ABSTRACT

Probabilistic Category Learning and Memory Systems Functioning
in Those At-Risk for Alcohol Abuse

Meilin Jia-Richards, M.A.

Mentor: Sara L. Dolan, Ph.D.

The transition from non-problematic to problematic drinking may be related to neuropsychological functioning, especially difficulties in memory functioning. The goal of this study was to examine declarative and non-declarative memory functioning in high-risk drinking college students using the Weather Prediction Task (WPT). We recruited 20 high-risk and 44 low-risk participants. We hypothesized that high-risk drinkers would perform worse on the WPT, as well as a reversal learning component of the WPT. We also examined the relationship between executive functioning and WPT performance as well as if impulsivity was related to WPT performance. Overall our results did not confirm our primary hypotheses. However, our exploratory analyses revealed in interesting relationship between WPT performance and facets of impulsivity. Future research is needed to further examine declarative and non-declarative memory process in high-risk drinkers, as there were several limitations in our study.

Probablistic Category Learning and Memory Systems Functioning in High-Risk Drinkers

by

Meilin Jia-Richards, B.S.

A Thesis

Approved by the Department of Psychology and Neuroscience

_____

Charles A. Weaver III, Ph.D., Chairperson

Submitted to the Graduate Faculty of
Baylor University in Partial Fulfillment of the
Requirements for the Degree
of

Master of Arts

Approved by the Thesis Committee

_____

Sara L. Dolan, Ph.D., Chairperson

_____

Shawn J. Latendresse, Ph.D.

_____

Tonya N. Davis, Ph.D.

Accepted by the Graduate School

December 2018

_____

J. Larry Lyon, Ph.D., Dean

Page bearing signatures is kept on file in the Graduate School.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

ACKNOWLEDGMENTS

I would first like to acknowledge my advisor, Dr. Sara Dolan. Thank you for your endless encouragement and academic guidance. I could not have asked for a better mentor. I would also like to thank Drs. Shawn Latendresse and Tonya Davis for serving on my committee, as well as everyone in Department of Psychology and Neuroscience at Baylor. I am grateful to be a part of such a wonderful group of people. Lastly, I would like to thank my friends and family for the moral and emotional support during the many years of study that have lead up to this point.

CHAPTER ONE

Introduction

According to a recent study, almost 30% of people in the United States have experienced an alcohol use disorder (AUD[1]) in their lifetime, and less than 20% of those people received treatment (Grant et al., 2015). While the consequences of AUD are fairly well known, the factors influencing the transition from non-problematic drinking to alcohol dependence is less clear. Several risk factors have been identified, including genetic predisposition (Verhulst, Neale, & Kendler, 2015), elevated impulsive personality traits and neuropsychological impairment (Dolan, Bechara, & Nathan, 2008), however processes such as specific learning and memory mechanisms are not yet fully known.

Despite evidence for genetic risk factors (Verhulst et al., 2015) AUD and problem drinking[1] can also be characterized as learned behaviors. Through repeated use of alcohol, an individual learns that the alcohol can be rewarding and can relieve anxiety. As alcohol use quantity and frequency increases, this behavior may or may not lead to compulsive drinking. Kalivas and O'Brien (2008) proposed three stages of learning in the transition to addiction. The first is the "social use" phase. In this phase, alcohol use is non-problematic and is usually restricted to social situations. For example, the individual learns that alcohol relieves anxiety in social situations and elevates their mood. The second stage, the "regulated relapse" phase, is characterized by conscious declarative

[1]AUD refers to DSM-5 Alcohol Use Disorder. "Problem drinking" refers to alcohol use that results in negative consequences but does not meet criteria for AUD. "Heavy drinking" and "binge drinking" are considered problem drinking.

decisions to consume or not to consume alcohol outside of just social situations. In this stage, the individual considers whether it is appropriate to drink, and is usually able to abstain when needed. However, in the last phase, the "compulsive relapse" phase, the individual transitions from making conscious, declarative decisions to unconscious, non-declarative decisions. The learned behavior of drinking becomes compulsive and is no longer controlled by declarative processes. The first two phases, "social use" and "regulated relapse" do not necessarily always lead to "compulsive relapse," which is why it is important to examine why some people make this transition, and why others do not. Since drinking is a learned behavior, examining learning and memory in the context of AUD may improve our understanding of this transition from controlled declarative processes to uncontrolled non-declarative processes

The Multiple Memory Systems Theory

Current research suggests that learning and memory rely on multiple, distinct memory systems in the brain. The multiple memory systems theory partially originates from the distinction between declarative and non-declarative memory. Declarative memory is factual knowledge that can be verbalized, whereas non-declarative memory refers to memory of learned behaviors, or associative learning. Or, as Cohen and Squire (1980) wrote, it is the difference between "knowing that" and "knowing how." While people are consciously aware of the facts they do and do not know, non-declarative memory operates outside of awareness. This is seen in patients with damage to the medial temporal lobe (MTL)—a region that includes the hippocampus and is essential for declarative memory (Milner, 2005). Patient HM is perhaps the most famous case of this type of impairment. After bilateral removal of his MTLs, HM suffered from anterograde

and temporally graded retrograde amnesia, resulting in significant impairment to his declarative memory. However, he retained non-declarative memory as evidenced by the fact that he could still learn motor tasks. Korsakoff's syndrome is another classic example. Caused by thiamine deficiency due to chronic, excessive alcohol consumption, patients experience severely impaired declarative memory yet relatively intact non-declarative memory (Hayes, Fortier, Levine, Milberg, & McGlinchey, 2012; Oudman et al., 2016).

Another consequence of multiple memory systems is that some tasks may be completed successfully using either or both memory systems, so having a deficit in one system does not necessarily mean that an individual cannot complete a task. For example, one individual may solve a maze task using hippocampal-based declarative memory, and another may solve the same task using caudate-based non-declarative memory; however, both individuals successfully complete the task, as demonstrated in a study by Schwabe, Bohbot, and Wolf (2012). Based on verbal reports, participants were categorized as using either declarative (i.e. spatial and easily verbalized, dependent on the hippocampus) or non-declarative (i.e. stimulus-response and automatic, dependent on the caudate) strategies. Categorization was supported by behavioral data indicating that declarative learners—who heavily utilized spatial cues around the maze—were significantly impaired when spatial cues were removed when compared to non-declarative learners. Additionally, participants were asked to draw as much as they could remember of the virtual maze, including spatial cues. Declarative learners were able to recall multiple spatial cues around the maze, whereas non-declarative learners recalled very few, if any. This does not mean that multiple memory systems solve all tasks equally efficiently,

evidenced by the fact that both declarative and non-declarative learners were able to learn the task. Instead, it is more likely the case that distinct memory systems are better suited for different tasks, and there may be factors predisposing an individual towards particular memory systems. For example, Schwabe et al. (2012) demonstrated this effect in individuals predisposed towards stress. They found that individuals who had been exposed to prenatal stress were significantly more likely to rely on non-declarative strategies than those who had not. While these memory systems have been relatively well studied in some populations, little is known about how they function in AUD. Since these memory systems likely drive many of the behaviors associated with addiction, it is important to study them in the context of AUD.

Sub-Cortical Memory Systems Functioning in Alcohol Use Disorder

In the case of AUD, cognitive dysfunction is both a consequence of (Vetreno, Hall, & Savage, 2011) and a risk factor (Dolan et al., 2008) for addiction. An estimated 50 to 75% of detoxified alcoholics experience cognitive problems including memory dysfunction (Vetreno et al., 2011). This cognitive dysfunction can be found in acute detoxification and generally resolves with abstinence, but it can still be found in some alcoholics after years of sobriety. Additionally, synaptic functioning and synaptic plasticity in the hippocampus and cortex are adversely affected by chronic alcohol consumption (Lovinger & Roberto, 2010; McCool, 2011), brain regions essential for learning and memory. The hippocampi of actively drinking and abstinent alcoholics are also smaller than controls, even after over 200 days of abstinence (Hoefer et al., 2014), suggesting that AUD have long-lasting effects on declarative memory in some individuals (e.g., Sullivan, Fama, Rosenbloom, & Pfefferbaum, 2002).

The dorsal and ventral striatum have also been examined in regard to AUD. In a meta-analysis, Tomasi and Volkow (2013) found that 67% of brain activation differences between alcoholics and controls were in the striatum. The dorsal striatum is comprised of the caudate and putamen, while the ventral striatum is comprised of the nucleus accumbens (NAc). Vollstädt-Klein and colleagues (2010) suggest that the ventral striatum controls the declarative aspects of alcohol consumption, while the dorsal striatum controls the compulsive, non-declarative aspects of consumption. They found that social drinkers have greater ventral striatal activation in response to alcohol cues, whereas heavy drinkers have greater dorsal striatal activation. This may indicate a shift from ventral to dorsal striatal activity as alcohol use becomes problematic and compulsive.

The function of the NAc mainly lies in the dopaminergic reward system and instrumental conditioning (Corbit, Muir, & Balleine, 2001). As a result, dopamine release into the NAc motivates animals to work to earn rewards (Salamone, Correa, Farrar, & Mingote, 2007). Deep brain stimulation of the NAc may be a promising treatment for severe alcoholism (Müller et al., 2009). Out of three patients who received the treatment, two continued to be abstinent one year later while the other significantly decreased his alcohol consumption. This indicates that under-activation of the NAc may contribute to the compulsive, non-declarative behaviors seen in alcoholism. Altogether, this suggests that regions of the brain supporting declarative and non-declarative memory are affected in AUD, and that alcoholics may not have the capacity to efficiently utilize different memory systems. Additionally, deficits in declarative or non-declarative memory may

increase an individual's risk for transitioning from the "regulated relapse" phase to the "compulsive relapse" phase.

The California Verbal Learning Test – 2nd Edition (CVLT-II; Delis, Kramer, Kaplan, & Ober, 2000) is a neuropsychological assessment commonly used to measure declarative memory. The CVLT-II measures encoding, consolidation, retrieval, and recognition of verbal information. Recently detoxified alcoholics tend to perform worse than healthy controls (Goldstein et al., 2004), and Korsakoff's patients are more severely impaired (Wester, Roelofs, Egger, & Kessels, 2014). Non-declarative memory is commonly assessed using procedural motor tasks such as the mirror-tracing task. Participants trace figures as seen through a mirror as quickly and as accurately as possible. Mirror-tracing ability appears to be spared in AUD (Junghanns, Horbach, Ehrenthal, Blank, & Backhaus, 2009), as well as in Korsakoff's syndrome (Oudman, Nijboer, Postma, Wijnia, & Van der Stigchel, 2015). Together this suggests that declarative memory is impaired in AUD, while non-declarative memory remains intact.

In order to understand how these memory systems may be a factor in AUD, it is important to examine how these systems normally function. One way to examine both declarative and non-declarative memory systems simultaneously is by using a probabilistic category learning task such as the Weather Prediction Task (WPT; Knowlton, Squire, & Gluck, 1994). The WPT employs aspects of both declarative and non-declarative processes. A participant is presented with any combination of four different cards and learns how likely that combination of cards will predict rainy or sunny weather. Each of the four cards is assigned a probability of predicting a weather outcome. Poldrack and colleagues (2001) demonstrated that the MTL is more activated during

declarative aspects of the task, and the caudate is more activated during non-declarative aspects. To demonstrate this effect, two versions of the WPT were used. One group performed the original WPT task, also called the feedback-based (FB) task, while another performed a paired associate (PA) task. In the PA task, the stimuli and correct responses were presented together. This is thought to activate declarative processes as the participant is being told the correct response, rather than learning the response implicitly through feedback via operant conditioning. Poldrack et al. (2001) found that the caudate was significantly activated during the FB task, while the MTL activity was diminished to below baseline. Furthermore, during the PA task, the MTL was significantly activated while the caudate deactivated, demonstrating a double-dissociation of these memory processes. Additional analyses revealed a significant negative correlation between activity in the MTL and activity in the caudate, specifically the left MTL and the right caudate. Additionally, the changes of these regions during an extended number of FB trials revealed that the MTL was activated and the caudate was deactivated during the initial phase of the task. As training progressed, the MTL quickly deactivated while the caudate activated. Together this suggests that the MTL and caudate support declarative and non-declarative memory respectively, and that these two regions appear to compete with one another during declarative and non-declarative processes.

There is also evidence to suggest that these memory systems are not directly connected to each other, but rather mediated by other regions (Poldrack & Rodriguez, 2004). Path analysis of event-related fMRI WPT data revealed several significant negatively correlated paths between the hippocampus and prefrontal cortex (PFC). Additionally, significant positive paths were found between striatal regions (including the

caudate) and the MTL, as well as the striatum and PFC. Although there are direct pathways between the MTL and striatum, their activation patterns suggest that these memory systems are predominantly mediated by frontal regions.

There are few studies examining substance use disorders (SUDs) and the WPT. While one study failed to find differences between cocaine users and healthy controls (Vadhan et al., 2008), another study with similar methods by the same group found that cocaine users performed worse than controls, but only after controlling for marijuana and alcohol use (Vadhan et al., 2014). Because these are the only two published studies in regard to the WPT and SUDs, it is still unclear how AUD or SUD in general may affect performance on the WPT.

Eating disorders share many similarities with alcohol addiction in terms of cognitive functioning and behavior (Goodman & Packard, 2016). In a study examining sub-threshold bulimics (individuals who do not meet the frequency requirement of bingeing for full bulimia, but who still binged once per week) performed similarly on the WPT compared to controls (Celone, Thompson-Brenner, Ross, Pratt, & Stern, 2011). However, interestingly, fMRI revealed different activation patterns during the task. Sub-threshold bulimics had decreased activity in the MTL, retrosplenial cortex, middle frontal gyrus, and anterior and posterior cingulate cortex compared to controls during initial learning. Additionally, sub-threshold bulimics showed increased activity in the dorsolateral PFC (DLPFC) when compared to controls later in the task. Overall, the sub-threshold bulimic group had increased caudate nucleus and DLPFC activity. This study demonstrated that, even if behaviorally two groups may perform similarly, there may be underlying neural differences. As of yet, it is unknown how AUD may affect

performance on the WPT, and it is unclear whether or not dysfunctional prefrontal involvement mediates performance on the WPT in AUD.

CHAPTER TWO

Cortical Functioning in Alcohol Use Disorder

Since memory systems are likely mediated by PFC (Poldrack & Rodriguez, 2004), it is important to examine how these regions may differ functionally in AUD, and how they interact with memory systems. The PFC is comprised of several distinct regions, each with its own unique function. The four main subdivisions of the PFC are the dorsolateral prefrontal cortex (DLPFC), the orbitofrontal prefrontal cortex (OFC), the ventrolateral prefrontal cortex (VLPFC), and the motor cortex. The VLPFC and motor cortex are both involved with motor functioning—the motor cortex plans and executes movements, while the VLPFC inhibits movements (Aron, Robbins, & Poldrack, 2004). The function of the DLPFC can be described as executive functioning, which includes domains such as working memory (Petrican & Schimmack, 2008) and cognitive control (Gläscher et al., 2012). Lastly, the OFC is involved in some aspects of reward learning and behavioral flexibility (Everitt et al., 2007). Individuals with AUD have smaller PFCs compared to controls (Pfefferbaum, Sullivan, Mathalon, & Lim, 1997), and perform worse on measures of executive functioning (Stephan et al., 2017). Together the DLPFC and the OFC act to regulate behavior by maintaining attention and maintaining reward cues (Crews & Boettiger, 2009b; Schoenbaum, Roesch, & Stalnaker, 2006). A breakdown of these functions may lead to behaviors such as increased impulsivity, or an inability to regulate rewarding stimuli appropriately—behaviors often associated with

addiction. Given their importance to AUD, the DLPFC and the OFC are discussed in detail below.

Dorsolateral Prefrontal Cortex

The role of the DLPFC broadly lies in executive functioning. Lesions of the DLPC result in impaired cognitive control (e.g. response inhibition; Gläscher et al., 2012), as well as impaired working memory (Petrican & Schimmack, 2008), indicating that it plays a role in the regulation of both impulsivity and memory. Bechara (2005) has noted the similarities between patients with DLPC lesions and alcoholics, as many of the cognitive and behavioral changes seen in lesion patients (i.e. impaired executive functioning, increased impulsivity) are also seen in alcoholics. Additionally, a recent meta-analysis of volumetric differences due to chronic alcohol use found that the DLPC is significantly smaller in alcoholics when compared to healthy controls (X. Yang et al., 2016).

Resting state functional imaging studies have found that the DLPC of alcoholics is overactive when processing emotions—especially negative emotions (Goldstein & Volkow, 2012). This suggests that alcoholics' DLPC is generally dysregulated. Treatments targeting the DLPC provide further evidence for its involvement in AUD. Repetitive transcranial magnetic stimulation (rTMS) of the DLPC has been used to reduce craving, drug-seeking, and consumption (Boggio et al., 2008), and also reduces behavioral impulsivity (Del Felice et al., 2016). Together this further suggests that the DLPC is dysregulated in alcoholics. Since the DLPC may also regulate subcortical memory systems, this dysregulation could impact how subcortical memory systems function.

Orbitofrontal Cortex

Another prefrontal region playing a role in SUD is the orbitofrontal cortex (OFC; Everitt et al., 2007). The OFC is thought to be important for behavioral flexibility, i.e. the ability to alter or inhibit a previously learned response (Elliott, Dolan, & Frith, 2000). The OFC is involved in the maintenance, but not acquisition, of conditioned rewards (Pears, Parkinson, Hopewell, Everitt, & Roberts, 2003; Pickens et al., 2003). For example, pre-training OFC lesions in rats do not impair task acquisition; however, they do impair reinforcer devaluation after initial training. The OFC is also heavily implicated in reversal learning—a form of reward maintenance (Everitt et al., 2007). Reversal learning requires participants to relearn responses by reversing which responses are rewarded and which are not during testing. For example, on the WPT, if a combination of cards had previously predicted sunny weather, those cards would no longer predict sunny weather following reversal learning. Reversal learning requires behavioral flexibility and the ability to update previously conditioned rewards. An inability to properly update and manage conditioned rewards is an important characteristic of addiction. If an individual is unable to alter their behavior towards a reward (e.g. alcohol) they may be more likely to develop a AUD.

Humans with OFC lesions have many of the same behavioral deficits as chronic substance abusers. Patients with OFC lesions are characterized as being impulsive, emotional, and impaired at decision-making (Bechara, 2004). Patients with OFC lesions perform poorly on impulsivity tasks similarly to those with substance use disorders (Körner, Schmidt, & Soyka, 2015). Exacerbating the problem is the fact that drugs themselves alter OFC functioning (Everitt et al., 2007; J D Jentsch & Taylor, 1999). For

example, rodent and primate studies have found that administration of cocaine, even after withdrawal, results in impaired reversal learning (Jentsch, Olausson, De La Garza, & Taylor, 2002; Schoenbaum, Saddoris, Ramus, Shaham, & Setlow, 2004). In humans, other studies have noted changes in dopaminergic functioning in substance-dependent individuals. Detoxified alcoholics administered methylphenidate showed significantly attenuated levels of dopamine in the striatum compared to controls, and that OFC metabolism was significantly negatively correlated with dopamine increases in the striatum (Volkow et al., 2007). This perhaps indicates that OFC dysfunction leads to changes in memory systems, leading to behaviors such as impaired reversal learning. In the case of AUD, OFC dysfunction may lead to dysfunctional memory systems, which in turn may lead to an inability to adapt or reduce alcohol use even in the face of negative consequences. Additionally, as the disorder progresses and alcohol intake increases, this may lead to progressively worse OFC functioning, and in turn, even worse memory system functioning.

Neural Pathways Between PFC and Memory Systems

In regards to non-declarative memory, several pathways between the striatum and the PFC have been established, and these pathways appear to be dysfunctional addictive disorders (Tomasi & Volkow, 2013). In particular, DLPC projects to the dorsal striatum (nucleus accumbens) while the OFC projects to the ventral striatum (caudate and putamen). These two pathways are weaker in addicted individuals compared to non-addicted individuals (Yuan et al., 2016), suggesting that regulation of non-declarative memory systems via the PFC is abnormal in addiction. These two frontostriatal circuits have unique functions. Since the DLPC is associated impulsivity and the NAc is involved

with reward and motivation, dysfunction in this circuit may predispose an individual towards engaging in risky but rewarding behaviors such as substance use. On the other hand, dysfunction in the OFC-caudate circuit may result in an inability to adapt alcohol use even in the face of negative consequences, as is often the case in addiction.

There are several pathways between cortical areas and the hippocampus, including the OFC and hippocampus (Catenoix et al., 2005; Ranganath, Heller, Cohen, Brozinsky, & Rissman, 2005) that support declarative memory. For example, functional connectivity between these regions is associated with successful memory formation (Ranganath et al., 2005). While the OFC and hippocampus have been well-examined in regards to AUD and other SUDs individually, functional connectivity between the two has not. However, since these regions are negatively affected in AUD, it seems likely that this pathway would be dysfunctional. Since AUD manifests from the transition from declarative to non-declarative behaviors, studying hippocampal connectivity is important in our understanding of the development of this disorder. While yet to be demonstrated, these systems' functionality may be involved in memory tasks such as the WPT, which involves interactions between distinct memory systems and prefrontal areas.

Risk in Alcohol Use Disorders

Important to note is the fact that almost all studies examining AUD and learning and memory are in the context of already-developed disorders. A handful of risk factors for AUD have been identified, however it is still difficult to predict—and even more so prevent—the development of AUD in individuals. Some of the aforementioned differences seen in alcoholics and controls may be due to alcohol consumption, but some may be indicative of premorbid differences. However, with very few studies examining

potential premorbid neurological differences, premorbid differences at the neural level are largely unknown, and such studies are difficult and expensive to perform. By looking at potential neurological factors, we hope to gain further insight into the underlying mechanisms of risk.

In regard to connectivity between PFC and memory systems, there may be premorbid differences associated with risk for future SUDs, and these differences may be impacted by alcohol use. Dysfunctional connectivity between frontal regions and memory systems may influence how effectively an individual can utilize each memory system, which may put that individual at risk for developing problematic drinking patterns. In conjunction with structural changes due to alcohol use, this may exacerbate the consequences of problematic drinking.

In addition to dysfunctional connectivity, deficits in executive functioning, originating in frontal cortex, may add a further level of risk. The Wisconsin Card Sorting Test (WCST; Grant & Berg, 1948) is a neuropsychological assessment of executive functioning. Imaging studies indicate that DLPC is activated during the WCST (Berman et al., 1995; Nagahama et al., 1996), an area that is likely affected in AUD (Bechara, 2005). Alcoholics and adult children of alcoholics tend to perform worse than controls on the WCST (Du, Guo, & Jian, 2002; Fama, Pfefferbaum, & Sullivan, 2004; Gierski et al., 2013), indicating executive dysfunction. Since memory systems are mediated by the PFC, poorer performance on the WPT associated with poorer performance on the WCST may indicate that executive dysfunction and memory system dysregulation are risk factors for AUD. In addition, since the OFC is involved in reversal learning, and it is impaired in AUD, adding a reversal learning component to the WPT may reveal premorbid

dysfunctional connectivity between memory systems and the OFC. This may suggest that individuals at-risk for AUD do not effectively utilize their multiple memory systems, or that there is dysfunctional connectivity between the memory systems and frontal regions. Additionally, if an individual has poor executive functioning, they may not have the capacity to utilize their memory systems efficiently.

One risk factor that has already been established is impulsivity (Sher, Bartholow, & Wood, 2000). Impulsivity can be defined as a tendency to act quickly without thinking, or as a preference for immediate rather than delayed rewards. Those who score high on impulsivity scales are more likely to develop a substance-use disorder (Verdejo-Garcıá, Lawrence, & Clark, 2008). Although increased impulsivity may be a result of chronic alcohol exposure, there is evidence to suggest that it is also a pre-existing trait (Dolan et al., 2008). Impulsive behaviors also seem to resemble some of the automatic, non-declarative behaviors seen in addiction (e.g. acting without thinking); however, automatic behaviors do not necessarily equate to impulsive behaviors. It may be the case that impulsive behaviors predispose an individual to develop a pattern of automatic, non-declarative behaviors. Elevated impulsivity is associated with lower executive functioning and poorer performance on tests such as the WCST (Dolan et al., 2008), however how exactly impulsivity maps onto the functions of memory systems is yet unclear. Given the lack of information on this topic, an exploratory aim of this current study is to examine how impulsivity is related to performance on the WPT. If demonstrated, this would confirm that one of the symptoms of dysregulated memory systems is increased impulsivity.

Another risk factor is problem drinking. Problem drinking, or a pattern of drinking which borderlines that seen in AUD but does not yet meet the diagnostic criteria, is a significant predictor of AUD and medical complications related to alcohol (Conigrave, Hall, & Saunders, 1995). While problem drinking does not guarantee a later AUD, it represents a potential steppingstone between the "regulated relapse" and "compulsive relapse" phases in Kalivas and O'Brien's (2008) model. Problem drinking is also associated with greater impulsivity (MacKillop, Mattson, Anderson Mackillop, Castelda, & Donovick, 2007), further implicating its role as a risk factor. The Alcohol Use Disorders Identification Test (AUDIT; Saunders, Aasland, Babor, de la Fuente, & Grant, 1993) is a screening questionnaire sensitive to detecting problem drinking in adults (Conigrave et al., 1995; Reinert & Allen, 2002). As with other risk factors, problem drinking does not always lead to AUD, although it is highly correlated (r = .86; Dawson, Grant, Stinson, & Zhou, 2005). Examining those who are, and those who are not, problem drinkers provides an opportunity to explore how memory systems may differ in those at risk for AUD.

CHAPTER THREE

Objectives and Hypotheses

Risk for AUD is difficult to assess, and there is a gap in the literature examining the neural and behavioral components of risk factors for AUD. The goal of this study was to examine if the memory systems of individuals at-risk for AUD (determined by problem drinking) perform differently than those of healthy controls. The original feedback-based version of the WPT was as it utilizes two distinct memory systems—the declarative and non-declarative systems. These two memory systems were examined because the pattern of behaviors seen in AUD appear to reflect a shift from controlled declarative processes to compulsive non-declarative processes. In addition, since memory systems likely interact with each other via the PFC, a second goal of this study was to examine how PFC regions may function differently in those at-risk. Given the OFC's importance in addiction, a reversal learning component was introduced in the WPT to see if individuals at-risk were able to re-learn the task similarly to controls. Additionally, a separate task specifically aimed to measure executive functioning (the WCST) was used to examine if prefrontal dysfunction affects memory system functioning.

Lastly, given that the WPT has not previously been used in this population, an exploratory aim of this study was to probe the relationship between impulsivity and WPT performance. Since impulsivity is a marker of risk and is also related to executive functioning, this may provide further insight into how the functioning of memory systems is related to the behavioral makers of risk.

We hypothesized that:

1. On the feedback-based WPT, there would be a within-subject effect of block, where participants' performance (percent of optimal choices) improves over time. Additionally, there would be a between-subjects effect, with high-risk drinkers making fewer optimal choices than low-risk drinkers. Even though there are very few studies looking at substance use and the WPT, and the findings from these studies are mixed (Vadhan et al., 2008, 2014), there is evidence suggesting that the memory systems involved in the WPT are impaired in AUD (Lovinger & Roberto, 2010; McCool, 2011; Tomasi & Volkow, 2013).

2. During the reversal learning portion of the feedback-based WPT, high-risk drinkers would make fewer optimal choices than low-risk drinkers. Given that one of the functions of the OFC is to update the associations of previous rewards (Pears et al., 2003; Pickens et al., 2003), and that OFC dysfunction has been observed in substance use disorders (Everitt et al., 2007), one risk factor for AUD may be a dysfunctional OFC resulting in impaired reversal learning.

3. Executive functioning, as measured by perseverative responses on the WCST, will be a significant covariate of WPT performance (percent of optimal choices) comparing high-risk drinkers and low-risk drinkers on initial learning of the WPT (pre-reversal learning). Perseverative responses were chosen as it is related to impulsivity, and because alcoholics tend to engage in more perseverative responses than controls (Fama et al., 2004). This was hypothesized because of evidence suggesting that the PFC mediates memory systems' activity during the WPT (Poldrack & Rodriguez, 2004), and that fact that executive functioning is impaired in AUD (Du et al., 2002; Fama et al., 2004; Oscar-Berman et al., 2009).

CHAPTER FOUR

Materials and Methods

Inclusion and Exclusion Criteria

Participants for this study were undergraduates at Baylor University. Participants were excluded from the study if any of the following criteria are met: self-reported neurological disorders (e.g., seizure disorders, prior stroke, tumor, or brain surgery), self-reported history of substance use disorder (including AUD), any score ≥ 5 on the Drug Abuse Screening Test (Skinner, 1982), and if they were under the age of 18.

Sample Characteristics

Participants were divided into two groups: high-risk and low-risk drinkers. Risk level was determined by scores on the Alcohol Use Disorder Identification Test (AUDIT; Saunders et al., 1993). A total of 243 participants completed Part 1 of the study. Of those participants, 158 were eligible and contacted for Part II. Ultimately, 64 participants completed the entirety of the study, and were included in analyses: 20 high-risk and 44 low-risk drinkers. The sample was mostly Caucasian (73.4%) and female (n = 42). Complete sample characteristics are in Table 1. Group analyses revealed a significant difference in age between low- and high-risk drinkers ($t(62) = -2.16$, $p = .035$), as well as ADHD medication use ($\chi^2(1) = 4.16$, $p = .041$). Therefore, in addition to the medication use variables already included *a priori* as control variables, we decided to also control for age in our analyses.

Table 1
Sample characteristics.

		Group		Comparison			
Demographic Variable	Category	Low	High	Statistic	Value	*p*	Total
N	--	44	20				64
Age *M*(*SD*)	--	18.68(.80)	19.60(2.58)	*t*(62)	-2.16	.035*	18.97(1.62)
Sex (*N*)	Male	13	9	$\chi^2(1)$	1.46	.228	22
	Female	31	11				42
Race (%)	American Indian/Alaska Native	2.3%	0	$\chi^2(4)$	.949	.917	1.6%
	Asian	9.1%	5.0%				7.8%
	Black/African American	9.1%	10.0%				9.4%
	White/Caucasian	72.7%	75.0%				73.4%
	Mixed	6.8%	10.0%				7.8%
Medication (*N*)	Anxiety	4	1	$\chi^2(1)$	.32	.572	5
	Depression	0	1	$\chi^2(1)$	2.24	.135	1
	ADHD	3	5	$\chi^2(1)$	4.16	.041*	8

Note. *$p < .05$; Low = low-risk drinkers; High = high-risk drinkers; ADHD = attention deficit hyperactivity disorder

Demographics and Screening Questions

The demographics included questions about the participant's background (sex, ethnicity, family income, school standing). The survey also included screening questions to identify any exclusionary criteria.

Drug Abuse Screening Test (DAST-10)

The DAST-10 (Skinner, 1982) consists of ten questions (e.g. "Have you engaged in illegal activities in order to obtain drugs?") answered yes/no. In our sample, the DAST-10 had a Cronbach's α of .58, however other larger studies have found higher internal reliability (Cronbach's α = .94; Carey, Carey, & Chandra, 2003). The DAST-10 is significantly correlated with other measures of problematic substance use (Yudko, Lozhkina, & Fouts, 2007). Participants who scored ≥ 5 (answering "yes" to eight or more questions) were excluded from the study. A score of 5 is the cutoff for a "moderate level" of drug-related problems.

Alcohol Use Disorder Identification Test (AUDIT)

The AUDIT (Saunders et al., 1993) is a 10-item measure of problematic drinking behavior. Questions are scored on a five-point Likert scale (0 to 4), and ask about frequency of alcohol use, dependence, and alcohol-related problems (e.g. "Have you or someone else been injured because of your drinking?"). Male participants scoring ≥ 8 and female participants scoring ≥ 6 were considered high-risk (Conigrave et al., 1995). Scores below these cutoffs were considered low-risk for AUD. In our sample the AUDIT had good internal reliability (Cronbach's α = .81)

Weather Prediction Task (WPT)

The WPT (Knowlton et al., 1994) is a computerized task measuring probabilistic category learning. Combinations of four different cards, each with a distinctive geometric pattern, are presented in one, two, or three-card combinations. Each card is assigned a probabilistic value (80%, 60%, 40%, and 20%) which reflects how likely that card will predict a sunny weather outcome. The participant pushes a button to select a whether or not the cards will predict sunny weather, after which feedback is provided. Participants complete 600 trials, and then the probabilities of the cards were reversed for another 200 trials. Trials will be broken down into blocks of 50 trials. Participants will not be informed of the switch. There are currently no studies examining AUD and the WPT. Data from cocaine users are mixed—some supports worse performance compared to controls, while others support no difference (Vadhan et al., 2008, 2014).

Wisconsin Card Sorting Test (WCST)

A computerized version of the WCST (D. Grant & Berg, 1948) was used as a measure of executive functioning. Participants have to match 128 cards from two decks of 64 cards to one of four target cards. The matching rule can be based either on color, form, and/or number. After a participant successfully sorts ten consecutive cards, the matching rule changes until the participant completes all 128 cards. Prior research shows that alcoholics perform worse on the WCST compared to healthy controls (Du et al., 2002; Fama et al., 2004).

UPPS Impulsive Behavior Scale (UPPS)

The UPPS (Whiteside & Lynam, 2003) is a 45-item measure of four subscales of impulsivity: Urgency, (Lack of) Premediation, (Lack of) Perseverance, and Sensation Seeking. The subscales had good internal consistency in our sample: Cronbach's α = .88, .89, .88, and .81, respectively. Questions are scored on a four-point Likert scale ranging from 1 ("I agree strongly") to 4 ("I disagree strongly") to statements such as, "When I am upset I often act without thinking". Subscale scores on the UPPS are predictive of drinking quantity, drinking frequency, drinking problems, and alcohol dependence (Coskunpinar, Dir, & Cyders, 2013).

Recruitment

Participants were recruited through Baylor University's SONA system. The study was completed in two phases. Part I consisted of a battery of questionnaires administered online through Qualtrics, including demographics and screening questions, DAST-10, AUDIT, and UPPS. Participants eligible for the study were invited to participate in Part II, which was conducted in the lab. Participants completed the WPT and WCST on a lab computer. As compensation for their time, participants received one SONA credit for Part I and two SONA credits for Part II, for a total of three possible credits.

Data Analysis

1. Hypothesis 1 was analyzed with a mixed (block x group) ANOVA using SPSS version 24. We used the first four blocks of the WPT to assess this hypothesis .
2. Hypothesis 2 was tested with an independent samples *t*-test in SPSS using the percent of optimal choices for the first block after the switch as the dependent variable.

3. Hypothesis 3 was tested using a mixed (block x group) ANCOVA in SPSS using data from the first four blocks of the initial feedback-based WPT. For this analysis, perseverative responses from the WCST served as the covariate. Due to a computer error, 9 (4 high-risk, 5 low-risk) participants were missing WCST data. We determined that data were missing completely at random (MCAR) as the reason for missingness was unrelated to subject variables. Missing data were replaced using multiple imputation (five imputations using predictive mean matching) in R.

CHAPTER FIVE

Results

Means and standard deviations for self-report measures and WCST scores are in Table 2, as well as results of *t*-tests comparing low- and high-risk drinkers. Table 3 contains zero order correlations between study measures.

Table 2
Self-report measures, WCST, and results of t-tests comparing high- and low-risk drinkers.

Measure	Low	High	*t*(62)	*p*
AUDIT *M*(*SD*)	1.66(2.33)	10.25(5.15)	-9.24	<.001**
UPPS *M*(*SD*)				
Urgency	23.45(6.63)	27.35(6.36)	-2.21	.031*
Premeditation	18.36(5.27)	21.25(5.26)	-2.03	.046*
Perseveration	16.61(4.89)	18.40(5.28)	-1.32	.191
Sensation Seeking	35.18(6.62)	35.30(5.50)	-.07	.95
WCST				
Total Trials	90.77(18.82)	104.55(21.03)	-2.62	.011*
% Correct Trials	.79(.11)	.76(.12)	.96	.343
% Perseverative Errors	.07(.02)	.08(.03)	-1.12	.266
% Perseverative Responses	.10(.04)	.12(.04)	-1.61	.112
Completed Categories	5.68(.96)	5.45(1.00)	.86	.38

Note. *$p < .05$, **$p < .001$; Low = low-risk drinkers; High = high-risk drinkers; *M* = mean; *SD* = standard deviation; AUDIT = Alcohol Use Disorder Identification Test; UPPS = UPPS impulsivity scale; WCST = Wisconsin Card Sorting Test.

Table 3
Zero Order Correlations Between Measures.

Measure	1	2	3	4	5	6	7	8	9
1. AUDIT	--								
2. UPPS Urgency	.24	--							
3. UPPS Premeditation	.25*	.29*	--						
4. UPPS Perseveration	.23	.37**	.36**	--					
5. UPPS Sensation Seeking	.05	< .001	.16	.08	--				
6. WCST Total Trials	.22	.22	.04	-.07	-.05	--			
7. WCST % Correct	-.12	-.12	.11	.06	.06	-.76**	--		
8. WCST % Persev. Errors	.18	.19	.06	.18	.05	-.39**	.35**	--	
9. WCST % Persev. Responses	.17	.17	.18	.17	.04	-.41**	.43**	.85**	--
10. WCST Categories	-.14	.07	.07	.01	-.04	-.64**	.83**	.48**	.54**

Note. *$p < .05$, **$p < .001$; AUDIT = Alcohol Use Disorder Identification Test; *UPPS* = UPPS Impulsive Behavior Scale; *WCST* = Wisconsin Card Sorting Test

High-risk drinkers had significantly higher AUDIT scores ($t(62) = -9.24$; $p < .001$), urgency scores ($t(62) = -2.21$, $p = .031$), and premeditation scores ($t(62) = -2.03$, $p = .046$). Furthermore, high-risk drinkers took significantly more trials to complete the WCST ($t(62) = -2.62$, $p = .011$).

WPT Performance

Initial Learning

Figure 1 shows performance of both groups over all blocks of trials. Results from analyses are in Table 4. Over the first four blocks, there was no main effect of performance for both groups ($F(3, 174) = 1.14$, $p = .335$, partial $\eta^2 = .019$). There were no differences in performance between groups ($F(1, 58) = .16$, $p = .687$, partial $\eta^2 = .003$). Depression, Anxiety, and ADHD medication use were dummy coded separately as three variables and were controlled for in analyses as covariates. Neither medication use nor age accounted for any significant amount of variance in within- and between-subjects effects.

Reversal Learning

An independent samples *t* test comparing the high- and low-risk groups' percent optimal choices the first block after the switch was non-significant ($t(62) = .12$, $p = .91$).

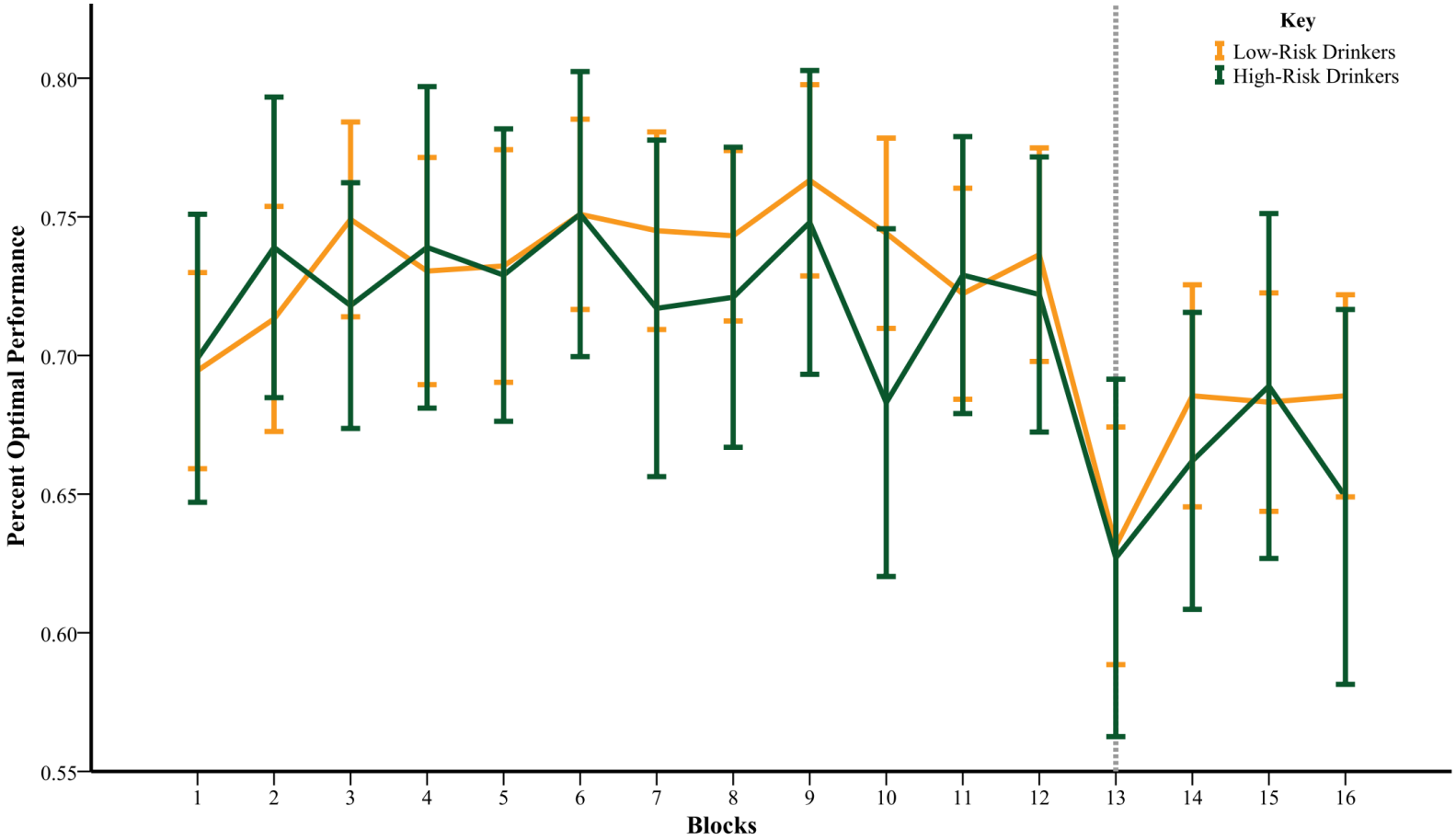

Figure 1. WPT performance for all groups for high- and low-risk drinkers. Error bars represent 95% confidence intervals. Dotted grey line marks beginning of reversal learning trials.

Table 4
Performance across blocks 1-4 of the WPT: Analysis of Variance (ANOVA).

Source	*SS*	*MS*	*F*(3, 174)	Par. η^2	*p*
Within-Subjects Effects					
Blocks	.020	.007	1.14	.019	.335
Blocks*Anxiety Meds	.012	.004	.67	.011	.569
Blocks*Depression Meds	.001	<.001	.03	.001	.992
Blocks*ADHD Meds	.030	.010	1.70	.028	.169
Blocks*Age	.022	.007	1.25	.021	.293
Blocks*Group	.018	.006	1.05	.018	.371
Source	*SS*	*MS*	*F*(1, 58)	Par. η^2	*p*
Between-Subjects Effects					
Intercept	.624	.624	14.82	.204	>.001**
Anxiety Meds	.021	.021	.50	.009	.482
Depression Meds	.121	.121	2.87	.047	.096
ADHD Meds	.008	.008	.17	.003	.669
Age	.009	.009	.22	.004	.643
Group	.007	.007	.16	.003	.687

Note. *$p < .05$, **$p < .001$; *SS* = sum of squares; *MS* = mean square; Par. η^2 = partial η^2; ADHD = attention deficit hyperactivity disorder.

Executive Functioning as a Covariate for WPT Performance

Table 5 contains results from our ANCOVA analysis, which included perseverative responses from the WCST, in addition to medication use variables, as a covariate. The main effect of block was still non-significant ($F(3, 171) = 1.02$, $p = .384$, partial $\eta^2 = .018$). There were no significant effects or interactions of depression, anxiety, and ADHD medication use, or age.

Table 5
Performance across blocks 1-4 of the WPT: Analysis of Covariance (ANCOVA).

Source	*SS*	*MS*	*F*(3, 171)	Par. η^2	*p*
Within-Subjects Effects					
Blocks	.018	.006	1.02	.018	.384
Blocks*Anxiety Meds	.012	.004	.67	.012	.573
Blocks*Depression Meds	<.001	<.001	.01	<.001	.998
Blocks*ADHD Meds	.028	.009	1.60	.027	.191
Blocks*Age	.021	.007	1.19	.020	.315
Blocks*Persev. Responses	.004	.001	.224	.004	.880
Blocks*Group	.016	.005	.93	.016	.427
Source	*SS*	*MS*	*F*(1, 57)	Par. η^2	*p*
Between-Subjects Effects					
Intercept	.472	.472	11.09	.163	.002*
Anxiety Meds	.021	.021	.48	.008	.490
Depression Meds	.133	.133	3.12	.052	.083
ADHD Meds	.013	.013	.31	.005	.578
Age	.013	.013	.32	.006	.576
Persev. Responses	.014	.014	.33	.006	.567
Group	.004	.004	.10	.002	.754

Note. *$p < .05$, **$p < .001$; *SS* = sum of squares; *MS* = mean square; Par. η^2 = partial η^2; ADHD = attention deficit hyperactivity disorder.

Exploratory Analysis

We first examined the relationship between WPT performance and impulsivity using a linear fixed effects model for the first 12 blocks of the WPT. The fixed effect for Sensation Seeking was significant ($t(759) = 4.06$, $p < .001$). Furthermore, the effects of anxiety and depression medication use were significant ($t(759) = 2.54$, $p = .011$; $t(759) = -5.10$, $p < .001$ respectively).

Next, we analyzed the reversal-learning blocks (blocks 13-16) in a second linear fixed effects model. The effect of Sensation Seeking was nearly significant ($t(247) =$

1.97, p = .050), while Urgency was (t(247) = -2.93, p = .004). The effect of anxiety medication use was also significant (t(247) = 2.67, p = .008). Table 6 contains the full results from both of the above analyses.

Table 6
Linear mixed model analysis of the WPT, relationship with impulsivity: Estimates of fixed effects

Blocks 1-12	Estimate	*SE*	*t*(759)	*p*
Parameter				
Intercept	.625	.07	9.28	<.001**
Anxiety Meds	.040	.01	2.54	.011*
Depression Meds	-.182	.04	-5.10	<.001**
ADHD Meds	-.003	.01	-.22	.830
Age	.001	<.01	.42	.674
UPPS				
Urgency	-.001	<.01	-1.59	.113
Premeditation	.001	<.01	1.16	.245
Perseveration	<.001	<.01	-.51	.610
Sensation Seeking	.003	<.01	4.06	<.001**
Blocks 13-16	Estimate	*SE*	*t*(247)	*p*
Parameter				
Intercept	.604	.13	4.65	<.001**
Anxiety Meds	.080	.03	2.67	.008*
Depression Meds	-.040	.07	-.58	.562
ADHD Meds	-.005	.03	-.158	.874
Age	-.001	.01	-.184	.854
UPPS				
Urgency	-.004	<.01	-2.93	.004*
Premeditation	.002	<.01	1.06	.292
Perseveration	.003	<.01	1.56	.120
Sensation Seeking	.003	<.01	1.97	.050

Note. *p < .05, **p < .001; *SE* = standard error; ADHD = attention deficit hyperactivity disorder; UPPS = UPPS impulsivity scale.

CHAPTER SIX

Discussion

The overall goal of this study was to examine declarative and non-declarative memory functioning in high-risk alcohol drinkers. Based on prior research, we formed a number of hypotheses to address the possibility that similar to individuals with AUD, high-risk drinkers would show behavioral deficits indicating non-declarative memory deficits when compared to low-risk drinkers. To address these hypotheses, we used the Weather Prediction Task, which is known to employ both declarative and non-declarative processes (Poldrack et al., 2001). By and large, our data did not support our hypotheses. Nonetheless, the data may still be informative for future studies on this topic.

In general, group differences on the UPPS, and WCST were as-expected. High-risk drinkers had elevated Urgency and Premeditation compared to low-risk drinkers. High-risk drinkers also took more trials to complete the WCST than low-risk drinkers.

Our first hypothesis was comprised of two parts. First, we predicted that participants' performance would improve as they learned the task. Second, we predicted a difference in performance between our high- and low-risk groups. The data did not support these. We did not see a main effect of performance across blocks. This is most likely due to considerable variation in performance across participants. Some participants learned the task very quickly, while others never achieved the same level of performance. From prior research, participants usually reach a level of approximately 80% optimal responding (Gluck, Shohamy, & Myers, 2002). However, we had several participants (*n* = 10, two high-risk and eight low-risk) fail to reach even 60% by block 12. Re-analyzing

the data excluding these participants did not meaningfully change our results, and there did not appear to be any characteristic differences compared to those who performed better on the task. Differences could be a lack of effort or motivation to properly learn the task.

There are several reasons why we may not have observed a difference between groups in addition to the above problem. The first and most obvious is that our high-risk group was quite small. While we had reached our enrollment goal, we did not have an alcohol-related WPT study on which to power ours. Instead, we based our power analysis on a study done in cocaine-dependent participants (Vadhan et al., 2014) who likely have more significant brain changes than our college student problem drinkers.

Behavioral tests may not always be able to capture subtle changes in deficits like those we would expect. The participants in our sample were all college students at a private university and were all relatively healthy and high-functioning. In the memory literature, relatively healthy older adults reporting cognitive complaints have significant neural changes similar to patients diagnosed with mild cognitive impairment (Rabin et al., 2006). However, this population of older adults perform normally on behavioral tests, despite showing executive functioning impairments on a self-report measure. Studies looking at high-risk drinkers also show mixed results on neuropsychological impairment. While performance on the WCST is generally considered vulnerable to the effects of alcohol (Stephan et al., 2017), and several studies have observed significant impairments in high-risk drinkers (e.g., Giancola, Zeichner, Yarnell, & Dickson, 1996; Houston et al., 2014; Rothlind et al., 2005), others have not been able to replicate those results (Blume, Marlatt, & Schmaling, 2000; Nigg et al., 2006; Parada et al., 2012). Lastly, Celone et al.

(2011) reported findings in their sub-threshold bulimic sample in demonstrating this problem. While the sub-threshold bulimic sample did not perform any differently from their healthy control sample on the WPT, the authors observed several neural differences between the groups. Altogether, this suggests that behavioral tests alone may not capture subtle deficits in relatively healthy, but still impaired, populations. When assessing these individuals, neuroimaging and self-report measures may be more useful for characterizing deficits than traditional behavioral tests.

We also predicted that high-risk drinkers would perform worse than low-risk drinkers on a reversal learning portion of the WPT. A *t*-test comparing the percent of optimal choices revealed no group differences, and thus our hypothesis was not supported. We based our initial predictions on the fact that OFC functioning is impaired in AUD (Everitt et al., 2007). Furthermore, executive dysfunction is generally regarded as a risk-factor for AUD. For example, individuals with a family history of AUD perform worse on tests of executive functioning than those without a family history of AUD (Dolan et al., 2008). Family history is also associated with differences in neural activation (Cservenka, Herting, & Nagel, 2012) and receptor functioning (Underwood, Mann, Huang, & Arango, 2008) in the PFC. We may not have seen any group differences in our study due to a large amount of variability in performance throughout the samples (see figure 1).

For our third analyses, we re-examined the same data from Hypothesis 1 with the addition of a measure of executive functioning as a covariate. We used the perseverative responses score from the WCST as our measure of executive functioning, as it has been shown previously to be susceptible to impairment in AUD (Stephan et al., 2017). We

hypothesized that executive functioning could be a significant covariate for WPT performance. After including perseverative responses as a covariate in our analysis, the main effect of block was effectively unchanged. As was previously discussed, the two main memory systems implicated in learning the WPT are likely communicating via the PFC. Furthermore, a transition from declarative (i.e. hippocampal) to non-declarative (caudate-based) memory is necessary to effectively learn the WPT (Poldrack & Rodriguez, 2004). Yang, Raine, Colletti, Toga, and Narr (2011) have demonstrated previously that a reduction of cortical thickness in the OFC is related to perseveration on the WCST, an area of the brain implicated in AUD. However, even though WCST impairment has been observed in some studies with high-risk drinkers (e.g., Houston et al., 2014), we were unable to replicate the effect.

Exploratory Analysis

Given that elevated impulsivity is also a risk factor for AUD (Crews & Boettiger, 2009a), we also examined how impulsivity would relate to performance on the WPT. Since no study has examined the relationship of impulsivity to the WPT, we considered our analysis exploratory. Overall, results suggested that lower levels of Urgency and elevated levels of Sensation Seeking, contributed most to better WPT performance. For the first 12 blocks, before reversal learning, only the effect of Sensation Seeking was significant. On the other hand, analysis of the reversal learning blocks (blocks 13-16) revealed a significant effect of Urgency and a near-significant effect of Sensation Seeking, perhaps suggesting a double-dissociation of the two impulsivity factors associated with initial and reversal learning.

Sensation seeking refers to a tendency towards engaging in risky, rewarding, and exciting behaviors (Zuckerman, 2008). In terms of AUD, sensation seeking is related to alcohol consumption quantity, but not alcohol-related problems (Magid & Colder, 2007). Individuals high in sensation seeking engage in riskier behaviors (e.g., drug use) than those low or moderate in sensation seeking (Zuckerman, Bone, Neary, Mangelsdorff, & Brustman, 1972). Additionally, high sensation seekers appear to process rewarding stimuli differently than low sensation seekers such that they require higher levels of stimulation to experience reward (Cservenka, Herting, Seghete, Hudson, & Nagel, 2013).

A few studies have found links between elevated levels of Sensation Seeking and improved automatic/non-declarative learning (e.g., Dietrich, de Wit, & Horstmann, 2016; Lawson, Gauer, & Hurst, 2012; Pleskac, Wallsten, Wang, & Lejuez, 2008). In the case of the WPT, non-declarative processes are activated after initial learning of the task (Poldrack & Packard, 2003), which may explain why we found a positive effect of Sensation Seeking on WPT performance in our sample.

Urgency, defined as a tendency to act impulsively to avoid negative emotions (Magid & Colder, 2007), is generally regarded as a predictor of alcohol-related problems (Anestis, Selby, & Joiner, 2007). . The negative effect of Urgency during reversal learning suggests that those higher in urgency performed worse on the reversal learning trials than those lower in urgency. Furthermore, in our sample, high-risk drinkers had significantly elevated levels of urgency compared to low-risk drinkers (see Table 2). Higher levels of urgency have been linked to increased craving for alcohol and increased activation of the ventromedial PFC in response to alcohol cues (Cyders et al., 2014), and intrinsic activity (i.e. slow changes in activity during resting state) in the DLPFC (Zhao et

al., 2017). Furthermore, the ventromedial PFC and DLPFC are both involved in emotion regulation (Etkin, Egner, & Kalisch, 2011; Goldin, McRae, Ramel, & Gross, 2008) and reward processing (Bechara, Damasio, Damasio, & Anderson, 1994; Wallis & Miller, 2003). Altogether this suggests that individuals with elevated urgency have dysfunctional reward and emotion regulation. This is also supported at the behavioral level, as individuals with elevated urgency tend to cope with negative emotions by drinking (Littlefield, Stevens, & Sher, 2014).

Why urgency relates to reversal learning on the WPT is unclear, and neuroimaging will likely be necessary to fully understand the brain processes involved. One possible explanation is that elevated urgency leads to increased perseveration. A study that induced feelings of urgency found that induced urgency decreased response time (suggesting tendency towards automatic responding), as well as changes in striatal activation (Jones, Minati, Harrison, Ward, & Critchley, 2011). As Poldrack and Packard (2003) have previously demonstrated, increased striatal activation is associated with learning on the WPT. Individuals who have elevated baseline levels of urgency may be predisposed towards falling back on automatic, unconscious, non-declarative behaviors. On the WPT this would manifest as difficulty relearning automatic responses to stimuli.

Limitations

The most impactful limitation of this study was sample size. We had difficulty recruiting a large number of self-reported high-risk drinkers, which resulted in decreased variability in performance on the WPT. However, it is possible that even if we had more high-risk drinkers in the study, we still would find the same results. Furthermore, our study was cross-sectional, and as such we cannot make definitive predictions regarding

individuals who will later go on to develop AUD. Lastly, our sample was a sample of convenience, which may have limited generalizability outside of the college student population.

We chose the WPT as it is known to employ both declarative and non-declarative processes, however we did not find the effects we predicted. As evidenced by Celone et al.'s (2011) study, we may need to employ neuroimaging techniques to observe any differences between high- and low-risk drinkers. Behavioral differences may be too subtle for the WPT to pick up alone. However, our results will add to a small body of literature, and hopefully inform future studies in this domain.

Our other measures, the UPPS and the WCST were chosen because they historically have proven useful measuring AUD-related deficits. However, they are not the only measures of impulsivity and executive functioning. As was discussed previously, the WCST does not always capture deficits in high-risk drinkers (e.g., Blume et al., 2000), and while WCST performance is sensitive to AUD (Stephan et al., 2017) it may have had high enough sensitivity in this sample. Future studies may benefit from considering alternate measures of impulsivity and executive functioning.

Conclusions

The goal of this study was to examine declarative and non-declarative memory functioning in high-risk drinkers. Caudate-based, non-declarative memory is impaired in AUD, but may also be a risk factor for development of AUD. Furthermore, declarative and non-declarative systems communicate through PFC, so executive dysfunction may also negatively impact memory systems' functioning. Overall, our results did not support our primary hypotheses. However, our exploratory analyses revealed that impulsivity—

specifically sensation seeking and urgency—was significantly related to task performance. Future studies will be needed to (1) replicate and confirm our results with a larger sample, (2) generalize results to a broader population and (3) further elucidate mechanisms for the relationship between impulsivity and the WPT, including via neuroimaging studies.

REFERENCES

Anestis, M. D., Selby, E. A., & Joiner, T. E. (2007). The role of urgency in maladaptive behaviors. *Behaviour Research and Therapy*, *45*(12), 3018–3029. http://doi.org/10.1016/J.BRAT.2007.08.012

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2004). Inhibition and the right inferior frontal cortex. *Trends in Cognitive Sciences*, *8*(4), 170–177. http://doi.org/10.1016/j.tics.2004.02.010

Bechara, A. (2004). The role of emotion in decision-making: Evidence from neurological patients with orbitofrontal damage. *Brain and Cognition*, *55*(1), 30–40. http://doi.org/10.1016/j.bandc.2003.04.001

Bechara, A. (2005). Decision making, impulse control and loss of willpower to resist drugs: a neurocognitive perspective. *Nature: Neuroscience*, *8*(11), 1458–1463. http://doi.org/Doi 10.1038/Nn1584

Bechara, A., Damasio, A. R., Damasio, H., & Anderson, S. W. (1994). Insensitivity to future consequences following damage to human prefrontal cortex. *Cognition*, *50*(1–3), 7–15. http://doi.org/10.1016/0010-0277(94)90018-3

Berman, K. F., Ostrem, J. L., Randolph, C., Gold, J., Goldberg, T. E., Coppola, R., … Weinberger, D. R. (1995). Physiological activation of a cortical network during performance of the Wisconsin Card Sorting Test: A positron emission tomography study. *Neuropsychologia*, *33*(8), 1027–1046. http://doi.org/10.1016/0028-3932(95)00035-2

Blume, A. W., Marlatt, G. A., & Schmaling, K. B. (2000). Executive cognitive function and heavy drinking behavior among college students. *Psychology of Addictive Behaviors*, *14*(3), 299–302. http://doi.org/10.1037/0893-164X.14.3.299

Boggio, P. S., Sultani, N., Fecteau, S., Merabet, L., Mecca, T., Pascual-Leone, A., … Fregni, F. (2008). Prefrontal cortex modulation using transcranial DC stimulation reduces alcohol craving: A double-blind, sham-controlled study. *Drug and Alcohol Dependence*, *92*(1), 55–60. http://doi.org/10.1016/j.drugalcdep.2007.06.011

Carey, K. B., Carey, M. P., & Chandra, P. S. (2003). Psychometric evaluation of the alcohol use disorders identification test and short drug abuse screening test with psychiatric patients in India. *The Journal of Clinical Psychiatry*, *64*(7), 767–74. http://doi.org/10.4088/JCP.v64n0705

Catenoix, H., Magnin, M., Guénot, M., Isnard, J., Mauguière, F., & Ryvlin, P. (2005). Hippocampal-orbitofrontal connectivity in human: An electrical stimulation study. *Clinical Neurophysiology*, *116*(8), 1779–1784. http://doi.org/10.1016/j.clinph.2005.03.016

Celone, K. A., Thompson-Brenner, H., Ross, R. S., Pratt, E. M., & Stern, C. E. (2011). An fMRI investigation of the fronto-striatal learning system in women who exhibit eating disorder behaviors. *NeuroImage*, *56*(3), 1749–1757. http://doi.org/10.1016/j.neuroimage.2011.03.026

Cohen, N. J., & Squire, L. R. (1980). Preserved Learning and Retention of Pattern-Analyzing Skill in Amnesia : Dissociation of Knowing How and Knowing that Author (s): Neal J . Cohen and Larry R . Squire Published by : American Association for the Advancement of Science Stable URL : http://. *Science*, *210*(4466), 207–210.

Conigrave, K. M., Hall, W. D., & Saunders, J. B. (1995). The AUDIT questionnaire: choosing a cutoff score. *Addiction*, *90*(10), 1349–1356. http://doi.org/10.1046/j.1360-0443.1995.901013496.x

Corbit, L. H., Muir, J. L., & Balleine, B. W. (2001). The Role of the Nucleus Accumbens in Instrumental Conditioning: Evidence of a Functional Dissociation between Accumbens Core and Shell. *The Journal of Neuroscience*, *21*(9), 3251–3260. http://doi.org/http://www.jneurosci.org/content/21/9/3251

Coskunpinar, A., Dir, A. L., & Cyders, M. A. (2013). Multidimensionality in impulsivity and alcohol use: A meta-analysis using the UPPS model of impulsivity. *Alcoholism: Clinical and Experimental Research*, *37*(9), 1441–1450. http://doi.org/10.1111/acer.12131

Crews, F. T., & Boettiger, C. A. (2009a). Impulsivity, frontal lobes and risk for addiction. *Pharmacology Biochemistry and Behavior*, *93*(3), 237–247. http://doi.org/10.1016/j.pbb.2009.04.018

Crews, F. T., & Boettiger, C. A. (2009b, September 1). Impulsivity, frontal lobes and risk for addiction. *Pharmacology Biochemistry and Behavior*. Elsevier. http://doi.org/10.1016/j.pbb.2009.04.018

Cservenka, A., Herting, M. M., & Nagel, B. J. (2012). Atypical frontal lobe activity during verbal working memory in youth with a family history of alcoholism. *Drug and Alcohol Dependence*, *123*(1–3), 98–104. http://doi.org/10.1016/j.drugalcdep.2011.10.021

Cservenka, A., Herting, M. M., Seghete, K. L. M., Hudson, K. A., & Nagel, B. J. (2013). High and low sensation seeking adolescents show distinct patterns of brain activity during reward processing. *NeuroImage*, *66*, 184–193. http://doi.org/10.1016/J.NEUROIMAGE.2012.11.003

Cyders, M. A., Dzemidzic, M., Eiler, W. J., Coskunpinar, A., Karyadi, K., & Kareken, D. A. (2014). Negative Urgency and Ventromedial Prefrontal Cortex Responses to Alcohol Cues: FMRI Evidence of Emotion-Based Impulsivity. *Alcoholism: Clinical and Experimental Research*, *38*(2), 409–417. http://doi.org/10.1111/acer.12266

Dawson, D. A., Grant, B. F., Stinson, F. S., & Zhou, Y. (2005). Effectiveness of the Derived Alcohol Use Disorders Identification Test (AUDIT-C) in Screening for Alcohol Use Disorders and Risk Drinking in the US General Population. *Alcoholism: Clinical & Experimental Research*, *29*(5), 844–854. http://doi.org/10.1097/01.ALC.0000164374.32229.A2

Del Felice, A., Bellamoli, E., Formaggio, E., Manganotti, P., Masiero, S., Cuoghi, G., … Serpelloni, G. (2016). Neurophysiological, psychological and behavioural correlates of rTMS treatment in alcohol dependence. *Drug and Alcohol Dependence*, *158*, 147–153. http://doi.org/10.1016/j.drugalcdep.2015.11.018

Delis, D. C., Kramer, J. H., Kaplan, E., & Ober, B. A. (2000). California Verbal Learning Test – second edition. Adult version. Manual. *Test*.

Dietrich, A., de Wit, S., & Horstmann, A. (2016). General Habit Propensity Relates to the Sensation Seeking Subdomain of Impulsivity But Not Obesity. *Frontiers in Behavioral Neuroscience*, *10*. http://doi.org/10.3389/fnbeh.2016.00213

Dolan, S. L., Bechara, A., & Nathan, P. E. (2008). Executive dysfunction as a risk marker for substance abuse: The role of impulsive personality traits. *Behavioral Sciences and the Law*, *26*(6), 799–822. http://doi.org/10.1002/bsl.845

Du, Guo, & Jian. (2002). Cognitive impairment of alcoholic dependents measured by the Wisconsin Card Sorting Test. *Chinese Mental Health Journal*, *16*(5), 296–298. http://doi.org/10.1037/t31298-000

Elliott, R., Dolan, R. J., & Frith, C. D. (2000). Dissociable functions in the medial and lateral orbitofrontal cortex: evidence from human neuroimaging studies. *Cerebral Cortex*, *10*(3), 308–317. http://doi.org/10.1093/cercor/10.3.308

Etkin, A., Egner, T., & Kalisch, R. (2011). Emotional processing in anterior cingulate and medial prefrontal cortex. *Trends in Cognitive Sciences*, *15*(2), 85–93. http://doi.org/10.1016/J.TICS.2010.11.004

Everitt, B. J., Hutcheson, D. M., Ersche, K. D., Pelloux, Y., Dalley, J. W., & Robbins, T. W. (2007). The orbital prefrontal cortex and drug addiction in laboratory animals and humans. *Annals of the New York Academy of Sciences*, *1121*, 576–597. http://doi.org/10.1196/annals.1401.022

Fama, R., Pfefferbaum, A., & Sullivan, E. V. (2004). Perceptual Learning in Detoxified Alcoholic Men: Contributions From Explicit Memory, Executive Function, and Age. *Alcoholism: Clinical & Experimental Research*, *28*(11), 1657–1665. http://doi.org/10.1097/01.ALC.0000145690.48510.DA

Giancola, P. R., Zeichner, A., Yarnell, J. E., & Dickson, K. E. (1996). Relation between executive cognitive functioning and the adverse consequences of alcohol use in social drinkers. *Alcoholism: Clinical and Experimental Research*, *20*(6), 1094–1098. http://doi.org/10.1111/j.1530-0277.1996.tb01952.x

Gierski, F., Hubsch, B., Stefaniak, N., Benzerouk, F., Cuervo-Lombard, C., Bera-Potelle, C., … Limosin, F. (2013). Executive functions in adult offspring of alcohol-dependent probands: toward a cognitive endophenotype? *Alcoholism, Clinical and Experimental Research*, *37 Suppl 1*, E356-63. http://doi.org/10.1111/j.1530-0277.2012.01903.x

Gläscher, J., Adolphs, R., Damasio, H., Bechara, A., Rudrauf, D., Calamia, M., … Tranel, D. (2012). Lesion mapping of cognitive control and value-based decision making in the prefrontal cortex. *Proceedings of the National Academy of Sciences of the United States of America*, *109*(36), 14681–6. http://doi.org/10.1073/pnas.1206608109

Gluck, M. A., Shohamy, D., & Myers, C. (2002). How do people solve the “weather prediction” task?: individual variability in strategies for probabilistic category learning. *Learning & Memory (Cold Spring Harbor, N.Y.)*, *9*(6), 408–418. http://doi.org/10.1101/lm.45202

Goldin, P. R., McRae, K., Ramel, W., & Gross, J. J. (2008). The Neural Bases of Emotion Regulation: Reappraisal and Suppression of Negative Emotion. *Biological Psychiatry*, *63*(6), 577–586. http://doi.org/10.1016/J.BIOPSYCH.2007.05.031

Goldstein, R. Z., Leskovjan, A. C., Hoff, A. L., Hitzemann, R., Bashan, F., Khalsa, S. S., … Volkow, N. D. (2004). Severity of neuropsychological impairment in cocaine and alcohol addiction: Association with metabolism in the prefrontal cortex. *Neuropsychologia*, *42*(11), 1447–1458. http://doi.org/10.1016/j.neuropsychologia.2004.04.002

Goldstein, R. Z., & Volkow, N. D. (2012). Dysfunction of the prefrontal cortex in addiction: neuroimaging findings and clinical implications. *Nature Review Neuroscience*, *12*(11), 652–669. http://doi.org/10.1038/nrn3119.Dysfunction

Goodman, J., & Packard, M. G. (2016). Memory Systems and the Addicted Brain. *Frontiers in Psychiatry*, *7*(February), 1–9. http://doi.org/10.3389/fpsyt.2016.00024

Grant, B. F., Goldstein, R. B., Saha, T. D., Chou, S. P., Jung, J., Zhang, H., … Hasin, D. S. (2015). Epidemiology of *DSM-5* Alcohol Use Disorder. *JAMA Psychiatry*, *72*(8), 757. http://doi.org/10.1001/jamapsychiatry.2015.0584

Grant, D., & Berg, E. (1948). A behavioral analysis of degree of reinforcement and ease of shifting to new responses in a Weigl-type card-sorting problem. *Journal of Experimental Psychology*, *38*(4), 404–411. http://doi.org/10.1037/h0059831

Hayes, S. M., Fortier, C. B., Levine, A., Milberg, W. P., & McGlinchey, R. (2012). Implicit memory in Korsakoff's syndrome: a review of procedural learning and priming studies. *Neuropsychology Review*, *22*(2), 132–53. http://doi.org/10.1007/s11065-012-9204-3

Hoefer, M. E., Pennington, D. L., Durazzo, T. C., Mon, A., Abé, C., Truran, D., … Meyerhoff, D. J. (2014). Genetic and behavioral determinants of hippocampal volume recovery during abstinence from alcohol. *Alcohol*, *48*(7), 631–638. http://doi.org/10.1016/j.alcohol.2014.08.007

Houston, R. J., Derrick, J. L., Leonard, K. E., Testa, M., Quigley, B. M., & Kubiak, A. (2014). Effects of heavy drinking on executive cognitive functioning in a community sample. *Addictive Behaviors*, *39*(1), 345–349. http://doi.org/10.1016/j.addbeh.2013.09.032

Jentsch, J. D., Olausson, P., De La Garza, R., & Taylor, J. R. (2002). Impairments of reversal learning and response perseveration after repeated, intermittent cocaine administrations to monkeys. *Neuropsychopharmacology*, *26*(2), 183–190. http://doi.org/10.1016/S0893-133X(01)00355-4

Jentsch, J. D., & Taylor, J. R. (1999). Impulsivity resulting from frontostriatal dysfunction in drug abuse: implications for the control of behavior by reward-related stimuli. *Psychopharmacology*, *146*(4), 373–90. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10550488

Jones, C. L., Minati, L., Harrison, N. A., Ward, J., & Critchley, H. D. (2011). Under Pressure: Response Urgency Modulates Striatal and Insula Activity during Decision-Making under Risk. *PLoS ONE*, *6*(6), e20942. http://doi.org/10.1371/journal.pone.0020942

Junghanns, K., Horbach, R., Ehrenthal, D., Blank, S., & Backhaus, J. (2009). Chronic and high alcohol consumption has a negative impact on sleep and sleep-associated consolidation of declarative memory. *Alcoholism, Clinical and Experimental Research*, *33*(5), 893–7. http://doi.org/10.1111/j.1530-0277.2009.00909.x

Kalivas, P. W., & O'Brien, C. (2008). Drug addiction as a pathology of staged neuroplasticity. *Neuropsychopharmacology : Official Publication of the American College of Neuropsychopharmacology*, *33*(1), 166–80. http://doi.org/10.1038/sj.npp.1301564

Knowlton, B. J., Squire, L. R., & Gluck, M. A. (1994). Probabilistic classification learning in amnesia. *Learn Mem*, *1*(2), 106–120. http://doi.org/10.1101/lm.1.2.106

Körner, N., Schmidt, P., & Soyka, M. (2015). Decision making and impulsiveness in abstinent alcohol-dependent people and healthy individuals: a neuropsychological examination. *Substance Abuse Treatment, Prevention, and Policy*, *10*(1), 24. http://doi.org/10.1186/s13011-015-0020-7

Lawson, A. L., Gauer, S., & Hurst, R. (2012). Sensation seeking, recognition memory, and autonomic arousal. *Journal of Research in Personality*, *46*(1), 19–25. http://doi.org/10.1016/j.jrp.2011.10.005

Littlefield, A. K., Stevens, A. K., & Sher, K. J. (2014). Impulsivity and Alcohol Involvement: Multiple, Distinct Constructs and Processes. *Current Addiction Reports*, *1*(1), 33–40. http://doi.org/10.1007/s40429-013-0004-5

Lovinger, D. M., & Roberto, M. (2010). Synaptic Effects Induced by Alcohol. In *Current topics in behavioral neurosciences* (Vol. 13, pp. 31–86). http://doi.org/10.1007/7854_2011_143

MacKillop, J., Mattson, R. E., Anderson Mackillop, E. J., Castelda, B. a, & Donovick, P. J. (2007). Multidimensional assessment of impulsivity in undergraduate hazardous drinkers and controls. *Journal of Studies on Alcohol and Drugs*, *68*(6), 785–788. http://doi.org/10.15288/jsad.2007.68.785

Magid, V., & Colder, C. R. (2007). The UPPS Impulsive Behavior Scale: Factor structure and associations with college drinking. *Personality and Individual Differences*, *43*(7), 1927–1937. http://doi.org/10.1016/j.paid.2007.06.013

McCool, B. A. (2011). Ethanol modulation of synaptic plasticity. *Neuropharmacology*, *61*(7), 1097–1108. http://doi.org/10.1016/j.neuropharm.2010.12.028

Milner, B. (2005). The medial temporal-lobe amnesic syndrome. *Psychiatric Clinics of North America*. http://doi.org/10.1016/j.psc.2005.06.002

Müller, U. J., Sturm, V., Voges, J., Heinze, H.-J., Galazky, I., Heldmann, M., … Bogerts, B. (2009). Successful treatment of chronic resistant alcoholism by deep brain stimulation of nucleus accumbens: first experience with three cases. *Pharmacopsychiatry*, *42*(6), 288–91. http://doi.org/10.1055/s-0029-1233489

Nagahama, Y., Fukuyama, H., Yamauchi, H., Matsuzaki, S., Konishi, J., Shibasaki, H., & Kimura, J. (1996). Cerebral activation during performance of a card sorting test. *Brain : A Journal of Neurology*, 1667–75. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/8931588

Nigg, J. T., Wong, M. M., Martel, M. M., Jester, J. M., Puttler, L. I., Glass, J. M., … Zucker, R. A. (2006). Poor response inhibition as a predictor of problem drinking and illicit drug use in adolescents at risk for alcoholism and other substance use disorders. *Journal of the American Academy of Child and Adolescent Psychiatry*, *45*(4), 468–475. http://doi.org/10.1097/01.chi.0000199028.76452.a9

Oscar-Berman, M., Valmas, M. M., Sawyer, K. S., Kirkley, S. M., Gansler, D. A., Merritt, D., & Couture, A. (2009). Frontal brain dysfunction in alcoholism with and without antisocial personality disorder. *Neuropsychiatric Disease and Treatment*, *5*(1), 309–326.

Oudman, E., Nijboer, T. C. W., Postma, A., Wijnia, J. W., & Van der Stigchel, S. (2015). Procedural Learning and Memory Rehabilitation in Korsakoff's Syndrome - a Review of the Literature. *Neuropsychology Review*, *25*(2), 134–48. http://doi.org/10.1007/s11065-015-9288-7

Oudman, E., Van der Stigchel, S., Nijboer, T. C. W., Wijnia, J. W., Seekles, M. L., & Postma, A. (2016). Route learning in Korsakoff's syndrome: Residual acquisition of spatial memory despite profound amnesia. *Journal of Neuropsychology*, *10*(1), 90–103. http://doi.org/10.1111/jnp.12058

Parada, M., Corral, M., Mota, N., Crego, A., Rodríguez Holguín, S., & Cadaveira, F. (2012). Executive functioning and alcohol binge drinking in university students. *Addictive Behaviors*, *37*(2), 167–72. http://doi.org/10.1016/j.addbeh.2011.09.015

Pears, A., Parkinson, J. a, Hopewell, L., Everitt, B. J., & Roberts, A. C. (2003). Lesions of the orbitofrontal but not medial prefrontal cortex disrupt conditioned reinforcement in primates. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *23*(35), 11189–11201. http://doi.org/23/35/11189 [pii]

Petrican, R., & Schimmack, U. (2008). *The role of dorsolateral prefrontal function in relationship commitment*. *Journal of Research in Personality* (Vol. 42).

Pfefferbaum, a, Sullivan, E. V, Mathalon, D. H., & Lim, K. O. (1997). Frontal lobe volume loss observed with magnetic resonance imaging in older chronic alcoholics. *Alcoholism, Clinical and Experimental Research*, *21*(3), 521–529. http://doi.org/10.1111/j.1530-0277.1997.tb03798.x

Pickens, C. L., Saddoris, M. P., Setlow, B., Gallagher, M., Holland, P. C., & Schoenbaum, G. (2003). Different roles for orbitofrontal cortex and basolateral amygdala in a reinforcer devaluation task. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *23*(35), 11078–84. http://doi.org/23/35/11078 [pii]

Pleskac, T. J., Wallsten, T. S., Wang, P., & Lejuez, C. W. (2008). Development of an automatic response mode to improve the clinical utility of sequential risk-taking tasks. *Experimental and Clinical Psychopharmacology*, *16*(6), 555–64. http://doi.org/10.1037/a0014245

Poldrack, R. A., & Rodriguez, P. (2004). How do memory systems interact? Evidence from human classification learning. *Neurobiology of Learning and Memory*, *82*(3), 324–332. http://doi.org/10.1016/j.nlm.2004.05.003

Poldrack, R. A, Clark, J., Paré-Blagoev, E. J., Shohamy, D., Creso Moyano, J., Myers, C., … Gluck, M. a. (2001). Interactive memory systems in the human brain. *Nature*, *414*(November), 546–550. http://doi.org/10.1038/35107080

Poldrack, R., & Packard, M. (2003). Competition among multiple memory systems: Converging evidence from animal and human brain studies. *Neuropsychologia.Special Issue: Functional Neuroimaging of Memory*, *41*, 245–251.

Rabin, L. A., Roth, R. M., Isquith, P. K., Wishart, H. A., Nutter-Upham, K. E., Pare, N., … Saykin, A. J. (2006). Self- and informant reports of executive function on the BRIEF-A in MCI and older adults with cognitive complaints. *Archives of Clinical Neuropsychology*, *21*(7), 721–732. http://doi.org/10.1016/j.acn.2006.08.004

Ranganath, C., Heller, A., Cohen, M. X., Brozinsky, C. J., & Rissman, J. (2005). Functional connectivity with the hippocampus during successful memory formation. *Hippocampus*, *15*(8), 997–1005. http://doi.org/10.1002/hipo.20141

Reinert, D. F., & Allen, J. P. (2002). The Alcohol Use Disorders Identification Test (AUDIT): A Review of Recent Research. *Alcoholism: Clinical and Experimental Research*, *26*(2), 272–279. http://doi.org/10.1111/j.1530-0277.2002.tb02534.x

Rothlind, J. C., Greenfield, T. M., Bruce, A. V., Meyerhoff, D. J., Flenniken, D. L., Lindgren, J. A., & Weiner, M. W. (2005). Heavy alcohol consumption in individuals with HIV infection: Effects on neuropsychological performance. *Journal of the International Neuropsychological Society*, *11*(1), 70–83. http://doi.org/10.1017/S1355617705050095

Salamone, J. D., Correa, M., Farrar, A., & Mingote, S. M. (2007). Effort-related functions of nucleus accumbens dopamine and associated forebrain circuits. *Psychopharmacology*, *191*(3), 461–482. http://doi.org/10.1007/s00213-006-0668-9

Saunders, J. B., Aasland, O. G., Babor, T. F., de la Fuente, J. R., & Grant, M. (1993). Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption--II. *Addiction*, *88*, 791–804. http://doi.org/10.1111/j.1360-0443.1993.tb02093.x

Schoenbaum, G., Roesch, M. R., & Stalnaker, T. A. (2006). Orbitofrontal cortex, decision-making and drug addiction. *Trends in Neurosciences*, *29*(2), 116–124. http://doi.org/10.1016/j.tins.2005.12.006

Schoenbaum, G., Saddoris, M. R., Ramus, S. J., Shaham, Y., & Setlow, B. (2004). Cocaine-experienced rats exhibit learning deficits in a task sensitive to orbitofrontal cortex lesions. *European Journal of Neuroscience*, *19*(7), 1997–2002. http://doi.org/10.1111/j.1460-9568.2004.03274.x

Schwabe, L., Bohbot, V. D., & Wolf, O. T. (2012). Prenatal stress changes learning strategies in adulthood. *Hippocampus*, *22*(11), 2136–43. http://doi.org/10.1002/hipo.22034

Sher, K. J., Bartholow, B. D., & Wood, M. D. (2000). Personality and substance use disorders: a prospective study. *Journal of Consulting and Clinical Psychology*, *68*(5), 818–829. http://doi.org/10.1037//0022-006x.68.5.818

Skinner, H. A. (1982). The drug abuse screening test. *Addictive Behaviors*, *7*(4), 363–371. http://doi.org/10.1016/0306-4603(82)90005-3

Stephan, R. A., Alhassoon, O. M., Allen, K. E., Wollman, S. C., Hall, M., Thomas, W. J., … Grant, I. (2017). Meta-analyses of clinical neuropsychological tests of executive dysfunction and impulsivity in alcohol use disorder. *The American Journal of Drug and Alcohol Abuse*, *43*(1), 24–43. http://doi.org/10.1080/00952990.2016.1206113

Sullivan, E. V., Fama, R., Rosenbloom, M. J., & Pfefferbaum, A. (2002). A profile of neuropsychological deficits in alcoholic women. *Neuropsychology*, *16*(1), 74–83. http://doi.org/10.1037//0894-4105.16.1.74

Tomasi, D., & Volkow, N. D. (2013). Striatocortical pathway dysfunction in addiction and obesity: differences and similarities. *Critical Reviews in Biochemistry and Molecular Biology*, *48*(1), 1–19. http://doi.org/10.3109/10409238.2012.735642

Underwood, M. D., Mann, J. J., Huang, Y.-Y., & Arango, V. (2008). Family history of alcoholism is associated with lower 5-HT2A receptor binding in the prefrontal cortex. *Alcoholism, Clinical and Experimental Research*, *32*(4), 593–9. http://doi.org/10.1111/j.1530-0277.2007.00610.x

Vadhan, N. P., Myers, C. E., Benedict, E., Rubin, E., Foltin, R. W., & Gluck, M. A. (2014). A decrement in probabilistic category learning in cocaine users after controlling for marijuana and alcohol use. *Experimental and Clinical Psychopharmacology*, *22*(1), 65–74. http://doi.org/10.1037/a0034506

Vadhan, N. P., Myers, C. E., Rubin, E., Shohamy, D., Foltin, R. W., & Gluck, M. A. (2008). Stimulus-response learning in long-term cocaine users: Acquired equivalence and probabilistic category learning. *Drug and Alcohol Dependence*, *93*(1–2), 155–162. http://doi.org/10.1016/j.drugalcdep.2007.09.013

Verdejo-Garcıá, A., Lawrence, A. J., & Clark, L. (2008). Impulsivity as a vulnerability marker for substance-use disorders: Review of findings from high-risk research, problem gamblers and genetic association studies. *Neuroscience and Biobehavioral Reviews*, *32*, 777–810. http://doi.org/10.1016/j.neubiorev.2007.11.003

Verhulst, B., Neale, M. C., & Kendler, K. S. (2015). The heritability of alcohol use disorders: a meta-analysis of twin and adoption studies. *Psychological Medicine*, *45*(05), 1061–1072. http://doi.org/10.1017/S0033291714002165

Vetreno, R. P., Hall, J. M., & Savage, L. M. (2011). Alcohol-related amnesia and dementia: Animal models have revealed the contributions of different etiological factors on neuropathology, neurochemical dysfunction and cognitive impairment. *Neurobiology of Learning and Memory*, *96*(4), 596–608. http://doi.org/10.1016/j.nlm.2011.01.003

Volkow, N. D., Wang, G. J., Telang, F., Fowler, J. S., Logan, J., Jayne, M., … Wong, C. (2007). Profound decreases in dopamine release in striatum in detoxified alcoholics: possible orbitofrontal involvement. *J Neurosci*, *27*(46), 12700–12706. http://doi.org/10.1523/JNEUROSCI.3371-07.2007

Vollstädt-Klein, S., Wichert, S., Rabinstein, J., Bühler, M., Klein, O., Ende, G., … Mann, K. (2010). Initial, habitual and compulsive alcohol use is characterized by a shift of cue processing from ventral to dorsal striatum. *Addiction*, *105*(10), 1741–1749. http://doi.org/10.1111/j.1360-0443.2010.03022.x

Wallis, J. D., & Miller, E. K. (2003). Neuronal activity in primate dorsolateral and orbital prefrontal cortex during performance of a reward preference task. *European Journal of Neuroscience*, *18*(7), 2069–2081. http://doi.org/10.1046/j.1460-9568.2003.02922.x

Wester, A. J., Roelofs, R. L., Egger, J. I. M., & Kessels, R. P. C. (2014). Assessment of Alcohol-related Memory Deficits: A Comparison between the Rivermead Behavioural Memory Test and the California Verbal Learning Test. *Brain Impairment*, *15*(01), 18–27. http://doi.org/10.1017/BrImp.2014.6

Whiteside, S. P., & Lynam, D. R. (2003). Understanding the role of impulsivity and externalizing psychopathology in alcohol abuse: Application of the UPPS Impulsive Behavior Scale. *Experimental and Clinical Psychopharmacology*, *11*(3), 210–217. http://doi.org/10.1037/1064-1297.11.3.210

Yang, X., Tian, F., Zhang, H., Zeng, J., Chen, T., Wang, S., … Gong, Q. (2016). Cortical and subcortical gray matter shrinkage in alcohol-use disorders: A voxel-based meta-analysis. *Neuroscience and Biobehavioral Reviews*, *66*(37), 92–103. http://doi.org/10.1016/j.neubiorev.2016.03.034

Yang, Y., Raine, A., Colletti, P., Toga, A. W., & Narr, K. L. (2011). Abnormal structural correlates of response perseveration in individuals with psychopathy. *The Journal of Neuropsychiatry and Clinical Neurosciences*, *23*(1), 107–10. http://doi.org/10.1176/jnp.23.1.jnp107

Yuan, K., Yu, D., Cai, C., Feng, D., Li, Y., Bi, Y., … Tian, J. (2016). Frontostriatal circuits, resting state functional connectivity and cognitive control in internet gaming disorder. *Addiction Biology*. http://doi.org/10.1111/adb.12348

Yudko, E., Lozhkina, O., & Fouts, A. (2007). A comprehensive review of the psychometric properties of the Drug Abuse Screening Test. *Journal of Substance Abuse Treatment*, *32*(2), 189–198. http://doi.org/10.1016/j.jsat.2006.08.002

Zhao, J., Tomasi, D., Wiers, C. E., Shokri-Kojori, E., Demiral, Ş. B., Zhang, Y., … Wang, G. J. (2017). Correlation between Traits of Emotion-Based Impulsivity and Intrinsic Default-Mode Network Activity. *Neural Plasticity*, *2017*. http://doi.org/10.1155/2017/9297621

Zuckerman, M. (2008). Sensation Seeking. In *The International Encyclopedia of Communication*. Chichester, UK: John Wiley & Sons, Ltd. http://doi.org/10.1002/9781405186407.wbiecs029

Zuckerman, M., Bone, R. N., Neary, R., Mangelsdorff, D., & Brustman, B. (1972). What is the sensation seeker? Personality trait and experience correlates of the Sensation-Seeking Scales. *Journal of Consulting and Clinical Psychology*, *39*(2), 308–321. http://doi.org/10.1037/h0033398