic brain injury. *Neuropsychology, 23*(2), 201.
McCauley, S. R., Wilde, E. A., Bigler, E. D., Chu, Z., Yallampalli, R., Oni, M. B., . . . Vásquez, A. C. (2011). Diffusion tensor imaging of incentive effects in prospective memory after pediatric traumatic brain injury. *Journal of neurotrauma, 28*(4), 503-516.
McDaniel, M. A., & Einstein, G. O. (2000). Strategic and automatic processes in prospective memory retrieval: A multiprocess framework. *Applied cognitive psychology, 14*(7), S127-S144.
McDaniel, M. A., & Einstein, G. O. (2011). The neuropsychology of prospective memory in normal aging: A componential approach. *Neuropsychologia, 49*(8), 2147-2155.
McDaniel, M. A., Glisky, E. L., Guynn, M. J., & Routhieaux, B. C. (1999). Prospective memory: A neuropsychological study. *Neuropsychology, 13*(1), 103.
McDaniel, M. A., Howard, D. C., & Butler, K. M. (2008). Implementation intentions facilitate prospective memory under high attention demands. *Memory & Cognition, 36*(4), 716-724.
McDaniel, M. A., LaMontagne, P., Beck, S. M., Scullin, M. K., & Braver, T. S. (2013). Dissociable neural routes to successful prospective memory. *Psychological science*, 0956797613481233.

Minati, L., Piacentini, S., Ferrè, F., Nanetti, L., Romito, L., Mariotti, C., . . . Albanese, A. (2011). Choice-option evaluation is preserved in early Huntington and Parkinson's disease. *NeuroReport: For Rapid Communication of Neuroscience Research, 22*(15), 753-757. doi:10.1097/WNR.0b013e32834acb6e

Mioni, G., Stablum, F., McClintock, S. M., & Cantagallo, A. (2012). Time-based prospective memory in severe traumatic brain injury patients: The involvement of executive functions and time perception. *Journal of the International Neuropsychological Society, 18*(4), 697-705. doi:10.1017/S1355617712000306

Montoya, A., Pelletier, M., Menear, M., Duplessis, E., Richer, F., & Lepage, M. (2006). Episodic memory impairment in Huntington's disease: a meta-analysis. *Neuropsychologia, 44*(10), 1984-1994.

Nasreddine, Z. S., Phillips, N. A., Bédirian, V., Charbonneau, S., Whitehead, V., Collin, I., . . . Chertkow, H. (2005). The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society, 53*(4), 695-699.

Nelson, A. B., & Kreitzer, A. C. (2014). Reassessing models of basal ganglia function and dysfunction. *Annual review of neuroscience, 37*, 117.

Neulinger, K., Oram, J., Tinson, H., O'Gorman, J., & Shum, D. H. (2015). Prospective memory and frontal lobe function. *Aging, Neuropsychology, and Cognition*, 1-13.

Nicoll, D. R., Pirogovsky, E., Woods, S. P., Holden, H. M., Filoteo, J. V., Gluhm, S., . . . Gilbert, P. E. (2014). "Forgetting to Remember" in Huntington's Disease: A Study of Laboratory, Semi-Naturalistic, and Self-Perceptions of Prospective Memory. *Journal of the International Neuropsychological Society, 20*(02), 192-199.

Novak, M. J., & Tabrizi, S. J. (2010). Huntington's disease. *Bmj, 340*.

Papoutsi, M., Labuschagne, I., Tabrizi, S. J., & Stout, J. C. (2014). The cognitive burden in Huntington's disease: pathology, phenotype, and mechanisms of compensation. *Movement Disorders, 29*(5), 673-683.

Patel, K. T., Stevens, M. C., Meda, S. A., Muska, C., Thomas, A. D., Potenza, M. N., & Pearlson, G. D. (2013). Robust changes in reward circuitry during reward loss in current and former cocaine users during performance of a monetary incentive delay task. *Biological psychiatry, 74*(7), 529-537.

Patton, J. H., & Stanford, M. S. (1995). Factor structure of the Barratt impulsiveness scale. *Journal of clinical psychology, 51*(6), 768-774.

Paulsen, J. S. (2011). Cognitive impairment in Huntington disease: diagnosis and treatment. *Current neurology and neuroscience reports, 11*(5), 474-483.

Paulsen, J. S., Hoth, K. F., Nehl, C., Stierman, L., & Group, H. S. (2005). Critical periods of suicide risk in Huntington's disease. *American Journal of Psychiatry, 162*(4), 725-731.

Paulsen, J. S., Ready, R., Hamilton, J., Mega, M., & Cummings, J. (2001). Neuropsychiatric aspects of Huntington's disease. *Journal of Neurology, Neurosurgery & Psychiatry, 71*(3), 310-314.

Paulsen, J. S., Smith, M. M., Long, J. D., investigators, P. H., & Group, C. o. t. H. S. (2013). Cognitive decline in prodromal Huntington Disease: implications for clinical trials. *Journal of Neurology, Neurosurgery & Psychiatry, 84*(11), 1233-1239.

Pavese, N., Andrews, T. C., Brooks, D. J., Ho, A. K., Rosser, A. E., Barker, R. A., . . . Piccini, P. (2003). Progressive striatal and cortical dopamine receptor dysfunction in Huntington's disease: a PET study. *Brain, 126*(5), 1127-1135.
Penningroth, S. L., & Scott, W. D. (2007). A motivational-cognitive model of prospective memory: The influence of goal relevance. *Psychology of motivation*, 115-128.
Perry, D. C., Sturm, V. E., Wood, K. A., Miller, B. L., & Kramer, J. H. (2015). Divergent processing of monetary and social reward in behavioral variant frontotemporal dementia and Alzheimer's disease. *Alzheimer disease and associated disorders*.
Pirogovsky, E., Woods, S. P., Filoteo, J. V., & Gilbert, P. E. (2012). Prospective memory deficits are associated with poorer everyday functioning in Parkinson's disease. *Journal of the International Neuropsychological Society, 18*(06), 986-995.
Ramanan, S., & Kumar, D. (2013). Prospective memory in Parkinson's disease: A meta-analysis. *Journal of the International Neuropsychological Society, 19*(10), 1109-1118.
Ramnani, N., & Owen, A. M. (2004). Anterior prefrontal cortex: insights into function from anatomy and neuroimaging. *Nature Reviews Neuroscience, 5*(3), 184-194.
Rao, J. A., Harrington, D. L., Durgerian, S., Reece, C., Mourany, L., Koenig, K., . . . Johnson, H. J. (2014). Disruption of response inhibition circuits in prodromal Huntington disease. *Cortex, 58*, 72-85.
Raskin, S. A., Woods, S. P., Poquette, A. J., McTaggart, A. B., Sethna, J., Williams, R. C., & Tröster, A. I. (2011). A differential deficit in time-versus event-based prospective memory in Parkinson's disease. *Neuropsychology, 25*(2), 201.
Redgrave, P., Rodriguez, M., Smith, Y., Rodriguez-Oroz, M. C., Lehericy, S., Bergman, H., . . . Obeso, J. A. (2010). Goal-directed and habitual control in the basal ganglia: implications for Parkinson's disease. *Nature Reviews Neuroscience, 11*(11), 760-772.
Rendell, P. G., Gray, T. J., Henry, J. D., & Tolan, A. (2007). Prospective memory impairment in "ecstasy"(MDMA) users. *Psychopharmacology, 194*(4), 497-504.
Rendell, P. G., Mazur, M., & Henry, J. D. (2009). Prospective memory impairment in former users of methamphetamine. *Psychopharmacology, 203*(3), 609-616.
Rose, N. S., Rendell, P. G., McDaniel, M. A., Aberle, I., & Kliegel, M. (2010). Age and individual differences in prospective memory during a" Virtual Week": The roles of working memory, vigilance, task regularity, and cue focality. *Psychology and aging, 25*(3), 595.
Schnitzspahn, K. M., Ihle, A., Henry, J. D., Rendell, P. G., & Kliegel, M. (2011). The age-prospective memory-paradox: An exploration of possible mechanisms. *International Psychogeriatrics, 23*(04), 583-592.
Schnitzspahn, K. M., Stahl, C., Zeintl, M., Kaller, C. P., & Kliegel, M. (2013). The role of shifting, updating, and inhibition in prospective memory performance in young and older adults. *Developmental psychology, 49*(8), 1544.
Scullin, M. K., McDaniel, M. A., Shelton, J. T., & Lee, J. H. (2010). Focal/nonfocal cue effects in prospective memory: Monitoring difficulty or different retrieval processes? *Journal of Experimental Psychology: Learning, Memory, and Cognition, 36*(3), 736.
Sesack, S. R., & Grace, A. A. (2010). Cortico-basal ganglia reward network: microcircuitry. *Neuropsychopharmacology, 35*(1), 27-47.
Shoulson, I., & Fahn, S. (1979). Huntington disease clinical care and evaluation. *Neurology, 29*(1), 1-1.

Sitek, E. J., Sołtan, W., Robowski, P., Schinwelski, M., Wieczorek, D., & Sławek, J. (2012). Poor insight into memory impairment in patients with Huntington disease. *Neurologia i neurochirurgia polska, 46*(4), 318-325.
Sjöwall, D., Roth, L., Lindqvist, S., & Thorell, L. B. (2013). Multiple deficits in ADHD: executive dysfunction, delay aversion, reaction time variability, and emotional deficits. *Journal of Child Psychology and Psychiatry, 54*(6), 619-627.
Slaughter, J. R., Martens, M. P., & Slaughter, K. A. (2001). Depression and Huntington's disease: prevalence, clinical manifestations, etiology, and treatment. *CNS spectrums, 6*(04), 306-308,325-326.
Smith, C. T., Wallace, D. L., Dang, L. C., Aarts, E., Jagust, W. J., D'Esposito, M., & Boettiger, C. A. (2016). Modulation of impulsivity and reward sensitivity in intertemporal choice by striatal and midbrain dopamine synthesis in healthy adults. *Journal of neurophysiology, 115*(3), 1146-1156.
Smith, G., Del Sala, S., Logie, R. H., & Maylor, E. A. (2000). Prospective and retrospective memory in normal ageing and dementia: A questionnaire study. *Memory, 8*(5), 311-321.
Smith, G. T., Fischer, S., Cyders, M. A., Annus, A. M., Spillane, N. S., & McCarthy, D. M. (2007). On the validity and utility of discriminating among impulsivity-like traits. *Assessment, 14*(2), 155-170.
Smith, R. E. (2003). The cost of remembering to remember in event-based prospective memory: investigating the capacity demands of delayed intention performance. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 29*(3), 347.
Snowden, J. S., Craufurd, D., Griffiths, H. L., & Neary, D. (1998). Awareness of involuntary movements in Huntington disease. *Archives of neurology, 55*(6), 801-805.
Sprengelmeyer, R., Lange, H., & Hömberg, V. (1995). The pattern of attentional deficits in Huntington's disease. *Brain, 118*(1), 145-152.
Stanford, M. S., Mathias, C. W., Dougherty, D. M., Lake, S. L., Anderson, N. E., & Patton, J. H. (2009). Fifty years of the Barratt Impulsiveness Scale: An update and review. *Personality and Individual Differences, 47*(5), 385-395.
Stout, J. C., Rodawalt, W. C., & Siemers, E. R. (2001). Risky decision making in Huntington's disease. *Journal of the International Neuropsychological Society, 7*(01), 92-101.
Tekin, S., & Cummings, J. L. (2002). Frontal–subcortical neuronal circuits and clinical neuropsychiatry: an update. *Journal of psychosomatic research, 53*(2), 647-654.
Terrett, G., McLennan, S. N., Henry, J. D., Biernacki, K., Mercuri, K., Curran, H. V., & Rendell, P. G. (2014). Prospective memory impairment in long-term opiate users. *Psychopharmacology, 231*(13), 2623-2632.
Thut, G., Schultz, W., Roelcke, U., Nienhusmeier, M., Missimer, J., Maguire, R. P., & Leenders, K. L. (1997). Activation of the human brain by monetary reward. *Neuroreport, 8*(5), 1225-1228.
Tversky, A., & Kahneman, D. (1991). Loss aversion in riskless choice: A reference-dependent model. *The quarterly journal of economics*, 1039-1061.
Van Duijn, E., Kingma, E., & Van der Mast, R. (2007). Psychopathology in verified Huntington's disease gene carriers. *The Journal of neuropsychiatry and clinical neurosciences, 19*(4), 441-448.
Verdejo-García, A., del Mar Sánchez-Fernández, M., Alonso-Maroto, L. M., Fernández-Calderón, F., Perales, J. C., Lozano, Ó., & Pérez-García, M. (2010). Impulsivity and

executive functions in polysubstance-using rave attenders. *Psychopharmacology, 210*(3), 377-392.
Vitale, C., Pellecchia, M., Grossi, D., Fragassi, N., Cuomo, T., Di Maio, L., & Barone, P. (2001). Unawareness of dyskinesias in Parkinson's and Huntington's diseases. *Neurological Sciences, 22*(1), 105-106.
Volkow, N. D., Wang, G.-J., Telang, F., Fowler, J. S., Alexoff, D., Logan, J., . . . Tomasi, D. (2014). Decreased dopamine brain reactivity in marijuana abusers is associated with negative emotionality and addiction severity. *Proceedings of the National Academy of Sciences, 111*(30), E3149-E3156.
Walker, F. O. (2007). Huntington's disease. *The Lancet, 369*(9557), 218-228. doi:10.1016/S0140-6736(07)60111-1
Walter, S., & Meier, B. (2014). How important is importance for prospective memory? A review. *Front. Psychol, 5*(657), 10.3389.
Wang, Y., Wu, L., Zhou, H., Lin, X., Zhang, Y., Du, X., & Dong, G. (2017). Impaired executive control and reward circuit in Internet gaming addicts under a delay discounting task: Independent component analysis. *European Archives of Psychiatry and Clinical Neuroscience, 267*(3), 245-255. doi:10.1007/s00406-016-0721-6
Weber, E., Woods, S. P., Delano-Wood, L., Bondi, M. W., Gilbert, P. E., Grant, I., & Group, H. N. R. P. (2011). An examination of the age-prospective memory paradox in HIV-infected adults. *Journal of Clinical and Experimental Neuropsychology, 33*(10), 1108-1118.
Weller, J. A., Levin, I. P., & Denburg, N. L. (2011). Trajectory of risky decision making for potential gains and losses from ages 5 to 85. *Journal of Behavioral Decision Making, 24*(4), 331-344.
West, R., Scolaro, A. J., & Bailey, K. (2011). When goals collide: the interaction between prospective memory and task switching. *Canadian Journal of Experimental Psychology/Revue canadienne de psychologie expérimentale, 65*(1), 38.
Woods, S. P., Iudicello, J. E., Moran, L. M., Carey, C. L., Dawson, M. S., & Grant, I. (2008). HIV-associated prospective memory impairment increases risk of dependence in everyday functioning. *Neuropsychology, 22*(1), 110.
Woods, S. P., Weinborn, M., Velnoweth, A., Rooney, A., & Bucks, R. S. (2012). Memory for intentions is uniquely associated with instrumental activities of daily living in healthy older adults. *Journal of the International Neuropsychological Society, 18*(01), 134-138.
Wu, Y., Van Dijk, E., Aitken, M., & Clark, L. (2016). Missed losses loom larger than missed gains: Electrodermal reactivity to decision choices and outcomes in a gambling task. *Cognitive, Affective & Behavioral Neuroscience, 16*(2), 353-361. doi:10.3758/s13415-015-0395-y
Zamboni, G., & Wilcock, G. (2011). Lack of awareness of symptoms in people with dementia: the structural and functional basis. *International journal of geriatric psychiatry, 26*(8), 783-792.
Zogg, J. B., Woods, S. P., Sauceda, J. A., Wiebe, J. S., & Simoni, J. M. (2012). The role of prospective memory in medication adherence: a review of an emerging literature. *Journal of behavioral medicine, 35*(1), 47-62.

Appendices

Appendix A: Semi-Structured Interview

Demographic Information

1. Gender: **Female** **Male**

2. Age: _____

3. Race and/or Ethnicity: _____

4. Handedness: **Right** **Left**

5. Education: _____

6. For Controls, what is the relationship to individual with HD? _____

Psychological and Medical History

7. Have you ever been diagnosed with either ADD or ADHD? **YES** **NO**
   7a. If yes, which one? **ADD** **ADHD**

8. Have you ever had open or closed head injury? **YES** **NO**
   8a. If yes, did you lose consciousness? **YES** **NO**
   8b. If yes, for how long? _____

9. Have you ever been diagnosed with a mental health disorder? **YES** **NO**
   9a. If yes, what was the diagnosis? _____

10. Are you currently taking any psychiatric medication? **YES** **NO**
    10a. If yes, what is the medication? _____

11. Have you ever been diagnosed with a neurological disorder such as a stroke, Parkinson's disease, epilepsy, etc.? **YES** **NO**
    11a. If yes, what was the diagnosis? _____
    11b. When were you diagnosed? _____

12. Have you been diagnosed with Huntington's disease? **YES** **NO**
    12a. If yes, when were you diagnosed? _____
    12b. If known, what is your CAG repeat? _____

Appendix B: Frequency data of correctly identified prospective memory (PM) cues during the Neutral block

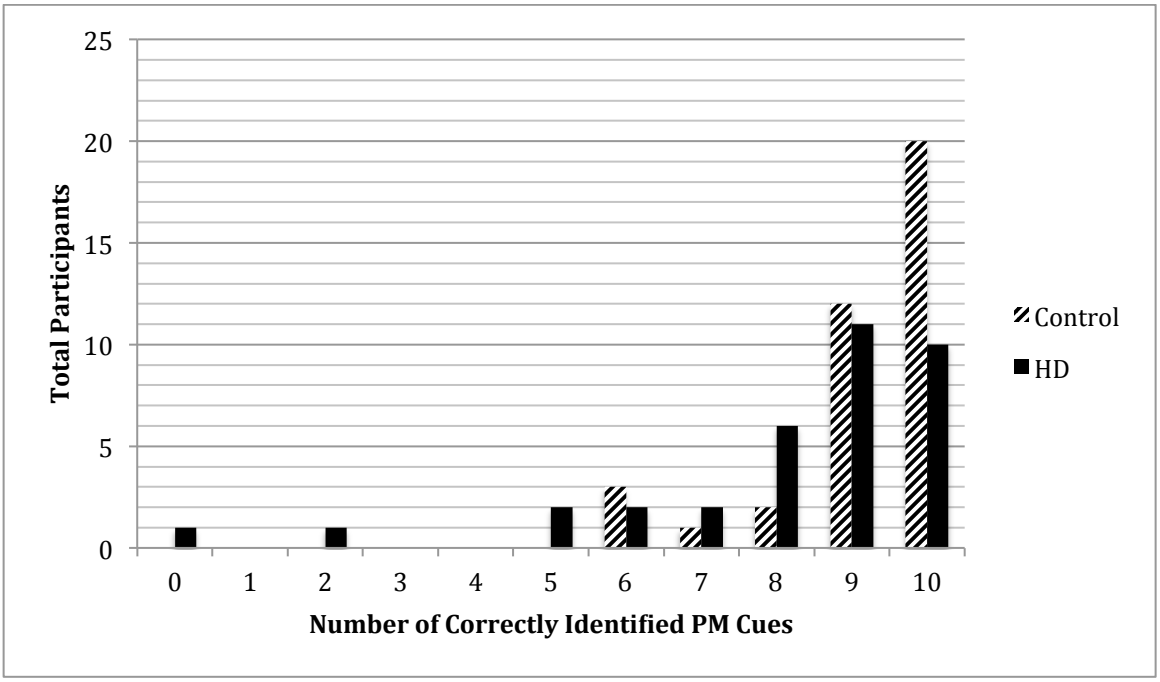

Figure 3. Frequency data of correctly identified prospective memory (PM) cues during the Neutral block

Appendix C: Frequency data of correctly identified prospective memory (PM) cues during the Reward block

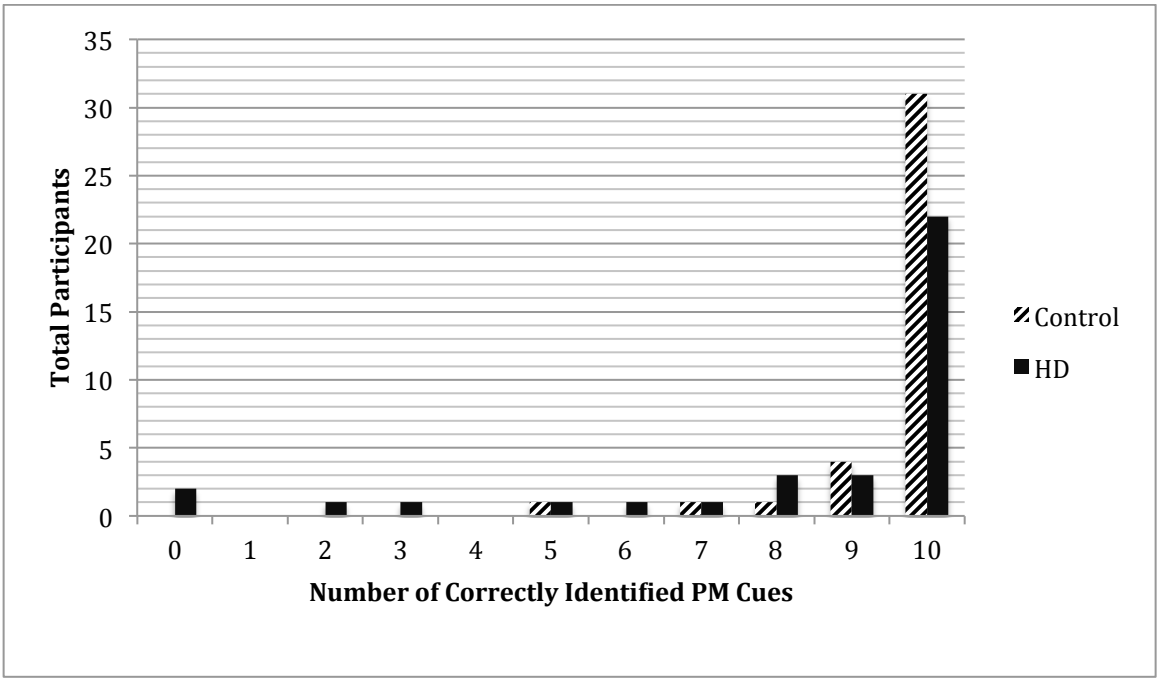

Figure 4. Frequency data of correctly identified prospective memory (PM) cues during the Reward block

Appendix D: Frequency data of correctly identified prospective memory (PM) cues during the Loss block

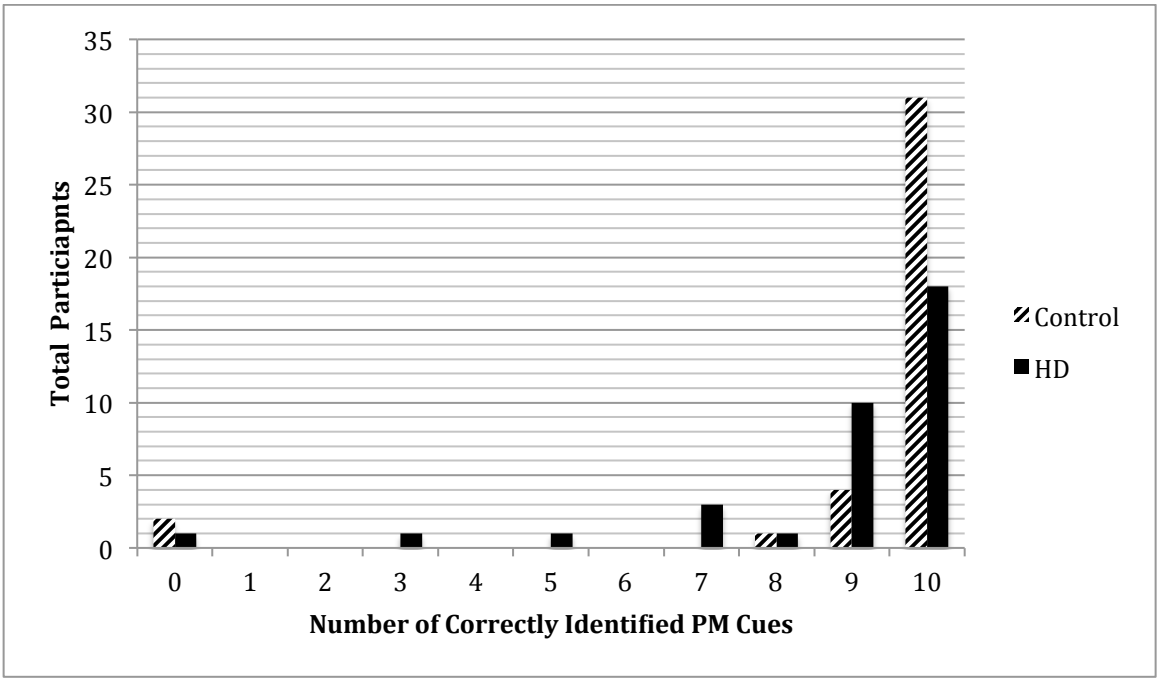

Figure 5. Frequency data of correctly identified prospective memory (PM) cues during the Loss block

Appendix E: IRB Approval Letter

USF
UNIVERSITY OF
SOUTH FLORIDA

RESEARCH INTEGRITY AND COMPLIANCE
Institutional Review Boards, FWA No. 00001669
12901 Bruce B. Downs Blvd., MDC035 • Tampa, FL 33612-4799
(813) 974-5638 • FAX (813) 974-7091

October 5, 2016

Emily Kellogg, B.S.
Psychology
Tampa, FL 33612

RE: **Expedited Approval for Initial Review**
IRB#: Pro00027851
Title: Factors Affecting Prospective Memory in Huntington's Disease

Study Approval Period: 10/5/2016 to 10/5/2017

Dear Ms. Kellogg:

On 10/5/2016, the Institutional Review Board (IRB) reviewed and **APPROVED** the above application and all documents contained within, including those outlined below.

Approved Item(s):
Protocol Document(s):
Study Protocol_Version 1_2016_0919

Consent/Assent Document(s)*:
Caregiver Consent.pdf
HD Consent.pdf

*Please use only the official IRB stamped informed consent/assent document(s) found under the "Attachments" tab. Please note, these consent/assent document(s) are only valid during the approval period indicated at the top of the form(s).

It was the determination of the IRB that your study qualified for expedited review which includes activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the categories outlined below. The IRB may review research through the expedited review procedure authorized by 45CFR46.110 . The research proposed in this study is categorized under the following expedited review category:

(7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

Your study qualifies for a waiver of the requirement for signed authorization as outlined in the HIPAA Privacy Rule regulations at 45CFR164.512(i) which states that an IRB may approve a waiver or alteration of the authorization requirement provided that the following criteria are met (1) the PHI use or disclosure involves no more than a minimal risk to the privacy of individuals; (2) the research could not practicably be conducted without the requested waiver or alteration; and (3) the research could not practicably be conducted without access to and use of the PHI. A partial waiver of HIPAA Authorization is granted for recruitment purposes only; written Authorization will be obtained as part of the informed consent process. Pursuant to this partial waiver, the study team is authorized to obtain PHI of patients diagnosed with Huntington's disease who provided their informed consent to participate in the USF IRB-approved Huntington's Disease Registry (USF Pro 10382).

As the principal investigator of this study, it is your responsibility to conduct this study in accordance with IRB policies and procedures and as approved by the IRB. Any changes to the approved research must be submitted to the IRB for review and approval via an amendment. Additionally, all unanticipated problems must be reported to the USF IRB within five (5) calendar days.

We appreciate your dedication to the ethical conduct of human subject research at the University of South Florida and your continued commitment to human research protections. If you have any questions regarding this matter, please call 813-974-5638.

Sincerely,

Kristen Salomon, Ph.D., Vice Chairperson
USF Institutional Review Board