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ALCOHOL-INDUCED FRAGMENTARY BLACKOUTS: ASSOCIATED MEMORY PROCESSES AND NEURAL CORRELATES

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ALCOHOL-INDUCED FRAGMENTARY BLACKOUTS: ASSOCIATED MEMORY PROCESSES AND NEURAL CORRELATES

by

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Alcohol-Induced Fragmentary Blackouts: Associated Memory Processes and Neural Correlates

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Alcohol-induced blackouts, or periods of anterograde amnesia without loss of consciousness, were a diagnostic indicator in Jellinek's (1952) theory of alcoholism and have been correlated with alcohol use problems (Campbell & Hodgins, 1993; Goodwin, Crane, & Guze, 1969; Ryback, 1970; Tarter & Schneider, 1976). Other findings suggest that blackouts are a warning sign of problem drinking, but not a predictor of alcohol use disorders (Anthenelli, Klein, Tsuang, Smith, & Schuckit, 1994). Most published research on blackouts focuses on cognitive deficits among older alcohol-dependent adults, yet recent research indicates prevalence rates for blackouts as high as 50% among college students (White, Jamieson-Drake, & Swartzwelder, 2002). In addition, young adults who reported experiencing a blackout were later told that they had vandalized property, driven a car, or engaged in other risky behaviors without remembering (Buelow & Koeppel, 1995). Despite their high prevalence and associated negative consequences, relatively little is known about alcohol-induced blackouts or their neural, social, and behavioral correlates among non-dependent populations. The current research explored individual variation in memory functioning under sober and intoxicated conditions and alcohol's effects on neural activation during memory processes.

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CHAPTER 1: INTRODUCTION

THE ETIOLOGY OF ALCOHOL USE DISORDERS

Interest in the etiology and temporal progression of alcohol use disorders dates back to the work of Jellinek (1946, 1952), who posited the existence of four phases of alcohol dependence: pre-alcoholic, prodromal, crucial, and chronic. During the pre-alcoholic phase, an individual's alcohol consumption is usually socially motivated and provides the person with psychological relief or enjoyment. The next phase, the prodromal phase, consists of drinking more often, experiencing blackouts, gulping and sneaking drinks, and having frequent hangovers. At this point, the individual is described as a "problematic drinker" and may enter the crucial phase, which involves loss of control over drinking, finding excuses and reasons for their drinking, consuming alcohol upon waking, changing drinking patterns (e.g., consuming a different type of alcohol or trying to quit drinking), engaging in anti-social behaviors, losing friends or a job, and seeking medical help for their alcohol-related problems. Jellinek's final, chronic phase of alcoholism is described as complete loss of control over drinking where the drinker experiences tremors, goes on benders, and often realizes that there are no more excuses for drinking beyond the fact that they "must" drink. Although Jellinek's phases of alcoholism were published over 50 years ago, subsequent studies have generally shown similar findings with the common progression including initial symptoms of abuse, impaired self-control, development of tolerance, and finally physiological dependence (e.g., Nelson, Heath, & Kessler, 1998; Shaffer & Eber, 2002).

According to Shaffer and colleagues (2004), there are three distinct phases in the development of alcohol use disorders: the distal precursors, the premorbid phase, and the expression of the disorder. Incorporating the temporal progression model suggests distal

precursors influence the occurrence of the initial symptoms of abuse, followed by impaired self-control and the premorbid phase of repeated use, followed by the manifestation of the disorder which includes the development of tolerance and physiological dependence. Thus, it is important to understand the early phases of development in order to design effective preventive interventions.

Several antecedents to alcohol use initiation include (but are not limited to) individual vulnerability (e.g., family history of alcoholism, Hussong, Bauer, & Chassin, 2008; comorbid psychopathology, Kaplow, Curran, Angold, & Costello, 2001) and exposure to alcohol (Shaffer et al., 2004). As such, adolescence is the most common time for alcohol use initiation because adolescence is a time when individuals begin spending more time with their peers than their family, engaging in behavioral risks and exploration, and developing an idea about their adult self (Arnett, 2000, 2005; Spear, 2000; Fromme, Corbin, & Kruse, 2008). In fact, an estimated 80% of high school students report having consumed alcohol at least once in their lifetime and 66% admit to drinking alcohol at least once during the previous 30 days (Johnston, O'Malley, Bachman, & Schulenburg, 2008). Heavy episodic drinking is also common, with 30% of twelfth graders and 18% of tenth graders consuming five or more drinks per occasion (Johnston, O'Malley, & Bachman, 2003). These patterns of alcohol consumption often continue and, in some cases, increase as adolescents enter emerging adulthood (Wetherill & Fromme, 2006). In fact, emerging adults who enter college drink more alcohol than other young adults, reporting past-month alcohol use (62%), binge drinking (43%), and frequent binge drinking (19%; ≥ 5 or more occasions in the past 30 days) at higher rates than same-aged non-college young adults (56%, 39%, and 14%, respectively; Substance Abuse and Mental Health Services Administration, 2005).

Effects of Alcohol on the Adolescent Brain

During adolescence (i.e., ages 12-18), substantial neuromaturation occurs. Much of the neuronal tissue that was overproduced during childhood is reorganized and pruned, or eliminated, through interactions with one's environment (Seeman, 1999). Specifically, the hippocampal regions grow, gray matter volume and density decreases (particularly in the frontal and parietal brain regions), and neuronal myelination continues (e.g., Giedd et al., 1999, Rubia et al., 2000, Sowell, Delis, Stiles, & Jernigan, 2001). These changes underlie maturation of cognitive processing and result in greater efficiency, as evidenced by decreased energy requirements and glucose metabolism (Chugani, 1998). Given the extensive changes that are occurring in the brain during adolescence, it is not surprising that alcohol affects adolescent brain development and cognitive functioning in several ways (Spear, 2002).

Both animal and human studies show that adolescents appear to be more sensitive to the learning and memory impairments caused by alcohol exposure, but less sensitive to the sedation, motor coordination, and temperature regulation effects (Smith, 2003). Alcohol has been shown to disrupt hippocampal functioning and establishment of long term potentiation (Swartzwelder, Wilson, & Tayyeb, 1995; White & Best, 2000). For example, in a recent study researchers administered multiple, large doses of alcohol to adolescent and adult rats in a manner that is similar to binge drinking in humans. The animals that received alcohol during adolescence showed greater spatial memory impairments than the animals that had only been given alcohol as adults (White, Ghia, Levin, & Swartzwelder, 2000). In a series of human studies, youth with and without alcohol use disorders were monitored longitudinally to investigate neuropsychological functioning over time (Tapert & Brown, 1999; Tapert, Granholm, Leedy, & Brown, 2002). Individuals who continued alcohol involvement and those who experienced

withdrawal symptoms four and eight years after initial assessment exhibited poorer attention and visual-spatial functioning.

Whereas these studies provide neurocognitive evidence for alcohol's effects on the adolescent brain, recent rodent research also supports neuroanatomical effects of alcohol use. For example, Crews and colleagues (2000) administered heavy doses of alcohol over a period of four days to adolescent and adult rats, and their brains were subsequently analyzed at autopsy. Both groups showed significant brain damage; however, only the adolescent brains were damaged in the frontal brain regions, suggesting that different brain regions may vary in vulnerability to alcohol effects during development (Crews, Braun, Hoplight, Switzer, & Knapp, 2000). The neurocognitive and neuroanatmical effects of alcohol on the adolescent brain alter neuronal functioning which may or may not be reversed. These neuronal changes, particularly in the frontal and hippocampal regions, may increase the likelihood of continued alcohol consumption and development of alcohol use disorders, as well as, increased sensitivity to alcohol-induced memory impairments later in life (White et al., 2000).

Given the increased likelihood of alcohol initiation and alcohol's effects on brain development during adolescence, it is not surprising that the median ages at onset for alcohol abuse symptoms and loss of control over drinking are ages 19-21 (Nelson et al., 1998). Alcohol abuse during adolescence and emerging adulthood has been defined as regular and frequent alcohol use over an extended period of time with several negative consequences (Martin, Kaczynski, Maisto, & Tarter, 1996; Winters, 2001). Shaffer and colleagues (2004) describe this pattern of behavior as the premorbid stage of the development of alcohol use disorder. During this premorbid stage, biopsychosocial factors may indicate vulnerability toward alcohol use disorders. Primary among these factors are alcohol-induced blackouts.

Premorbid Stage of Alcohol Use Disorders and Blackouts

Alcohol-induced blackouts are defined as amnesia for all or part of a drinking episode. These amnestic periods are primarily anterograde, meaning memory loss for events occurring after alcohol intake. Jellinek (1946) introduced blackouts to the clinical literature characterizing them as powerful indicators of alcoholism (Jellinek, 1952). Although several findings suggest blackouts are correlated with alcohol use problems (Campbell & Hodgins, 1993; Goodwin et al., 1969; Ryback, 1970; Tarter & Schneider, 1976), other findings suggest that blackouts are a warning sign of problem drinking, not a predictor of alcohol use disorders (Anthenelli et al., 1994). Overall, very few scientific papers have been published on this topic, and therefore, relatively little is known about blackouts and their neural, social, and behavioral correlates among non-dependent populations.

Blackouts are common in non-dependent heavy drinkers (Anthenelli et al., 1994; Jennison & Johnson, 1994; Wechsler, Lee, Kuo, & Lee., 2000). Specifically, blackouts are correlated with binge drinking frequency (Wechsler et al., 2000), gulping drinks (Goodwin et al., 1969a,b; Ryback, 1970), drinking on an empty stomach (Goodwin et al., 1969a,b), and frequency and quantity of alcohol consumption (Anthenelli et al., 1994; White et al., 2002). Whereas frequency and quantity of alcohol use, gulping drinks, and drinking on an empty stomach influence the likelihood of experiencing an alcohol-induced blackout (Goodwin, 1995; Ryback, 1970), research remains unclear as to why some individuals experience alcohol-induced blackouts whereas others do not, even after reaching similar blood alcohol concentrations. A recent study suggests that subjective response to alcohol may help explain the experience of alcohol-induced blackouts (Wetherill & Fromme, 2009). In an examination of 21st birthday celebrations greater levels of stimulation (e.g., talkative, euphoria) at the midpoint of celebration was

positively associated with the occurrence of alcohol-induced blackouts, even after controlling for 21st birthday alcohol consumption. Although these findings provide important information about blackouts and their correlates, these studies are limited by neglecting the variation in duration and magnitude of alcohol-induced memory loss.

Based on the duration and extent of alcohol-induced memory loss, researchers have described two qualitatively distinct types of blackouts: en bloc and fragmentary (Goodwin et al., 1969a,b). People experiencing an en bloc blackout have amnesia for a distinct period of time and often have a feeling of lost time. En bloc blackouts tend to have a distinct onset, but the end is often unclear due to passing out or falling asleep. In addition, individuals who experience en bloc blackouts are unable to recall the drinking episode even after receiving cues about the episode. Fragmentary blackouts (FBs) involve partial amnesia during a drinking episode, but one can recall events of the episode with relevant cues. FBs occur more frequently than en bloc blackouts (Hartzler & Fromme, 2003b; Goodwin et al., 1969b; White, Signer, Kraus, & Swartzwelder, 2004), but neither type appear to occur until blood alcohol concentrations (BACs) are .06% or greater (Hartzler & Fromme, 2003b). The etiology of FBs remains unclear, but research suggests poor memory functioning after alcohol intake but no differences prior to drinking (Hartzler & Fromme, 2003b; Miller, Hertel, Saucedo, & Hester, 1994). Specifically, Hartzler and Fromme (2003) assessed college students with and without a history of fragmentary blackouts (FBs) on a variety of memory tasks under sober and intoxicated conditions. In the sober condition, participants showed no differences on memory tasks, but while intoxicated, individuals with a history of FBs performed worse than those without a history of FBs. Thus, alcohol may have more effects on memory processes in individuals who experience fragmentary blackouts than individuals who do not.

The cue-related nature of recall with FBs has led to speculation that FBs are a case of state-dependent information storage, such that individuals could remember events that occurred when they were intoxicated if they were intoxicated again (Goodwin et al., 1969a; Goodwin, 1995). Thus, individuals who experience alcohol-induced FBs should be more prone to state-dependent learning. These ideas, however, are without empirical support. In fact, two recent studies tested the ability to learn and recall information that was encoded while intoxicated and later retrieved while intoxicated, but revealed no state-dependency effects for alcohol (Duka, Weissenborn, & Dienes, 2001; Weissenborn & Duka, 2000). Thus, it is unlikely that alcohol-induced FBs involve state-dependent information storage and subsequent retrieval.

NEURAL MECHANISMS ASSOCIATED WITH FRAGMENTARY BLACKOUTS

FBs are amnestic periods of episodic memory (memory for personally experienced events), not semantic memory (memory for general facts) (Hartzler & Fromme, 2003; White, 2003; White et al., 2004). For example, individuals who report experiencing an FB have difficulty remembering where they were, what time events occurred, and what events transpired, such as having a conversation, traveling from one location to another, when they left for home, etc. Episodic memory is subserved by a widely distributed network of cortical and subcortical brain regions that overlap and enable an individual to consciously re-experience a past experience (Tulving, 2002). Specifically, an individual experiences an event, a memory trace of the event is created, and as time passes, the memory trace remains and is retrieved such that the person remembers the event. Memory traces include source aspects of memory, which differentiate an event's spatial, temporal, and social context.

Source memory (memory for spatio-temporal and social context of events) is critical to episodic memory because it enables a person to remember particular events

based on contextual cues (Johnson, 2005; Swick, Senkfor, & Van Patten, 2006), which parallels the retrieval process of FBs. Based on the research in this area, it is hypothesized that FBs are a result of alcohol's effects on encoding and/or retrieval of material encountered during alcohol intoxication and are associated with alcohol's effects on the hippocampus, medial septum, and frontal lobes. White and colleges (2000) found that alcohol impairs memory formation and retrieval by altering hippocampal activity and its associated structures, which resulted in deficits in episodic memory. Research supporting the role of the hippocampus in memory function has included behavioral observation in patients or animals with lesions, assessment of neuronal tissue and cell cultures, and pharmacological techniques (for a review, see White, Matthews, & Best, 2000).

Similarly, individuals with frontal lobe damage, particularly damage to the prefrontal cortex (PFC), show deficits in episodic and source memory (Blumenfeld & Ranganath, 2006; Brassen, Weber-Fahr, Sommer, Lehmbeck, & Braus, 2006; Cabeza, 2001; Curtis & D'Esposito, 2003; Swick et al., 2006); however, it is difficult to know whether the memory impairments are solely from frontal lobe damage or secondary to deficits in other frontal functions (executive cognitive functions, ECFs). Several studies have demonstrated that alcohol disrupts ECFs, and alcohol abusers and their offspring show poor ECFs (Glenn et al., 1993; Weissenborn & Duka, 2003; White, 2003). Taken together, alcohol-induced FBs are memory phenomena that appear to result from alcohol's effects on the frontal lobes and medial temporal areas, which subsequently alter encoding of material and retrieval processes. In addition, the detrimental effects of drinking on memory appear to be pharmacological in nature, as no placebo effects have been found for memory processes (Assefi & Garry, 2003; Mintzer & Griffiths, 2005; Nelson, McFadden, Fromme, & Marlatt, 1986).

FUNCTIONAL MAGNETIC RESONANCE IMAGING (FMRI), ALCOHOL, AND MEMORY

Whereas functional neuroimaging research has examined aspects of memory in a number of sub-groups, research has just begun to explore alcohol's effects on neural structures and cognitive processes, such as memory. The extant literature focuses primarily on alcohol's effects after alcohol abuse and dependence has developed. Structural and functional magnetic resonance imaging studies aimed at individuals with alcohol use disorders have explored brain shrinkage after chronic alcohol use (Jacobson, 1986; Mann, Batra, Gunter, & Scroth, 1992), hippocampal volumetric reductions (Agartz, Momenan, Rawlings, Kerich, & Hommer, 1999; Nagel, Schweinsburg, Phan, & Tapert, 2005), and cognitive processes, including spatial working memory (Caldwell et al., 2005; Schweinsburg et al., 2005; Tapert et al., 2004); craving (Tapert, Brown, Baratta, & Brown, 2004), and response inhibition (Anderson, Schweinsburg, Paulus, Brown, & Tapert, 2005; Schweinsburg et al., 2004) suggesting that alcohol has detrimental effects on the brain.

Although neuroimaging research has focused on chronic alcohol use effects, recent functional magnetic resonance imaging (fMRI) studies have shown decreased neural activation following alcohol intoxication (e.g., Calhoun, Altschul, McGinty, Shih, Scott et al., 2004; Van Horn, Yanos, Schmitt, & Grafton, 2006). Specifically, acute alcohol exposure suppressed frontal and parietal brain regions during a goal-directed task, which suggests alcohol affects cognitive regions necessary for ECF and higher-order processes (Van Horn et al., 2006). Further, alcohol decreased neural activation and behavioral performance associated with a visual perception task (i.e., Motor-Free Visual Perception Test-Revised, MVPT-R; Calhoun et al., 2004). Acute alcohol exposure has also been found to decrease neural activations and behavioral performance on tasks associated with episodic and working memory (Gundersen, Specht, Gruner, & Ersland,

2008; Soderlund, Grady, Easdon, & Tulving, 2007). Using a balanced placebo design to study expectancies and working memory, alcohol intoxication decreased neural activation in prefrontal and dorsal anterior cingulate cortex regions, while the placebo (expectancy) group showed increased activation in these same areas, showing alcohol and expectancy have opposite effects on neural activation (Gundersen et al., 2008). Soderlund and colleagues (2007) examined alcohol-induced memory impairment during episodic encoding and found decreased activation in the left frontal regions was associated with decreased memory performance. This finding suggests that the left frontal brain region is important for encoding episodic memory. In sum, acute alcohol intoxication appears to suppress neural activation and behavioral performance on a variety of cognitive tasks.

An extensive review of the literature indicated that no fMRI studies have explored memory processes in conjunction with alcohol-induced blackouts. The fundamental biological changes underlying reduced and sometimes absent episodic memory during alcohol-induced blackouts remain uncertain, but hints regarding compromised brain structures come from studies on alcoholics and individuals with focal lesions (Goodwin et al., 1969a,b; Ryback, 1970). Similar episodic memory impairments are seen between blackout amnesia and individuals who have damage to the thalamus, medial temporal and hippocampus (MT), and PFC structures (Huppert & Piercy, 1978; Scoville & Milner, 1957; Talland, 1965).

In a recent review, White (2003) suggested that alcohol-induced blackouts result from disruption of hippocampal function and PFC circuitry. Research supporting the role of the hippocampal memory function has included behavioral observation in patients or animals with lesions, assessment of neuronal tissue and cell cultures, and pharmacological techniques (for a review, see White et al., 2000). Much less is known, however, about the other brain structures involved in memory formation. Considerable

evidence suggests that the frontal lobes play important roles in the formation and retrieval of long-term explicit memories (e.g., Blumenfeld & Ranganath, 2006; Brassen et al., 2006; Cabeza, 2001; Chiu, Schmithorst, Brown, Holland, & Dunn, 2006; Gallo, Kensinger, & Schacter, 2006). Brassen and colleagues (2006) explored the connection between the prefrontal (PFC) and hippocampal regions and found that the stronger the relational binding between the PFC and the hippocampus, the more successful the recall. Thus, successful functioning of one structure clearly depends on the functioning of the other structure. As such, alcohol-induced amnesia may be associated with altered functioning in the PFC, the medial temporal lobe, or the interactions between the two regions. Thus, it is hypothesized that individuals who experience FBs have altered functioning of hippocampal and PFC circuitry, and this altered functioning may result from alcohol's pharmacological effects on the frontal and hippocampal areas. Furthermore, individuals who have experienced alcohol-induced FBs are likely to show differences in episodic and source memory, neural processes after alcohol ingestion compared to individuals who have not experienced FBs.

OVERVIEW OF RESEARCH & HYPOTHESES

The overall goal of the research was to examine the etiology of alcohol-induced fragmentary blackouts (FBs), as blackouts may be important indicators of alcohol misuse and prognostic indicators of alcohol use disorders. Previous research indicates that alcohol effects on memory may be more pronounced in some individuals than others, which may lead some people to experience alcohol-induced FBs (Hartzler & Fromme, 2003; Soderlund et al., 2007). Two studies tested the extent to which alcohol affects memory performance in individuals who have experienced a FB compared to individuals who have not experienced a FB, and examined the neural correlates that are associated with these differences. Study 1 combined questionnaire and experimental methodologies

in non-dependent college students to (a) test the differences in memory performance between FB+ and FB- groups under no alcohol and alcohol conditions and (b) examine the effects of alcohol on acute memory. We hypothesized that alcohol intoxication would lead to greater impairment in episodic and source memory in individuals who have experienced FBs compared to those who have not experienced FBs. By combining fMRI techniques and standardized alcohol administration procedures, Study 2 explored alcohol's acute effects on encoding and retrieval of source memory and compared neural activations (within- and between-group) for individuals who have and have not experienced a FB both before and after alcohol exposure (between-group comparisons). We hypothesized that alcohol intoxication would lead to greater memory impairments and decreased activations in individuals who have experienced a FB than individuals who have not.

CHAPTER 2: METHODS COMMON TO BOTH STUDIES

PARTICIPANT CHARACTERISTICS AND SUBJECT RECRUITMENT

All participants were initially enrolled as first-time freshmen at The University of Texas at Austin (UT) in 2004. They were selected from a large pool of approximately 2,600 individuals participating in a National Institute on Alcohol Abuse and Alcoholism (NIAAA)-funded longitudinal study ("The UT Experience!", RO1-AA01397, Principal Investigator: Kim Fromme, Ph.D.). All participants were healthy, right-handed, native English speakers in order to control for cerebral differences in individuals who differ in handedness and multilingualism. Participant's data from the previous four years of longitudinal assessments (the last three months of high school through the Fall semester of their senior year in college) were analyzed in order to select individuals who have and have not experienced an alcohol-induced FB. Based on these analyses, 21-23 year old, male and female individuals were screened for participation. Of these individuals, 41.3% endorsed experiencing an alcohol-induced blackout during the previous four years.

Inclusion criteria for all participants included classification as non-abstainer and drinking to an average BAC of .06% (e.g., endorsement of at least one instance of drinking three or more drinks in the past three months and an average BAC of .06% based on gender and drinking calculations determined at time of phone screening); as well as the absence of symptoms of substance dependence, head injury, ADHD and/or contraindications (medical, neurological, personal, or ethical) to the ingestion of alcohol. The fragmentary blackout positive (FB+) sample also reported experiencing at least one alcohol-induced FB during the previous year; the fragmentary blackout negative (FB-) sample did not experience alcohol-induced FB during the previous four years. Eligible participants were randomly assigned into alcohol or no alcohol conditions for both

studies. Qualified individuals were scheduled for participation and instructed to refrain from the use of alcohol or other psychoactive substances for 24 hours prior to their scheduled appointment(s).

SELF-REPORT MEASURES (SEE APPENDIX A)

Demographics. Participants provided their age, gender, ethnicity, socio-economic status (SES), history of psychological/psychiatric treatment, whether currently in medical treatment, and lifetime difficulty with day-to-day memory (e.g., naming objects, naming people, naming places; recalling important events, recalling things said or done, and remembering to complete tasks).

Family History of Alcohol Problems. The Family Tree Questionnaire (FTQ; Mann, Sobell, Sobell, & Pavan, 1985) assessed the history of alcohol-related problems in the biological parents, grandparents, and siblings of participants. The FTQ has demonstrated satisfactory test-retest reliability for use in clinical and research samples (Mann et al., 1985), and evidence for the criterion validity of the FTQ is based on consistent findings that alcohol abusers report a higher number of family history positive relatives than non-alcohol abusers (e.g., Wilhelmsen et al., 2003). In order to control for potential differences between those with and without a family history of alcohol problems, data from the FTQ was used during the screening process to select participants from the longitudinal sample who did not have a family history of alcohol problems.

Alcohol Consumption. Typical alcohol consumption during the past three months was measured with the widely used Daily Drinking Questionnaire (DDQ; Collins, Parks, & Marlatt, 1986). The DDQ yields estimates of the frequency (i.e., number of drinking episodes) and average quantity (i.e., number of standard drinks per drinking episode) of alcohol consumption for a typical week during the previous three month period.

The Time-Line Follow-back (TLFB; Sobell & Sobell, 1992) assessed recent drinking frequency (episodes), quantity (number of drinks per episode), and illicit drug use (frequency, type, and quantity). Consistent with established assessment procedures, participants were presented with 1-month calendars and asked to describe drinking episodes within the 1-month interval. The TLFB was modified to also assess blackouts (Hartzler & Fromme, 2003b). For each reported drinking episode, participants were asked if memory loss for intoxicated events had occurred. Reports of memory loss were followed by the questions, "Had you used any drugs besides alcohol when you experienced memory loss?"; "Were you able to remember your intoxicated experience(s) when later reminded of them?" Individuals who reported drug use other than alcohol when the memory impairment occurred were ineligible to participate in Study 2. Affirmative responses to being able to remember their intoxicated experience were coded as FBs, and negative responses were coded as en bloc blackouts. For each reported blackout, participants provided a subjective rating of their evaluation of the blackout experience (1= bad, 2= slightly bad, 3= neutral, 4= slightly good, 5= good).

Alcohol-Related Consequences. Taken from the most recent semi-annual survey, the experience of negative alcohol-related consequences during the past three months was obtained from the Rutgers Alcohol Problem Index (RAPI; White & Labouvie, 1989). The 23-item RAPI assesses physical (e.g., had withdrawal symptoms, passed out or fainted suddenly), psychological (e.g., noticed a change in your personality, felt that you had a problem with alcohol), and social (e.g., caused shame or embarrassment to someone, had a fight, argument, or bad feelings with a friend) consequences of alcohol consumption and is a widely used index of adolescent problem drinking. RAPI scores were used as a baseline measure to compare alcohol-related consequences between individuals with and without a history of fragmentary blackouts.

Blackouts. Initial screening for a history of blackouts was determined using the following question from the RAPI during the previous semi-annual survey: "During the past three months, how many times did you wake up in a place and did not know how you got there?" Based on this initial screen (as well as the additional inclusion criteria discussed in the previous section), a subsequent telephone screen assessed additional information regarding alcohol-induced blackouts. The telephone screen included the following questions: (1) "Have you awakened the morning after a good bit of drinking and found that you could not remember part of the evening before?" from the Young Adult Alcohol Problems Screening Test (YAAPST; Hurlbut & Sher, 1992); (2) "After drinking heavily, have you ever experienced a period of time that you could not remember things you said or did?" and to determine the type of blackout (i.e., fragmentary or en bloc); (3) "For times when you could not remember things you did or said while drinking, were you able to later recall them when reminded by others or cued by the setting?" These items have been used previously by Hartzler and Fromme (2003a) and Wetherill and Fromme (unpublished data).

Blood Alcohol Concentration. As part of the telephone screen, participants were asked about the episode when they consumed the most alcohol over the past three months and past month, the number of drinks consumed during that episode, and how long the drinking episode lasted. From this information, an estimated BAC was calculated and used as inclusion criteria (a recent BAC of at least .06%). This BAC calculation ensured that all participants had consumed adequate alcohol for blackouts to have occurred. Thus, memory and neural processes can be examined between those who have and have not experienced alcohol-induced blackouts even when controlling for comparable levels of drinking at which blackouts can occur.

CHAPTER 3: STUDY 1

RATIONALE, AIMS, AND HYPOTHESES

Preliminary research demonstrated that FB+ individuals show deficits in delayed recall of details and source memory after alcohol consumption, but not when sober (Hartzler & Fromme, 2003a). As a replication and extension of previous findings, this study combined longitudinal survey data, an alcohol administration, and experimental methodologies to assess alcohol's acute effects on memory in FB+ and FB- groups by assessing source memory, immediate, delayed, and next day free and cued recall in a 2 (FB+, FB-) X 2 (Alcohol, No Alcohol) between subjects design.

As a replication of Hartzler and Fromme (2003a), it was hypothesized that alcohol would lead to greater memory impairment in FB+ individuals than in FB- individuals. Consistent with previous research, there would be no differences in memory performance between FB+ and FB- individuals when sober. After alcohol intoxication, however, FB+ individuals would show greater impairment in episodic and source memory than FB- individuals. It was also expected that FB+ participants would display deficits in next day free and cued recall after the alcohol session, but not after a no alcohol laboratory session.

PARTICIPANTS

Both FB+ (n = 44) and FB- (n = 44) participants were recruited from the pool of 2,177 longitudinal participants who were aged 21-23 during time of recruitment. Eligible participants were randomly assigned to alcohol or no alcohol conditions.

STUDY 1 MEMORY TASKS (SEE APPENDIX B)

Digit Span. The Digit Span subtest of the Wechsler Adult Intelligence Scale-III (WAIS-III; Psychological Corp., 1997) assessed working memory, and includes the standard forward and backward components.

Logical Stories. The Logical Stories subtest from the Wechsler Memory Scale-III (WMS-III; Psychological Corp., 1997) measured immediate, delayed, and cued recall of details and themes from two brief narratives. Administration procedures were modified for this research such that the first narrative was completed before beverage (alcohol or no alcohol) consumption and the second narrative was presented after beverage consumption. The day after the experimental session, participants were contacted and free and cued recalls were assessed for the second narrative.

Source Memory. The computerized source memory task (modified from Dobbins, Foley, Schacter, & Wagner, 2002) assessed recollections of specific contextual details of earlier events (i.e., episodic memory). Participants were shown a series of images (2 separate study trials of 64 items) and asked to make semantic decisions (i.e., a total of 8 blocks of 8 pleasant/unpleasant items and 8 blocks of 8 living/nonliving items) on individual items by using the 1 or 2 button on a computer keyboard. Each study item was shown for approximately 4.25 seconds. Participants were then presented with three-alternative forced choice (3AFC) triplets for approximately 5 seconds to test source and item memory. Triplets consisted of a new item and items encoded under pleasant/unpleasant and under living/nonliving orienting study blocks. During item recognition, participants were instructed to identify the new item in the triplet, which should be an easy distinction based on familiarity. The baseline task consisted of viewing a blank (white) screen between each block of stimuli. The source memory task required selection of the item that was associated with a previous semantic orienting task

(e.g., select the item that they earlier rated as "pleasant"). For the 3AFC items, participants responded to each probe by using the 1 (left image), 2 (middle image), or 3 (right image) on the number key pad of a computer keyboard.

PROCEDURES

Following the initial RAPI screen from data during the previous four years (previous year for those FB+) to determine possible blackout status, individuals were contacted and screened through telephone interviews to determine eligibility based on blackout history, blackout type, and BAC during heaviest drinking episode. Qualified participants were scheduled for a session in our simulated bar laboratory and randomized to condition (i.e., alcohol, no alcohol).

Alcohol/No Alcohol Conditions. Upon arrival at our laboratory, participants provided informed consent, showed photo ID as proof of legal drinking age, were advised that participation was confidential, were weighed, and provided a breathalyzer test (Intoxilyzer 5000, CMI, Inc Owensboro, KY) to ensure .00% blood alcohol concentration (BAC). Females self-administered hormonal pregnancy tests and no one tested positive. Participants completed self-report questionnaires, baseline memory tasks, and were then taken to a simulated bar.

Participants (N = 88; FB+ 44, FB- 44) were given 10 minutes to consume each of three beverages (volume was determined by gender and body weight). Similar beverage preparation procedures were used in the alcohol and no alcohol beverage condition; however, the only difference was the beverage content. Specifically, drinks for those assigned to the alcohol condition (combined at a 3:1 ratio of mixer to vodka) were targeted at a .08% peak BAC. Those assigned to the no alcohol condition (n = 44; FB+ 22, FB- 22) received a non-alcoholic beverage. After a 30-minute absorption period, breathalyzer samples were recorded and then standardized false BAC feedback (of .06%)

was given to alcohol participants, whereas actual .00% feedback was given to no alcohol participants.

Participants were read and asked to recall the second WMS-III narrative with a delay and cued recall 30 minutes later. Each participant was then administered the digit span and source memory task. For these memory tasks, alcohol and no-alcohol participants were yoked to control for time differences between intoxicated and sober participants. To account for absorption in the alcohol condition, for each alcohol-dosed participant, a no-alcohol participant was administered measures at the same time intervals. Participants in the no-alcohol group were debriefed, compensated ($5 per hour), and reminded that they would be contacted by telephone the next day. Participants in the alcohol group remained in the laboratory until their BAC dropped to .02% and their observed behavior returned to normal (in accordance with NIAAA Guidelines). Participants were fully debriefed, paid $5 per hour (to a maximum of $30) for their participation and reminded that they would be contacted by telephone the next day. Finally, participants were then driven home by licensed and insured project staff.

RESULTS

Sample Description

Descriptive statistics were computed for self-reported age, lifetime memory difficulty, drinking frequency and quantity, alcohol-related problems (i.e., alcohol-related problems without the item assessing alcohol-induced blackouts), and blackout incidence (any type) in the past month. Independent-sample *t*-tests and multivariate analysis of variance (MANOVA) assessed differences among those who did and did not report fragmentary blackouts during the prior year. T-tests did not detect differences in age or lifetime memory difficulty (t values < 1.44, p values $> .16$). For drinking variables,

MANOVA revealed a significant multivariate effect, $F(1, 83) = 8.42$, $p < .001$; as well as univariate effects for alcohol-related problems, $F(1, 88) = 9.59$, $p < .003$ and past month incidence of blackouts, $F(1, 88) = 27.22$, $p < .001$. The group differences in drinking frequency and quantity failed to reach statistical significance. Participants who reported fragmentary blackouts in the prior year indicated more alcohol-related problems and blackouts in the prior month than their counterparts. Means for the overall sample and by group for these variables are listed in Table 1.

Blackout Description

Frequencies for the incidence of blackouts were computed using the Timeline Follow-back, as well as their descriptive aspects (i.e., overall, by type: fragmentary, en bloc). Of the current sample, 46% (N = 41; 22 men, 19 women) reported a blackout (any type) during the prior month (range of 1-4; $M = 1.41$; $SD = .78$). Of the FB+ participants, 93.2% had experienced a blackout in the past 30 days; whereas, none of the FB- participants reported experiencing a blackout during the prior month. Of the 62 blackouts that were reported, 13 were en bloc and the remaining 49 (79%) were fragmentary.

En Bloc Blackouts. The 13 reported en bloc blackouts were experienced by nine individuals. The range of estimated BACs corresponding to these blackouts were .20 to .33 ($M = .27$, $SD = 0.06$). Subjective evaluations for the en bloc blackouts were slightly negative ($M = 2.25$; $SD = .98$).

Fragmentary Blackouts. The 49 reported fragmentary blackouts were experienced by 35 individuals. Corresponding BACs for these experiences ranged from .07 to .31 ($M = .19$; $SD = .09$). Subjective evaluations for the fragmentary blackouts were slightly negative ($M = 2.33$; $SD = .91$) and did not significantly differ from the evaluations for en bloc blackouts ($t = 0.28$, $p = 0.78$).

Baseline Measurements

Participants who reported experiencing a fragmentary blackout during the past year and those who did not report experiencing fragmentary blackouts during the past four years were compared on a number of baseline measures. The groups were compared on measures of working memory, immediate, and delayed free and cued recall.

Memory Performance Prior to Beverage Challenge. Indices of baseline memory performance included the number of correct WAIS-III Digit Span trials, the number of WMS-III narrative details and themes freely recalled immediately, and after a 30-minute delay. A 2 (past year fragmentary blackouts: yes, no) X 2 (beverage condition: alcohol, no alcohol) X 2 (gender: male, female) MANOVA examined variation in these indices, but indicated no significant multivariate effects (F values, < 2.21, p values > .12). Group means for all indices of baseline memory performance are listed in Tables 2 and 3.

Measurements After Beverage Consumption

BACs were assessed at 30-minutes post-drinking and each 30-minute interval thereafter for FB+ and FB- individuals. Independent t-tests on BAC prior to and during memory assessments revealed no differences between the FB+ and FB- groups, p values > .07.

Narrative Recall. Separate 2 (past year fragmentary blackouts: yes, no) X 2 (beverage condition: alcohol, no alcohol) analysis of covariance (ANCOVA) assessed the following indices of narrative recall from the WMS-III. For the 30-minute delay, the immediate recall performance was entered as a covariate and the score from the subsequent administration (30-minute delay recall) served as a dependent variable. Similarly, an ANCOVA on next-day recall performance used immediate and 30-minute

delay recall performances as covariates. Group means for indices of recall at each of narrative details, narrative themes, and cued recall are depicted in Figure 1.

ANCOVA indicated beverage effects for 30-minute delay recall of details, F (1, 88) = 13.01, $p < .001$; and themes, F (1, 88) = 4.87, $p < .03$, but no effects of fragmentary blackout history or interaction. In both instances, those assigned to the alcohol condition exhibited poorer recall. Main effects for FB history were found for delayed recall of details, $F(1, 88) = 15.01$, $p < .001$. Thus, FB+ individuals recalled fewer narrative details at 30-minute delay than other participants. Analyses of narrative recall the day following a beverage challenge revealed effects of beverage condition, F (1, 83) = 11.45, $p < .001$, as well as next day recall of narrative themes, F (1, 83) = 6.85, $p < .01$. Although significant main effects were found for next day free recall, there were no significant differences between the alcohol or fragmentary blackout groups on next day cued recall.

Source and Item Memory. Source and item memory from the computerized source memory task was examined by way of a 2 (FB+, FB-) X 2 (alcohol, no alcohol) X 2 (gender) analysis of variance (ANOVA) with percent correct for item or source memory hits as the dependent variable. For item memory ("new?"), analyses indicated significant effects for beverage condition, F (1, 87) = 6.14, $p < .02$. Analyses for source memory ("living/pleasant?") revealed significant effects for beverage condition, F (1, 87) = 16.81, $p < .001$, history of fragmentary blackouts, F (1, 87) = 4.78, $p < .03$, and the interaction between fragmentary blackouts and beverage condition, F (1, 87) = 6.92, $p < .01$, but not for gender or any other interactions. Individuals who consumed alcohol performed more poorly on item recognition whereas individuals with a history of fragmentary blackouts and consumed alcohol performed more poorly on source recall than did other participants. Group means for the item recognition and source memory task are presented in Figure 2.

DISCUSSION

Study 1 was designed to examine alcohol-induced blackouts and memory processes associated with fragmentary blackouts. Findings confirm and expand what is known about the prevalence and experience of blackouts. For example, blackouts were reported by 41.3% of the longitudinal sample from which the current sample was drawn, which is comparable to published prevalence rates of 40% (White et al., 2002). Within the current sample of individuals who reported a blackout in the past year (i.e., FB+ participants), 93.2% had also experienced a blackout in the past 30 days. Of the two types of blackouts, fragmentary blackouts occurred nearly four times more often than en bloc blackouts. Similarly, White and colleagues (2004) found that fragmentary blackouts occurred four out of five times more often than en bloc blackouts. Consistent with previous research (Hartzler & Fromme, 2003b), fragmentary blackouts occurred at estimated BACs above .07%, but typically occurred around BACs of .19%. En bloc blackouts occurred at much higher BACs of at least .20% and most often around .27%. On average, blackouts occurred at BACs that are 2-4 times the legal level of intoxication (.08%). Participants described the experience of fragmentary and en bloc blackouts as "slightly negative," which differs from the White and colleagues (2004) finding that individuals felt "frightened" by the blackout experience and subsequently changed their drinking behavior. Differences in subjective ratings of the blackout experience may be attributed to the differences between the White sample (i.e., $N = 50$, 70% female, average age of 19) and the current sample (i.e., $N = 88$, 50% female, average age of 21). For example, women may be more fearful of experiencing a blackout than men. Further, differences between the two studies could also be due to research methodologies. White and colleagues (2004) assessed experiential aspects of blackouts via a paper-and-pencil

survey; however, we asked participants about blackout experiences during a face-to-face interview, which may have influenced participants' subjective ratings.

In terms of memory processes associated with fragmentary blackouts, current findings were consistent with previous studies. Baseline comparisons between individuals with and without a history of fragmentary blackouts revealed no significant differences in self-reported lifetime memory difficulty or self-reported alcohol use. Further, there were no significant differences between individuals with and without a history of fragmentary blackouts on memory performance prior to beverage challenge as measured by standardized neuropsychological assessments (i.e., indices of working memory and narrative recall). After the beverage challenge, individuals with a history of fragmentary blackouts showed greater source memory impairment than those without a history of fragmentary blackouts. As such, alcohol disrupts source memory processes in individuals with a history of fragmentary blackouts, which suggests that some individuals have an inherent vulnerability to alcohol-induced memory impairments and that this vulnerability makes them more susceptible to experiencing fragmentary blackouts. Further, this finding indicates that the effects of alcohol on source memory could be the mechanism through which fragmentary blackouts occur.

Contrary to Study 1 hypotheses, individuals with a history of fragmentary blackouts did not show significant differences in the other memory tasks (i.e., narrative recall or next day recall) after alcohol consumption. The lack of significant differences between the fragmentary blackout groups on the other memory assessments after alcohol consumption was surprising given that the current study aimed at replicating the findings of Hartzler and Fromme (2003a) and used the same research protocol and neuropsychological memory assessments. Although these studies were similar, the current study examined fewer individuals and may lack the power needed to find

significant differences between the fragmentary blackout groups post-alcohol consumption. Further, participant recruitment strategies and beverage challenges differed between the studies and may also account for these distinct findings. Specifically, the current study recruited participants from a longitudinal study; whereas, the Hartzler and Fromme study participants were from a community sample, which could yield differences in previous experiences of fragmentary blackouts. The longitudinal nature of the current study allowed for the review of several years of data on whether participants experienced fragmentary blackouts or not, and as such, the current procedures might have yielded a more pure sample of individuals with and without a history of fragmentary blackouts. In addition, participants in the current study were all college students, but the Hartzler and Fromme sample was comprised of college and non-college students. Thus, the current sample could have better working memory to compensate for the effects of alcohol.

Although fragmentary blackout groups did not differ on recall performance, alcohol showed main effects on memory processes. Individuals who consumed alcohol performed more poorly on delayed recall of narrative details and themes, cued narrative recall, next day recall of narrative details and themes, and source memory. These findings provide additional evidence for alcohol's detrimental effects on recall of verbal and auditory information, as well as memory for source and context. Similar alcohol-induced impairments have been observed previously (Soderlund, Parker, Schwartz, & Tulving, 2005), and it has been posited that these memory deficits result from reduced encoding rather than retrieval (LePage, Habib, & Tulving, 1998; Petersen, 1977). It remains unclear, however, whether alcohol-induced memory impairments result from decreased encoding or retrieval difficulties. For example, Fillmore and colleagues (1999) examined automatic and intentional retrieval after acute alcohol intoxication and

demonstrated that alcohol reduced verbal memory, whereas automatic processes were unchanged. Further, an investigation of associative learning, picture recognition, and free recall performance during the ascending and descending limbs of the blood alcohol concentration curve found that alcohol had a more general effect (i.e., both limbs of the BAC curve) on retrieval but encoding was only affected during the ascending limb (Soderlund et al., 2005). Together, these findings suggest that alcohol alters encoding and retrieval of information, regardless of stimulus type and timing of retrieval. Future research should examine the effects of alcohol on memory with reference to distinguishing differential effects on encoding and retrieval and the neurological substrates associated with alcohol's effects on these processes.

In addition to the main effects of alcohol on immediate, delayed, cued, and source memory, individuals in the alcohol group showed deficits in next day free recall. This finding is consistent with previous research showing memory impairment the day after a night of drinking (McKinney & Coyle, 2007; Verster, van Duin, Volkerts, Schreuder, & Verbaten, 2003). Next day cued recall, however, was not significantly impaired and suggests that individuals were able to recall information when cues were provided even after failing to recall this information at free recall. These findings seem particularly important for college students who consume alcohol the night prior to an exam because those students will likely do poorly on an essay exam that requires free recall of information. Individuals may not, however, do as poorly on a multiple choice exam, which provides cues for better recall. Similar memory patterns were found for verbal and visual memory performance the day following (i.e., 13 hours) an alcohol administration (Kim, Yoon, Lee, Choi, & Go, 2003). Kim and colleagues (2003) demonstrated that alcohol decreased free recall of information, whereas recognition of familiar and new stimuli remained intact. Further, a recent review of the effects of cannabinoids on

memory reported similar memory impairments the day following acute drug exposure with decreased performance on verbal recall, but no effect on recognition recall (Ranganathan & D'Souza, 2006). Even though alcohol and cannabinoids affect different receptors and neurotransmitters, comparable memory deficits occurred the day following acute exposure. These findings provide evidence for similar effects of sedative drugs on memory processes whereby free recall of information is impaired, but cued recognition remains intact. Thus, it appears that encoding is not affected by these drugs, but the information and processes used for free recall are impaired and are accessible only after additional cues or prompts are provided.

In summary, the results of Study 1 provide additional information about alcohol-induced memory impairments and the memory processes that may underlie their occurrence. Memory deficits occurred after alcohol consumption, with significant, specific differences between individuals with and without a history of fragmentary blackouts. These findings are consistent with previous research and provide additional evidence that fragmentary blackouts reflect source memory deficits that emerge for certain individuals after alcohol consumption. Specifically, it appears that alcohol alters source memory processes such that access and evaluation processes of remembering are impaired in some individuals more than others. Although alcohol impairs source memory processes, next day cued recall remains intact and does not differ between those who have and have not experienced a fragmentary blackout. Together, these findings provide information regarding a potential mechanism through which fragmentary blackouts occur, that is through altering source monitoring and memory. Further, extensive research examining source memory provides information about the possible neurological correlates and processes associated with source memory and the effects of alcohol on these brain structures. Specifically, functional magnetic resonance imaging

studies have implicated the left prefrontal cortex structures and the medial temporal lobes as brain regions associated with source and episodic memory (e.g., Mitchell, Raye, Johnson, & Greene, 2006; Slotnick, Moo, Segal, & Hart, 2003). In fact, it appears that the source memory deficits observed after acute alcohol consumption parallel source memory deficits observed in older adults. Compared to young adults, older adults show greater source memory deficits relative to other episodic memory tasks (e.g., Simons, Dodson, Bell, & Schacter, 2004). These age-related deficits are consistent with anatomical and neuroimaging evidence of prefrontal cortex changes in structure and function with age (e.g., Cabeza, Anderson, Locantore, & McIntosh, 2002; Dennis, Hayes, Prince, Madden, Huettel, & Cabeza, 2008). Following up on these findings and drawing from the similarities between the effects of alcohol on memory and age-related memory deficits, Study 2 was conducted to examine the neural correlates associated with alcohol intoxication and source memory in individuals with and without a history of alcohol-induced fragmentary blackouts.

CHAPTER 4: STUDY 2

RATIONALE, AIMS, AND HYPOTHESES

Findings from Study 1 indicated that individuals with a history of fragmentary blackouts show decreased source memory performance after alcohol consumption compared to those without a history of fragmentary blackouts. Further, fragmentary blackout groups did not exhibit any other significant differences in memory processes (i.e., free recall or recognition) when sober or intoxicated. As such, Study 2 examined similar neural correlates of source memory in individuals with and without a history of fragmentary blackouts in hopes to better understand the neural correlates of fragmentary blackouts. Using an alcohol administration protocol with functional magnetic resonance imaging (fMRI) techniques, Study 2 aimed to (1) examine neural activations of source memory processes affected by alcohol consumption (within-person comparison, no alcohol versus alcohol) and (2) determine whether alcohol differentially affects neural structures and functioning in individuals with and without a history of fragmentary blackouts (between-group comparison, neural activations between FB+ and FB- groups).

Based on Study 1 and previous research (Hartzler & Fromme, 2003a), it was hypothesized that alcohol would impair memory performance and modulate neural activations (as measured by fMRI) associated with these memory processes. That is, after alcohol consumption, individuals would show: (1) memory impairment when completing a source memory task and (2) decreased activation in brain regions associated with source memory. It was also expected that individuals with a history of FBs would show differences in neural activations after consuming alcohol. Specifically, FB+ individuals were expected to show: (1) greater source memory impairments and (2) less

activation in the left prefrontal cortex when completing a source memory task after drinking.

PARTICIPANTS

Equal numbers of men and women who are FB+ (N=15) and FB- (N=15) were thoroughly screened for eligibility to ensure there were no medical, personal, or ethical contra-indications for magnetic resonance research or alcohol ingestion, as well as the absence of family history of alcoholism, symptoms of alcohol dependence/abuse, attention-deficit/hyperactivity disorder (ADHD), head injury, or claustrophobia for eligibility.

PROCEDURES

Interested participants were screened through telephone interviews to determine eligibility (see Study 1) and qualified volunteers (N = 30) were scheduled for two sessions at the Imaging Research Center (i.e., alcohol and no alcohol) counterbalanced to control for order effects.

Scanning Procedures. Participants were scanned during the block design source memory task. Specifically, scanning occurred during item and source retrieval following the same Source Memory task procedure described in Study 1, which lasts for approximately 30 minutes (also see Appendix B for a detailed description of stimuli presentation).

Alcohol Session. At the time of scheduling, participants were instructed to eat a full meal 4 hours prior to their scheduled appointment and informed that transportation home would be provided at the end of the protocol. Participants completed the identical alcohol administration procedure as described in Study 1. BACs were recorded at 15 and 27 minutes after drinking ended, and at 30 minutes participants entered the scanner to

begin the scanning procedures. Sixty-five minutes after drinking began, participants were administered the block-design source memory task during fMRI acquisition. Functional imaging occurred only during the first 30 minutes while in the scanner, as data suggests encoding and retrieval of memories (except visual/spatial memory) are affected during the ascending limb of the BAC (Schweizer, Vogel-Sprott, Danckert, Roy, Skakum, & Broderick., 2006).

After imaging, participants exited the scanner and BACs were assessed every 30 minutes until BAC was < .02%. At that point, participants were debriefed, reminded that they would be contacted the next day, and either scheduled for their second laboratory session or received compensation at their final session ($50 for completing both scanning sessions). Participants were then driven home by licensed and insured project staff.

No Alcohol Session. Procedures for the no alcohol session were identical to the alcohol session, but non-alcoholic beverages were consumed. The same 30 minute scanning procedure with the source memory task was followed to make this session and fMRI acquisition comparable to the alcohol session. At the conclusion of the scanning protocol, participants were debriefed and scheduled for their second laboratory session or received compensation.

MRI Acquisition. Functional and structural images were acquired using a 3 Tesla General Electric Signa MRI scanner with an 8-channel phased array head coil. Functional images were obtained during the testing phase of each run, using a parallel acquisition (GRAPPA) echo-planar image (EPI) sequence that reduces typical EPI distortions and susceptibility artifacts. Images were collected using whole-head coverage with slice orientation to reduce artifact (approximately 20° off the anterior commissure-posterior commissure (AC-PC) plane, TR = 2 s, parallel acceleration factor of 3, TE = 30 ms, 35 axial slices oriented for best whole-head coverage, acquisition voxel size = 3.125

X 3.125 X 3 mm with a 0.3 mm interslice gap). The first four EPI volumes were discarded to allow scans to reach equilibrium. Stimuli were viewed through a back projection screen and a mirror mounted on the head coil. Responses were made using an MR compatible button box.

One high-resolution T1 spoiled gradient echo (SPGR) scan that has been empirically optimized for high contrast between gray matter (GM) and white matter (WM) and between GM and cerebrospinal fluid (CSF) was acquired. These images were acquired in the sagittal plane using a 1.3 mm slice thickness with 1 mm^2 in-plane resolution.

MRI Processing and Analysis. Preprocessing and data analysis were conducted using FEAT (FMRI Expert Analysis Tool) version 5.63, part of FMRIB Software Library (FSL; www.fmrib.ox.ac.uk/fsl). Preprocessing included motion correction using FMRIB's Linear Imaging Registration Tool (MCFLIRT; Jenkinson, Bannister, Brady, & Smith, 2002), non-brain removal using the Brain Extraction Tool (BET; Smith, 2002), high-pass temporal filtering with a 100 s cutoff, and spatial smoothing with a Gaussian kernel of 6 mm full width at half maximum (FWHM), and normalization to a 2 mm resolution Montreal Neurological Institute (MNI) template brain. Data from each run of each participant were analyzed separately at a first level of analysis. Item recognition blocks and source memory blocks were modeled separately as two predictors. Stimulus time onsets for the rest and memory blocks were convolved with a canonical hemodynamic response function and were entered as predictors into a general linear model to estimate β-weights. Within-person analyses (alcohol versus no alcohol) examined activation or deactivation during the source memory task, and group level analyses (alcohol versus no alcohol; FB+ versus FB-) combined data from each participant in their prospective grouping in a random effects analyses using ordinary least

squares (OLS). For all analyses, individual voxels were considered active when reaching $Z > 2.3$ and survived a whole-brain cluster size threshold set at $p < .05$ (Worsley, 2001).

In addition to the whole-brain analysis, a region of interest (ROI) was defined based on task activations in the left prefrontal cortex. This area has been implicated in source memory processes (Demb et al., 1995; Dobbins et al., 2002; Gabrieli, Desmond, Demb, & Wagner, 1996). The left PFC ROI consisted of FSL Harvard-Oxford atlas defined precentral, middle frontal, and superior frontal gyri overlapped with the source memory, between group functional activation map. Activation in the ROI was assessed using the Featquery tool of FEAT, which examines lower-level FEAT results within the designated ROI and provides percent signal change data associated with the modeled experimental paradigm.

RESULTS

Sample Description

Descriptive statistics were computed for self-reported age, lifetime memory difficulty, drinking frequency and quantity, alcohol problems, and blackout incidence (any type) in the past month. Independent-sample *t*-tests assessed the differences among those who did and did not report fragmentary blackouts. *T*-tests did no detect differences in age, lifetime memory difficulty, drinking frequency, or quantity of alcohol consumed (t values < 1.25, p values > 0.23).

Behavioral Performance

For main analyses of behavioral performance, the two source memory block responses were pooled to total a possibility of 32 items, and a total of 32 items assessed item recognition. Accuracy was calculated by dividing the total number of correct responses by the total number of source items and item recognition items, respectively.

Order Effects. First, order effects were examined to determine whether order of sober/alcohol session affected performance. Independent sample *t*-tests by session order (alcohol session first vs. alcohol session second; sober session first vs. sober session second) showed no significant differences in memory performance for session order (*t* values $< 0.50, p > 0.62$).

Accuracy Across Retrieval Tasks. Using similar analyses to Study 1, source and item memory performance was examined by way of repeated measures 2 (source, item memory) X 2 (alcohol, no alcohol) within subjects X 2 (FB+, FB-) between subjects (mixed model) ANOVA. Given the small sample size, it was not surprising that findings were not significant (*F* values < 0.73, $p > 0.40$). As such, an alternative analytical approach was used to examine source and item memory performance. Specifically, paired *t*-tests were employed and showed participant's accuracy across no alcohol retrieval tasks differed significantly ($t(28) = 13.60$, $p < .001$) with accuracy for item recognition ("new?", $M = 0.81$, $SD = 0.03$) higher than source recognition ("living/pleasant?", $M = 0.71$, $SD = 0.04$).[1] Similar patterns emerged for the retrieval tasks after intoxication as well ($t(28) = 35.36$, $p < .001$) with accuracy for item recognition ("new?", $M = 0.75$, $SD = 0.04$) higher than source recognition ("living/pleasant?", $M = 0.64$, $SD = 0.05$). Subsequent analyses examined between group differences (fragmentary blackout groups) on memory performance during no alcohol and alcohol sessions. During no alcohol sessions, no significant differences emerged between the two fragmentary blackout groups ($t < 0.63$, $p > .53$). After alcohol consumption, a trend emerged with individuals with a history of fragmentary blackouts

[1] There were no differences between accuracies achieved on the two source sets (living/nonliving versus pleasant/unpleasant).

showing poorer memory performance compared to individuals without a history of fragmentary blackouts ($t(28) = 1.93, p = .06$). See Table 4 for behavioral data.

Analyses also examined mean reaction times between memory type and alcohol conditions. Mean reaction times differed between the item and source tasks by approximately 0.2 s, with source retrieval responses ($M = 2.731$ sec, $SD = 0.096$) taking significantly longer than item retrieval responses ($M = 2.488$ sec, $SD = 0.102$; $t(28) = 6.26, p < 0.001$). Mean reaction times for source retrieval ($M = 3.132$, $SD = 0.15$) were significantly longer than item retrieval responses ($M = 2.686$, $SD = 0.18$); $t(28) = 6.86$, $p < .001$. Subsequent analyses examined mean reaction times between individuals with and without a history of fragmentary blackouts and found that there were no significant differences between the two fragmentary blackout groups (F values $< 0.43, p > 0.51$).

Neuroimaging Data

Within-Group Analyses

To examine brain activity during the source memory and item recognition tasks and the effects of alcohol on this activity, individual's fMRI images obtained during the source memory and item recognition condition were contrasted to those obtained at fixation baseline during alcohol and no alcohol sessions. Differences in activation between the alcohol and no alcohol sessions in association with a difference in performance would suggest that the area in question is a target for alcohol-induced source memory impairment.

Source Memory. During no alcohol sessions, a network of regions in which the source memory task showed significantly greater activation compared to the fixation baseline (see Table 5) included areas involved in visual perception and object identification (occipital and fusiform areas, areas associated with source memory (left

inferior frontal cortex, left middle frontal cortex, and left superior frontal cortex), and an area associated with episodic memory (medial temporal lobe).

A number of regions in which the source memory task showed greater activation compared to fixation baseline were also identified for the alcohol sessions (see Table 5). Specifically, these areas included regions of the occipital lobe, left superior parietal lobe, the caudate, left parahippocampus, left inferior frontal gyrus, and the left middle frontal gyrus.

Paired *t*-tests (alcohol versus no alcohol) assessing differences in mean activation during the source memory task revealed that there were no areas of greater activation during the alcohol sessions. The source memory task during the no alcohol sessions, however, showed greater neural activations in the left precentral gyrus, left inferior parietal regions, left middle frontal gyrus, and left superior frontal gyrus compared to the alcohol sessions. The list of identified regions is provided in Table 5, contrast activation maps are provided in Figure 3.

Item Recognition. Several regions were activated during the item recognition task. Specifically, no alcohol session activations occurred in the fusiform and occipital regions during the item recognition task relative to fixation baseline. During the alcohol session, the item recognition task was associated with greater activations in the fusiform/occipital regions, the right parietal lobe, the right middle frontal gyrus, right inferior frontal gyrus, and the right superior frontal gyrus. Paired *t*-tests revealed no areas of item recognition activation during alcohol sessions, but significantly greater activation in the bilateral occipital regions during the no alcohol sessions.

Between-Group Analyses

A 2 (FB+, FB-) X 2 (alcohol, no alcohol) ANOVA assessed differential activation on the source memory task compared to fixation baseline between FB+ and FB- groups

under both alcohol and no alcohol. For no alcohol sessions, there were no significant differences between the two groups. Significant differences were found between the FB+ and FB- groups under alcohol with the FB- group showing greater activation in the left lateral prefrontal cortex, including the left precentral and middle frontal gyrus, and the FB+ group showing greater activation in the right occipital and parietal regions (see Table 6, Figure 4).

Similarly, a 2 X 2 ANOVA examined differential activation on the source memory task compared to the item recognition task. The direct contrast revealed a significant Alcohol X FB- group interaction with greater activations in the left orbital cortex, left anterior cingulate, left superior frontal gyrus, and left medial frontal gyrus (see Table 6, Figure 4). The contrast between item recognition and the source memory task did not indicate significant differences between the FB groups on item recognition.

ROI Analysis

For the ROI analysis, the left prefrontal cortex mask (i.e., left PFC overlapped with the source memory functional map) was used to extract mean percent signal changes for source memory. Significant positive correlations between source memory task accuracy and the magnitude of brain activation during the source memory task was observed in the left precentral and middle frontal gyrus ($r = 0.71$, $p < .001$). Comparisons between the FB+ and FB- groups were conducted and showed no significant difference between mean percent signal change during no alcohol conditions ($p > .68$), but significant differences between alcohol conditions ($t(24) = 2.12$, $p < .04$)).

DISCUSSION

Study 2 was designed to examine neural correlates of source memory in individuals with and without a history of fragmentary blackouts. This is the first study to

identify neural correlates of alcohol-induced memory impairment in humans during retrieval of source information. It was hypothesized that individuals with a history of fragmentary blackouts would show differences in memory performance and neural activations after alcohol consumption. Specifically, individuals with a history of fragmentary blackouts were expected to show less activation in the left prefrontal cortex when completing a source memory task after alcohol consumption.

Alcohol Effects

The first finding was that source memory performance was impaired after alcohol consumption and that alcohol decreased neural activations. Comparable to Study 1 and previous research (Hartzler & Fromme, 2003), alcohol interfered with source memory. Further, there were common areas of activation in the alcohol and no alcohol groups during recognition of source material compared to a resting state condition, including the medial temporal lobe, left inferior frontal, left middle frontal, and left superior frontal cortices. These regions have been associated with source memory-related activity (e.g., Mitchell et al., 2004; Dobbins et al., 2002; Slotnick et al., 2003); thus, across studies, the left prefrontal cortex appears to be most consistently active during source memory processes.

The administration of alcohol compared to no alcohol resulted in significant differences in neural activations. Specifically, the left prefrontal and left parietal cortices exhibited greater source memory-related activations during no alcohol sessions, indicating less activation in these regions after alcohol consumption. As previously stated, activations in these areas have been associated with both immediate and long-term source memory (e.g., Dobbins et al., 2002; Dobbins, Rice, Wagner, & Schacter, 2003; Mitchell et al., 2006). It should be noted that the significant differences in neuronal activation were observed in the left parietal regions (i.e., precuneus, inferior parietal

regions). These areas have been shown to be involved in visuo-spatial information processes (Leichnetz, 2001; Shapiro, Hillstrom, & Husain, 2002), attention and attention shift (Behrmann, Geng, & Shomstein, 2004; Nagahama et al., 1999), and episodic memory retrieval (Cabeza, Ciaramelli, Olson, & Moscovitch, 2008). In fact, Lundstrom and colleagues (2003, 2005) examined the neural correlates of source memory retrieval of words paired with corresponding imagined or viewed pictures and found that the left parietal and left lateral prefrontal cortex were selectively activated during retrieval. Together, these findings suggest that alcohol modulates neural activation and alters processes associated with source memory.

Fragmentary Blackout Effects

Comparisons between individuals who have and have not experienced fragmentary blackouts indicated significant differences in neural activation during alcohol sessions, but no significant differences during no alcohol sessions. This finding was expected given that there were no significant differences on memory performance during no alcohol sessions during Study 1 and the current study. Analyses also revealed that those with a history of fragmentary blackouts who consumed alcohol (i.e., FB+ X Alcohol) exhibited greater activations in the right hemisphere, including the occipital and parietal regions. The right occipital and parietal regions have been associated with visual perception and object identification (Beck, Muggleton, Walsh, & Lavie, 2008; Harris, Benito, Ruzzoli, & Miniussi, 2008). Individuals with no prior history of fragmentary blackout who consumed alcohol (i.e., FB- X Alcohol), however, showed greater activation in the left prefrontal and left parietal regions than individuals with a history of fragmentary blackouts during a source memory task. Previous research found that alcohol decreased activation of the frontoparietal network during tasks that required visual perception and feedback (Van Horn et al., 2006), which could play an important

role in perceiving source-related stimuli and subsequent source retrieval. Together, these findings suggest that individuals with and without a history of fragmentary blackouts may engage in different memory strategies. Specifically, individuals with a history of fragmentary blackouts may utilize more visual strategies (i.e., occipital and parietal activations), whereas individuals without a history of fragmentary blackouts may use verbal strategies (i.e., left prefrontal activations) during recall and recognition tasks. Further, given the cue-related nature of fragmentary blackouts and source memory, deficits in source memory and decreased activation in areas related to source memory in individuals with a history of fragmentary blackouts suggests that fragmentary blackouts likely occur due to altered processing in the left prefrontal and parietal regions after alcohol consumption.

It is interesting that the current findings parallel those demonstrated in studies comparing source memory performance and processes between young and older adults. Individuals with a history of fragmentary blackouts show a pattern of results similar to older adults with lower accuracy and decreased activation in the left prefrontal cortex compared to young adults (Dennis et al., 2008; Mitchell et al., 2006). These findings are also consistent with the idea that memory impairments may be due to deficits in engaging the left prefrontal cortex to monitor specific memory-related information. Future research that links decreased activity in these areas with impaired memory performance is warranted. Further, more data are needed to determine whether the differences found between individuals with and without a history of fragmentary blackouts are a result from altered encoding. For example, if individuals with a history of fragmentary blackouts show differential activation in the fusiform gyrus during encoding, it might suggest that these individuals are encoding less source-specifying information for subsequent retrieval

and may have binding deficits similar to those in older adults (e.g., Li, Naveh-Benjamin, & Lindenburger, 2005; Naveh-Benjamin, Guez, Kilb, & Reedy, 2004).

In summary, the results of Study 2 provide additional information about fragmentary blackouts and the neural correlates and memory processes that may be associated with their occurrence. Similar to Study 1, individuals with a history of fragmentary blackouts displayed source memory deficits after alcohol consumption. Furthermore, alcohol interfered with neural activity of regions involved in source memory processes, such as the left prefrontal cortex. The comparison between alcohol and no alcohol sessions revealed that source memory was associated with greater activation during no alcohol sessions in the left prefrontal cortex, left parietal regions, and medial temporal lobe compared to alcohol sessions. After alcohol consumption, those without a history of fragmentary blackouts (i.e., FB-) showed greater activation in the left prefrontal areas during source recognition; whereas, individuals with a history of fragmentary blackouts (i.e., FB+) had greater activations in the right occipital and parietal regions when alcohol was consumed. Thus, it appears that alcohol alters neural activity in some individuals more than others, which seems to subsequently affect source memory. Specifically, alcohol may alter source memory processes in the left prefrontal regions such that access and evaluation processes of remembering are impaired in some individuals more than others, which may lead to alcohol-induced fragmentary blackouts. Together, these findings provide a potential mechanism through which fragmentary blackouts occur, that is through altering neural activity in areas associated with source memory.

CHAPTER 5: GENERAL DISCUSSION

Research indicates that alcohol-induced fragmentary blackouts are signs of alcohol misuse and may be prognostic indicators of alcohol use disorders (e.g., Wechsler et al., 2000, White et al., 2002). Although alcohol-induced blackouts are common, potentially dangerous, and suggestive of alcohol abuse, surprisingly little is known about these memory impairments. The primary motivation for this research was to examine memory processes that may be correlated with the experience of an alcohol-induced fragmentary blackout. Given the cue-related nature of alcohol-induced fragmentary blackouts and source memory deficits observed in some individuals after alcohol consumption, the current paradigm was designed to assess episodic memory, including source memory, processes during alcohol and no alcohol conditions Questionnaires, neuropsychological assessments, and fMRI techniques were used to compare memory performance and neural activation between individuals with and without a history of fragmentary blackouts. Results revealed differential performance on memory tasks after alcohol consumption, with individuals who had experienced a fragmentary blackout showing the poorest source memory performance compared to individuals who had not experienced a prior fragmentary blackout. Source memory performance was correlated with neural activity in the left prefrontal cortex with less activation during alcohol sessions when comparing source memory activations during alcohol and no alcohol sessions and differential activation during alcohol sessions between individuals with and without a history of fragmentary blackouts.

EFFECTS OF ALCOHOL ON MEMORY AND NEURAL ACTIVATIONS

Decades of research indicate that alcohol intoxication affects memory processes and typically leads to memory impairment. The current studies advance understanding of

the effects of alcohol on memory processes and provide a potential mechanism through which alcohol-induced episodic memory impairment may occur. Overall, alcohol impaired memory performance on a variety of episodic memory tasks, including recall of narrative details and themes, cued narrative recall, and source memory. Alcohol altered memory performance at immediate, delayed, and next day recall, which provides additional evidence for differential functioning of episodic memory during both intoxication and after detoxification. This finding is consistent with previous research showing episodic memory impairment after alcohol consumption (e.g., Duka et al., 2001; Petros, Kerbel, Beckwith, Sacks, & Sarafolean, 1985; Saults, Cowan, Sher, & Moreno, 2007; Soderlund et al., 2005), including impaired memory performance the day after alcohol intoxication (e.g., McKinney & Coyle, 2007; Spinetta, Woodlee, Feinberg, Stroud, Schallert et al., 2008; Prat, Adan, Perez-Pamies, & Sanchez-Turet, 2008). Although it remains unclear whether alcohol-induced memory impairments are a result of encoding, consolidation, or retrieval deficits, these data provide additional evidence that alcohol impairs memory processes across a variety of episodic memory tasks and at varying recall delays.

The detrimental effects of alcohol on memory performance have also been observed in recent fMRI studies showing alcohol impaired memory performance and modulated neuronal activity associated with the memory tasks (e.g., Gundersen et al., 2008; Soderlund et al., 2007; Van Horn et al., 2006). In the current study, alcohol intoxication led to decreased activations in areas associated with source and item memory compared to a resting state. The left prefrontal cortex and medial temporal lobe showed less activation in the alcohol group during source recall when source memory was impaired. Although results provide additional information regarding the effects of alcohol on memory processes and neural correlates of source memory, it will be

important to examine factors that may contribute to these effects and to determine the stages during which alcohol alters memory processes (e.g., encoding, consolidation, or retrieval).

Based on anecdotal and recent research evidence, it has been posited that the effects of alcohol on memory may be more pronounced in some individuals than others, which may lead some people to experience alcohol-induced fragmentary blackouts (Hartzler & Fromme, 2003; Nelson et al., 2004). In fact, the current study demonstrated that individuals with a history of fragmentary blackouts showed greater source memory impairment after alcohol consumption compared to those without a history of fragmentary blackouts. In other words, after alcohol consumption, individuals who reported experiencing a fragmentary blackout in the past exhibited the poorest source memory performance. Further, results revealed significant differences in activation patterns between individuals with and without a history of fragmentary blackouts during the source memory task. Specifically, individuals with and without a history of fragmentary blackouts showed similar left prefrontal activations during no alcohol sessions, with no significant differences between the two groups when sober; however, individuals with a history of fragmentary blackouts exhibited less neural activation in regions associated with source memory processes after alcohol consumption compared to individuals without a history of fragmentary blackouts. These activations were also correlated with behavioral performance on the source memory task, suggesting that alcohol affects some individuals more than others. These findings replicate and extend those of Hartzler and Fromme (2003) and provide additional support for the idea that some individuals have an inherent vulnerability to alcohol-induced memory impairments, including fragmentary blackouts. The potential for such vulnerabilities to the effects of alcohol are also strengthened by several studies showing prenatal alcohol exposure and

genetic contributions for experiencing alcohol-induced memory impairments (Baer, Sampson, Barr, Connor, & Streissguth, 2003; Nelson et al., 2004). Together, these findings strongly suggest that some individuals are simply built in a way that makes them more vulnerable to alcohol-induced memory impairments, particularly memory for source information.

METHODOLOGICAL ADVANCES

In addition to providing important information about fragmentary blackouts and the effects of alcohol on memory processes and neural activations, the current research represents an innovative approach to examining vulnerabilities to alcohol use disorders. By combining standardized human alcohol administration procedures and fMRI techniques, we were able to assess individual differences that may predispose a person to alcohol misuse and alcohol use disorders. Further, the current approach moves beyond the extant literature examining the effects of alcohol on memory by allowing us to not only evaluate behavioral data, like typical laboratory studies using neuropsychological assessments, but also to assess the neural activations that are associated with this behavioral data. As such, we can directly and objectively correlate neural activation with behavior and better understand how alcohol affects the brain and cognitive processes. This research also improves upon the growing literature on fMRI of vulnerable populations by examining the neural mechanisms that underlie individual differences in response to alcohol rather than assessing neural activations associated with encoding or retrieval among vulnerable populations when they are sober (e.g., Schweinsburg et al., 2005; Tapert et al., 2004). Although this latter approach is informative, the most important questions remain unanswered. That is, do these vulnerable populations respond to alcohol differently, and if so, in what ways? The current approach provides insight to these unanswered questions and presents unique opportunities to better

understand the diverse effects of alcohol on the brain and behavior. Similar studies could provide important insights to understanding other vulnerabilities and endophenotypes that place a person at greater risk to alcohol use disorders.

Beyond the current focus on memory processes and fragmentary blackouts, other individual differences in the vulnerability to alcohol use disorders could be examined by research that combines alcohol administration procedures with fMRI techniques. For example, subjective responses to alcohol (e.g., Schuckit, 1994, 1998, 1999; Schuckit and Smith, 1996), affect regulation (e.g., Sher & Slutske, 2003; Simons & Carey, 2006), age of drinking onset (e.g., Ehlers, Slutske, Gilder, Lau, & Wilhelmsen, 2006; Nagel et al., 2005), and personality traits (e.g., Jackson & Sher, 2003; Trull, Waudby, & Sher, 2004) have all been associated with alcohol use and the development of alcohol use disorders. These factors have been evaluated using a variety of methodologies including laboratory studies, physiological measures, neuropsychological assessments, and self-report measures; however, few (if any) studies have directly examined the neural mechanisms that underlie these individual differences in vulnerability to alcohol use disorders. In fact, we were unable to find any published studies investigating the effects of alcohol on neural activations among individuals who differ on any of these factors. Thus, there is a substantial gap within the alcohol literature in efforts to relate the brain-behavior connection and subsequent alcohol use trajectories. By employing alcohol administration and fMRI techniques among individuals with potentially different vulnerabilities, we may be able to address this gap by making the connections between differences in neural structures and processes and individual differences in the development of alcohol use disorders. Further, by understanding the neural substrates that underlie inherent vulnerabilities to alcohol use disorders, we may be able to one day use brain activation

patterns in response to alcohol as measures for the risk of developing alcohol use disorders.

LIMITATIONS AND FUTURE DIRECTIONS

Although the present data provide compelling evidence for a potential mechanism through which alcohol-induced fragmentary blackouts occur, several limitations must be addressed. First, the moderate alcohol dose manipulation (target BAC of .08%) was not comparable to the levels of intoxication which frequently lead to the occurrence of fragmentary blackouts. Even given ethical restraints prohibiting the administration of alcohol to higher BACs, previous studies and the current data suggest that dosing participants to a .08% BAC causes memory impairments that differentiate individuals who have and have not previously experienced fragmentary blackouts (Hartzler & Fromme, 2003). Given research findings, it is possible that alcohol affects source-related memory at lower BACs and other memory-related processes become altered at higher doses. Thus, current findings may underestimate the effects of alcohol on memory processes at greater levels of intoxication.

Another possible limitation of the current research is the absence of an active placebo condition to assess expectancy effects. When individuals expect alcohol or know they are consuming alcohol, a set of outcome expectancies (i.e., beliefs about the effects of drinking) are elicited that may influence a person's cognitions, moods, and behavior (e.g., Petrovic et al., 2005; Wager et al., 2004). An active placebo provides a way to account for these expectancies and separate the pharmacological effects of alcohol from the psychological effects of expectancies. Although alcohol expectancies have been shown to influence cognition and behavior, previous studies on memory performance and expectancy effects of various drugs have consistently shown that expectancy effects from substances do not influence memory performance (Assefi & Garry, 2003; Nelson et al.,

1986). As such, an active placebo condition was not included in the current research. Recent fMRI research, however, indicates that expectancy modulates neuronal activity (Gundersen et al., 2008). Thus, current neuroimaging findings could be confounded by alcohol expectancies. That is, participants in the current studies both expect and receive alcohol, and as a result, we are unable to separate expectancy from drug effects. Future research should address the interaction between alcohol intoxication and expectancy affects on source memory and other cognitive processes when conducting alcohol administrations with fMRI research.

The potential for practice effects on memory tasks (i.e., narrative recall, source memory) must be acknowledged. Although content was dissimilar, administration procedures were identical and could have facilitated later performances. Practice effects, however, were not found for the proposed narrative recall or source memory tasks in previous (Hartzler & Fromme, 2003b; Dobbins et al., 2002) or the present study. Furthermore, the current studies focused on memory tasks specific to the ascending limb of the blood alcohol concentration curve and not other cognitive mechanisms that may influence the occurrence of fragmentary blackouts (e.g., inhibitory processing, attentional bias, descending limb effects).

The screening process and experimental protocol relied on self-report, specifically of previously forgotten experiences. Recent analyses, however, indicated that self-report measures of blackouts are internally consistent with Cronbach alphas of 0.84 (en bloc) and 0.93 (fragmentary blackouts; Wetherill & Fromme, unpublished data). In addition, fragmentary blackouts and alcohol use were assessed multiple times using multiple modalities that have been shown to have strong reliability for drinking data (Needle, Jou, & Su, 1989). Overall, the use of self-report measures is supported by findings that self-report is both reliable and valid (Babor & Del Boca, 1992; Babor et al., 1994).

It is important to note that there are two interpretations for the current findings, both of which support the idea that some people are more susceptible to fragmentary blackouts than others. Based on our findings, we posit that individuals in the fragmentary blackout have always been more vulnerable to alcohol-induced memory impairments, and as a result, perform more poorly on source memory tasks after alcohol consumption and why they are members of the fragmentary blackout group in the first place. An alternative interpretation is that individuals who have experienced fragmentary blackouts performed more poorly on the source memory task after alcohol consumption because of substance use in the past, which has caused permanent damage and increased alcohol-induced memory impairments. That is, prior exposure to alcohol damaged the brain of these individuals in a way that predisposed them to experiencing future memory impairments. In order to determine the direction of effects, a prospective, longitudinal study could track individuals prior to drinking onset and examine alcohol consumption and the occurrence of memory impairments.

Most importantly, the relatively small number of participants in the present studies may constrain broad population generalizability and statistical power. Future research with larger and more diverse samples (in terms of drinking history) is needed in order to better characterize the memory processes and neural correlates associated with alcohol-induced fragmentary blackouts. Future fMRI research based upon these findings will seek to maximize cohort size, broaden the scope, and examine more closely the differences between individuals with and without a history of fragmentary blackouts. Based on findings that the frontoparietal network is important in attention and the ability to shift one's attention (Cusack, Mitchell, & Duncan, 2009; Rushworth, Krams, & Passingham, 2001), it will be important to examine the role of the frontal and parietal

lobes in association with attention and attention shift among individuals with and without a history of fragmentary blackouts.

Despite limitations, the current research provides important information regarding the effects of alcohol on memory processes and the neural mechanisms that underlie alcohol-induced memory impairments. Study findings suggest that fragmentary blackouts may result from the effects of alcohol the neural correlates associated with source memory. Findings also indicate that some people appear to have inherent vulnerabilities to alcohol-induced source memory impairment, which may explain why some people experience blackouts while others do not, even at comparable blood alcohol concentrations. These findings are quite promising and provide important information regarding the effects of alcohol on the brain and associated behaviors. Further, this research provides a methodological approach that could enable researchers to identify neural systems that contribute to a wide range of cognitive and affective processes that predispose individuals to alcohol use disorders. Taken together, these findings expand the growing alcohol and imaging literature by integrating human alcohol administration procedures and fMRI techniques to better understand alcohol-induced fragmentary blackouts.

Table 1. Study 1 Sample Description and Group Comparisons

	Overall Sample	FB +	FB –
	M (SD)	*M (SD)*	*M (SD)*
Age	21.62 (0.51)	21.58 (0.49)	21.66 (0.53)
Drinking Quantity	3.83 (2.18)	4.25 (1.98)	3.38 (2.29)
Drinking Frequency	2.88 (1.51)	3.18 (1.45)	2.57 (1.52)
Alcohol Problems*	4.13 (4.87)	5.66 (5.54)	2.59 (3.53)
Blackouts (Past Month)**	0.47 (0.82)	0.86 (0.98)	0.07 (0.25)
	% endorsed	% endorsed	% endorsed
Lifetime Difficulty With:			
Names of Objects	7.9	11.1	4.5
Names of People	47.2	48.9	45.5
Things Said or Done	13.5	17.8	9.1
Names of Places	2.2	0.0	4.5
Important Events	5.6	6.7	4.5
Tasks to Complete	12.4	11.1	13.6

Notes. * reflects statistically significant group differences at $p < .05$; ** = $p < .001$. FB = fragmentary blackouts. Drinking quantity ranges from 0 to ∞. Drinking frequency ranges from 1 to 7. Alcohol problems = total RAPI score minus the blackout item. Blackouts range from 1 to ∞.

Table 2. Baseline Memory by Beverage Condition for Those Reporting a History of Fragmentary Blackouts

	Alcohol *M (SD)*	No Alcohol *M (SD)*
Correct Digit Span Trials (Range: 0 - 26)	19.43 (2.25)	20.25 (3.77)
Immediate Recall of Narrative Details (Range: 0 - 25)	15.48 (3.15)	15.23 (3.44)
Immediate Recall of Narrative Themes (Range: 0 - 7)	5.74 (1.36)	5.68 (1.09)
Delayed Recall of Narrative Details (Range: 0 - 25)	15.00 (3.11)	15.13 (3.72)
Delayed Recall of Narrative Themes (Range: 0 - 7)	5.50 (1.19)	5.67 (0.92)
Delayed Cued Recall of Narrative Details (Range: 0 - 10)	8.14 (1.96)	8.22 (1.24)

Note. No statistical differences between beverage condition at baseline.

Table 3. Baseline Memory by Beverage Condition for Those Not Reporting a History of Fragmentary Blackouts

	Alcohol *M (SD)*	No Alcohol *M (SD)*
Correct Digit Span Trials (Range: 0 - 26)	20.87 (3.38)	20.82 (2.77)
Immediate Recall of Narrative Details (Range: 0 - 25)	15.39 (2.50)	16.10 (2.00)
Immediate Recall of Narrative Themes (Range: 0 - 7)	5.52 (1.24)	5.76 (0.77)
Delayed Recall of Narrative Details (Range: 0 - 25)	14.78 (3.15)	15.38 (2.91)
Delayed Recall of Narrative Themes (Range: 0 - 7)	5.13 (0.97)	5.57 (1.27)
Delayed Cued Recall of Narrative Details (Range: 0 - 10)	8.57 (1.81)	8.14 (1.80)

Note. No statistical differences between beverage condition at baseline.

Table 4. Behavioral Data for Study 2

	Fragmentary Blackouts +		Fragmentary Blackouts -	
	Alcohol	No Alcohol	Alcohol	No Alcohol
	M (SD)	*M (SD)*	*M (SD)*	*M (SD)*
Item Recognition	0.75 (0.04)	0.82 (0.06)	0.74 (0.05)	0.81 (0.02)
Source Recall	0.66 (0.05)	0.71 (0.04)	0.64 (0.07)	0.70 (0.05)

Note. Mean proportions with standard deviations.

Table 5. Regions Demonstrating Greater Activation from Within Group Comparisons

Region	Z score	x	y	z
Activations during No Alcohol Sessions				
R/L Medial Temporal Lobe (BA 39)	6.75	-32	-52	-24
R/L Occipital/Fusiform (BA 19)	6.66	24	-68	-14
	6.64	-30	-62	-18
L Inferior Frontal (BA 9, 13, 47)	5.72	-30	22	-8
	5.19	-48	18	22
	5.12	-38	26	12
L Middle Frontal (BA 6, 46)	5.32	-46	28	18
	4.74	-36	6	50
L Superior Frontal (BA 8)	5.03	-38	14	50
Activations during Alcohol Sessions				
R/L Occipital (BA 18, 19)	7.18	-28	-92	-14
	6.30	34	-92	-2
L Parietal (BA 7)	6.65	-26	-62	44
	6.56	-22	-66	42
L Caudate	4.69	-12	8	2
	4.62	-8	6	4
L Parahippocampus (BA 27)	4.48	-22	-30	-4
L Inferior Frontal (BA 45)	4.82	-28	26	2
L Middle Frontal (BA 6)	4.33	-38	8	52
Within Group: No Alcohol > Alcohol				
L Precuneus (BA 7)	3.76	-12	-56	38
	3.35	0	-66	34
L Inferior Parietal (BA 39, 40)	3.61	-44	-64	34
	3.12	-42	-56	48
	3.05	-40	-60	46
L Middle Frontal (BA 6, 9, 46)	3.18	-42	34	30
	3.14	-42	26	32

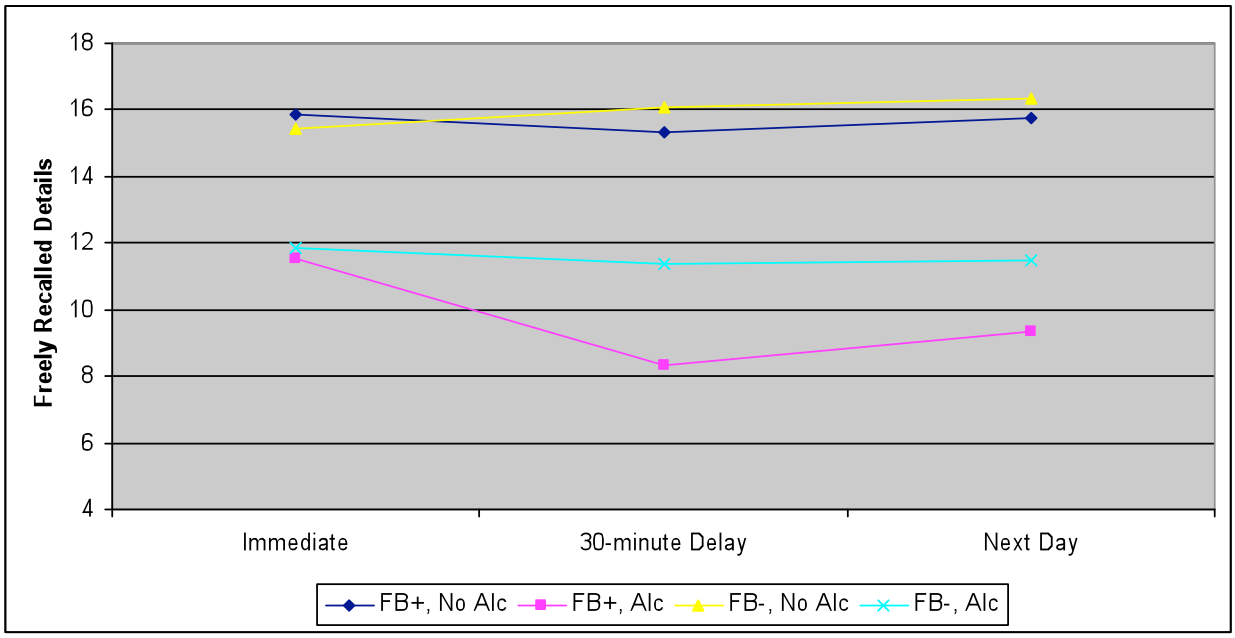
Notes. L = left, R = right, BA = Brodmann area.

Table 6. Regions Demonstrating Greater Activation from Between Group Comparisons

Region	Z Score	x	y	z
Between Group Interaction: FB+ > FB- (Alcohol > No Alcohol)				
R Parietal (BA 40, 7)	4.19	58	-58	44
	3.64	12	-46	46
R Occipital (BA 17, 18)	4.15	6	-102	-2
	3.65	8	-102	-14
Between Group Interaction: FB- > FB+ (Alcohol > No Alcohol)				
L Precentral (BA 4, 6)	3.72	-38	-22	66
	3.64	-40	-16	64
	2.64	-38	-20	54
	3.59	-44	-12	60
L Middle Frontal (BA 6)	3.68	-40	8	54
	2.65	-28	6	56
Between Group Interaction: FB- X Alcohol (Source-Fixation > Item-Fixation)				
L Orbital (BA 11)	3.67	-20	44	-26
L Anterior Cingulate (BA 10)	3.38	-18	46	8
L Superior Frontal (BA 10)	3.21	-22	60	12
	2.85	-16	50	16
L Medial Frontal (BA 9)	3.07	-16	52	4

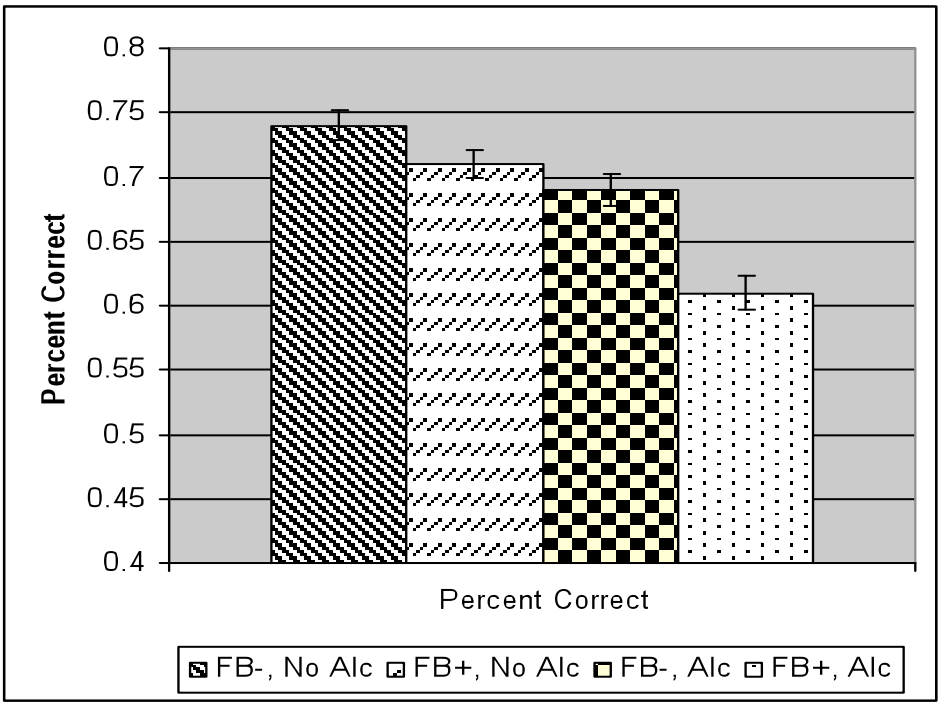
Notes. L = left, R = right, BA = Brodmann area.

Figure 1. Performances on Recall of Narrative Details



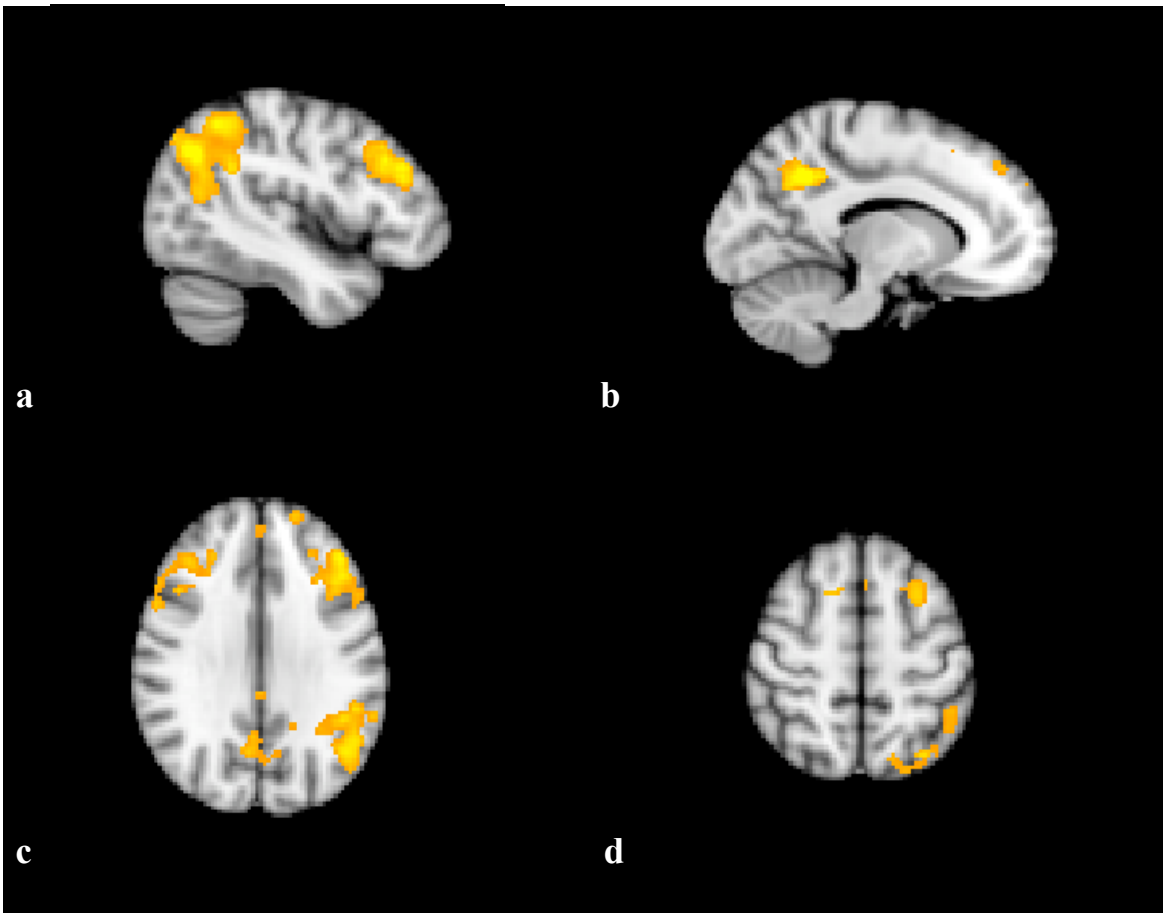
Notes. Immediate = Immediate free recall 30-minutes post-beverage consumption; 30-minute Delay = Free recall 30-minutes after immediate recall and 60-minutes post-beverage consumption; Next Day = Free recall 22-26 hours post-beverage challenge; FB+ = Fragmentary blackout history positive; FB- = Fragmentary blackout history negative; Alc = Alcohol session; No Alc = No alcohol session.

Figure 2. Performances on Source Recall



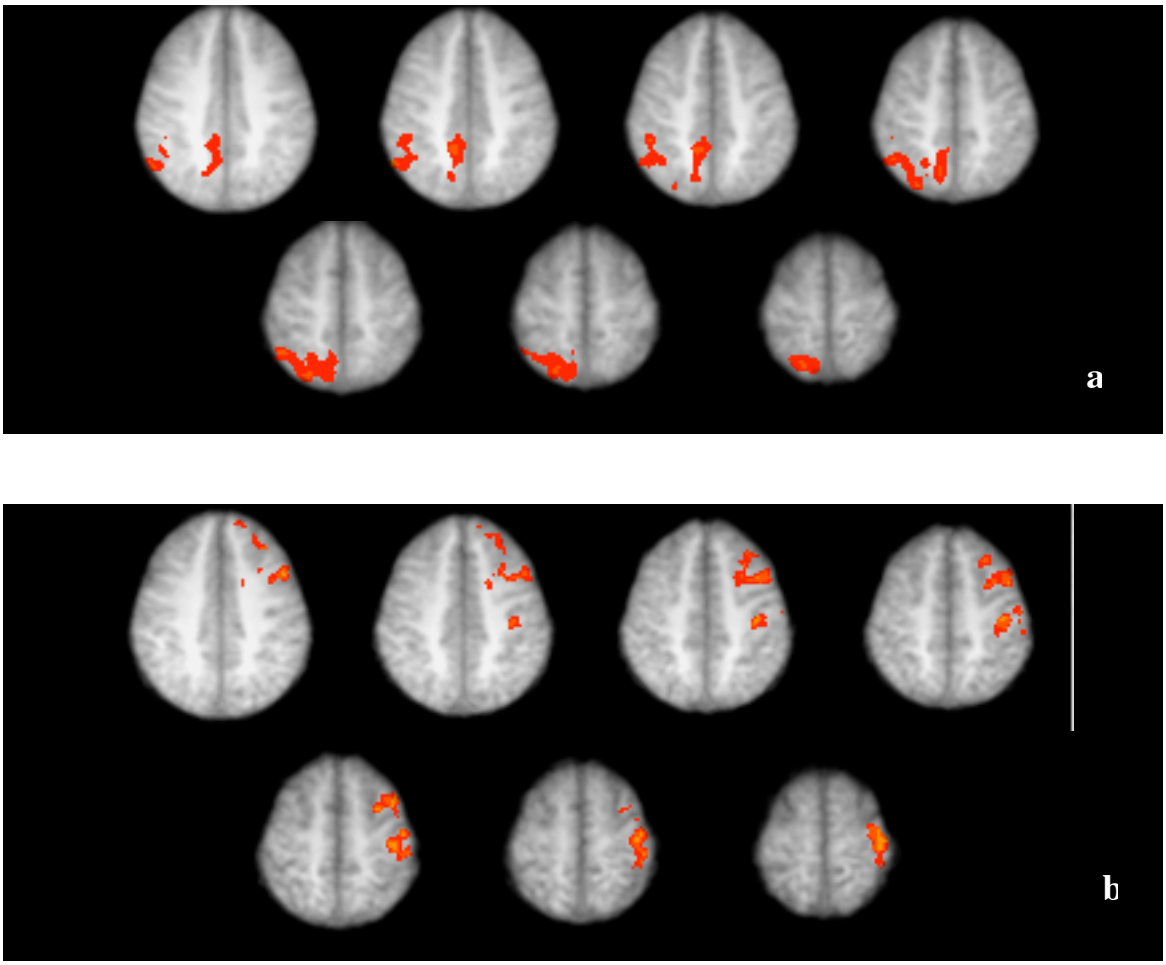
Notes. FB+ = Fragmentary blackout history positive; FB- = Fragmentary blackout history negative; Alc = Alcohol session; No Alc = No alcohol session.

Figure 3. Greater Activation during Source Memory Task Relative to Baseline Using Within-Group Analysis (No Alcohol > Alcohol)



Notes. No alcohol > alcohol activations during source memory task. a) Sagittal slice (x = -42) illustrating location of left middle frontal gyrus and left parietal regions that showed greater activation. b) Sagittal slice (x = -12) showing greater activation in the left precuneus. c,d) Axial slices (z = 30, 50) demonstrating greater activations in the middle frontal gyrus and left parietal regions.

Figure 4. Greater Activation during Source Memory Task Relative to Baseline between Groups



Notes. 2 (FB-, FB+) X 2 (Alcohol, No Alcohol) between group comparisons. a) Axial views demonstrating greater activation in the FB+ group under alcohol (FB+ X alcohol). b)Axial views demonstrating greater activation in the FB- group under alcohol (FB- X alcohol).

Figure 5. Greater Activation during Source Memory Task Relative to Item Recognition

Notes. 2 (FB-, FB+) X 2 (Alcohol, No Alcohol) between group comparisons. a) Sagittal and axial views demonstrating greater activation in the FB- group under alcohol (Source > Item).

APPENDIX A: SELF-REPORT MEASURES

A-1. Demographics

1. What is your age? a. 21 b. 22 c. 23

2. What is your biological sex? a. female b. male

3. What is your race/ethnicity?

a. African American or Black
b. American Indian/Alaskan Native
c. Asian
d. Hispanic or Latino/a
e. Hawaiian or Pacific Islander
f. White or Caucasian

4. What is your family's estimated annual income?

a. under $20,000
b. $20,000-$29,999
c. $30,000-$39,999
d. $40,000-$49,999
e. $50,000-$59,999
f. $60,000-$69,999
g. $70,000-$99,999
h. over $100,000

5. In your day-to-day experience do you have difficulty remembering/forget:

a the name of objects?	YES	NO
b. the name of people?	YES	NO
c to complete tasks?	YES	NO
d. you did or said?	YES	NO
e places you have been?	YES	NO
f. about important events (i.e., meetings, appointments)?	YES	NO

6. What time does your typical sleeping cycle:

begin? _____ am/pm end? _____ am/pm

7. Last night, what time did your sleep cycle:

begin? _____ am/pm end? _____am/pm

8. Have you or are you currently under the care of a psychiatrist and/or psychologist? YES NO

9. Are you currently undergoing medical treatment? YES NO

A-2. Family Tree Questionnaire (FTQ)

INSTRUCTIONS: For each relative listed below, we want to know your impressions of their drinking behavior. Please categorize each relative into the category you think best describes their drinking behavior. Only include blood relatives; that is, relatives by birth. Do not include relatives who are adopted, half-siblings, or step-relatives. If you have less than 4 brothers and/or 4 sisters, please mark "N/A" on any remaining lines for brothers (7-10) and sisters (11-14).

CODE EACH RELATIVE USING ONE OF THE FOLLOWING 5 CATEGORIES:

1. NEVER DRANK: A person who has never consumed alcoholic beverages (i.e., a lifelong abstainer or teetotaler).
2. SOCIAL DRINKERS: A person who you think drinks moderately and is not known to have a drinking problem.
3. POSSIBLE PROBLEM DRINKER: A person whom you or others believe may have a past or current drinking problem, but you are not actually certain whether they ever had a drinking problem.
4. DEFINITE PROBLEM DRINKERS: Only include persons who you think either have received treatment for a drinking problem (i.e., Alcoholics Anonymous), or who have experienced several negative consequences of their drinking.
5. DON'T KNOW/DON'T REMEMBER: Please indicate only if you do not know the relative, or have no memory of their drinking behavior.

	Family Member	[redacted]	1	2	3	4	5
01.	Maternal Grandmother (Mother's Mother)		1	2	3	4	5
02.	Maternal Grandfather (Mother's Father)		1	2	3	4	5
03.	Paternal Grandmother (Father's Mother)		1	2	3	4	5
04.	Paternal Grandfather (Father's Father)		1	2	3	4	5
05.	Mother		1	2	3	4	5
06.	Father		1	2	3	4	5
07.	Brother	N/A	1	2	3	4	5
08.	Brother	N/A	1	2	3	4	5
09.	Brother	N/A	1	2	3	4	5
10.	Brother	N/A	1	2	3	4	5
11.	Sister	N/A	1	2	3	4	5
12.	Sister	N/A	1	2	3	4	5
13.	Sister	N/A	1	2	3	4	5
14.	Sister	N/A	1	2	3	4	5

A-3. Daily Drinking Questionnaire (DDQ)

For the following questions, please think about your drinking behavior DURING THE LAST 3 MONTHS.

1 Standard Drink = 12 ounces of beer, 1 shot of liquor (straight or in mixed drink), or 5 ounces of wine

For a TYPICAL WEEK, please indicate the number of standard drinks you consumed each day:

Monday_____ Tuesday _____ Wednesday _____ Thursday _____

Friday _____ Saturday _____ Sunday _____

A-4. Timeline Follow-Back Interview (TLFB)

Instructions: The purpose of this task is to gather information about your drinking experiences during the past three months. Using this calendar (show the following page), we will be starting with your more recent drinking episodes and go backward until _____ (write day) of _____ (month). For each drinking episode, I will ask you how many standard drinks you consumed and over what period of time you drank. (present conversion scale). For each drinking episode, I'll ask you if you later had difficulty remembering intoxicated events, for instance when you awoke the next day. I'll be asking you questions to differentiate between intoxicated events that you have no recollection for, versus intoxicated events that you did not initially recall but could remember after someone described them. Before we begin, do you have any questions?

1 Standard Drink = 12 ounces of beer, 1 shot of liquor (straight or in mixed drink), or 5 ounces of wine

The following set of questions will be asked in the sequence listed below:

"When was your most recent experience?"	***Identify specific date. Use key dates (e.g., holidays, events) if he/she is unsure of date.***
"How may standard drinks did you consume?"	***Use actual examples of standard drinks (e.g., wine glass, shot glass, beer stein with colored sand marking ounces). Write amount on the calendar day.***
"Over what period of time did you consume those beverages?	***Identify specific time length. Write time on calendar day.***
"Did you awaken the next day and find that you could not remember things you had done or said?	***Obtain yes/no answer. If no, proceed to the next drinking episode. If yes, ask the following:***
"Were you later able to recall the forgotten events when later reminded of them?"	***Yes = fragmentary blackout. No = en bloc blackout. Probe as needed to differentiate and code as "FB" or "EBB" on calendar day.***
"Did you use other substances while intoxicated?	***If yes, determine what substance and note it on the calendar day.***
Which of the following labels best describes how you feel about having had difficulty recalling those experiences?"	***Obtain a specific rating label for the episode of memory loss and note on calendar day.*** ***Bad, Slightly Bad, Neutral, Slightly Good, or Good***

Repeat questions for prior drinking experiences during that previous month.

TLFB

Sunday	**Monday**	**Tuesday**	**Wednesday**	**Thursday**	**Friday**	***Saturday***
	1					

A-6. Rutgers Alcohol Problems Index (RAPI)

During the last 3 months, how many times did the following things happen to you while you were drinking alcohol or because of your alcohol use?

1.	Not able to do your homework or study for a test.	0	1 -2	3-5	6-10	>10
2.	Got into fights, acted badly, or did mean things.	0	1 - 2	3-5	6-10	>10
3.	Missed out in other things because you spent too much money on alcohol.	0	1 - 2	3-5	6-10	>10
4.	Went to work or school high or drunk.	0	1 - 2	3-5	6-10	>10
5.	Caused shame or embarrassment to someone.	0	1 - 2	3-5	6-10	>10
6.	Neglected your responsibilities.	0	1 - 2	3-5	6-10	>10
7.	Relatives avoided you.	0	1 - 2	3-5	6-10	>10
8.	Felt that you needed more alcohol than you used to use in order to get the same effect.	0	1 - 2	3-5	6-10	>10
9.	Tried to control your drinking by trying to drink only at certain times of the day or in certain places.	0	1 - 2	3-5	6-10	>10
10.	Had withdrawal symptoms (i.e. felt sick because you stopped or cut down on drinking).	0	1 - 2	3-5	6-10	>10
11.	Noticed a change in your personality.	0	1 - 2	3-5	6-10	>10
12.	Felt that you had a problem with alcohol.	0	1 - 2	3-5	6-10	>10
13.	Missed a day (or part of a day) of school or work.	0	1 - 2	3-5	6-10	>10
14.	Tried to cut down or quit drinking.	0	1 - 2	3-5	6-10	>10
15.	Suddenly found yourself in a place that you could not remember getting to.	0	1 - 2	3-5	6-10	>10
16.	Passed out or fainted suddenly.	0	1 - 2	3-5	6-10	>10
17.	Had a fight, argument, or bad feelings with a friend.	0	1 - 2	3-5	6-10	>10
18.	Had a fight, argument, or bad feelings with a family member.	0	1 - 2	3-5	6-10	>10
19.	Kept drinking when you promised yourself not to.	0	1 - 2	3-5	6-10	>10
20.	Felt you were going crazy.	0	1 - 2	3-5	6-10	>10
21.	Had a bad time.	0	1 - 2	3-5	6-10	>10
22.	Felt physically or physiologically dependent on alcohol.	0	1 - 2	3-5	6-10	>10
23.	Was told by a friend or neighbor to stop or cut down drinking.	0	1 - 2	3-5	6-10	>10

A-7. Blackout Items: Young Adult Alcohol Problems Screening Test (YAAPST)

For the following questions, please indicate the number of times you have experienced any of the following after drinking over the past 3 months.

If you did not experience any of the following during the past 3 months, please write "0."

1.	Have you been arrested, even for a few hours, because of other drunken behaviors?	times
2.	Have you awakened the morning after drinking and found that you could not remember something you did or said while drinking?	times
3.	For times when you could not remember things you did or said while drinking, were you able to later recall them when reminded by others or cued by the setting?	YES NO

APPENDIX B: MEMORY TASKS

B-1 & 2	Wechsler Adult Intelligence Scale-III: Digit Span
B-3 – B-6	Wechsler Memory Scale-III: Logical Stories
B-7	Source Memory Task

B-1. Digit Span (WAIS-III)

Read the digits at the rate of one per second *dropping your voice inflection slightly* on the last digit of the sequence. Pause to allow the participant to respond. DISCONTINUE AFTER A SCORE OF 0 ON ***BOTH*** TRIALS.

Digits Forward: ***"Now I am going to say some numbers. Listen carefully, and when I am through, I want you to say them right after me. Just say what I say."*** Proceed to trail 1 of digits 2 on Digits Forward.

DIGITS FORWARD					
Digits	Trial	Item	Response	Trial Score	Item Score (0,1,or 2)
2	1	1-7	(1-7)		
	2	6-3	(6-3)		
3	1	5-8-2	(5-8-2)		
	2	6-9-4	(6-9-4)		
4	1	6-4-3-9	(6-4-3-9)		
	2	7-2-8-6	(7-2-8-6)		
5	1	4-2-7-3-1	(4-2-7-3-1)		
	2	7-5-8-3-6	(7-5-8-3-6)		
6	1	6-1-9-4-7-3	(6-1-9-4-7-3)		
	2	3-9-2-4-8-7	(3-9-2-4-8-7)		
7	1	5-9-1-7-4-2-8	(5-9-1-7-4-2-8)		
	2	4-1-7-9-3-8-6	(4-1-7-9-3-8-6)		
8	1	5-8-1-9-2-6-4-7	(5-8-1-9-2-6-4-7)		
	2	3-8-2-9-5-1-7-4	(3-8-2-9-5-1-7-4)		
9	1	2-7-5-8-6-2-5-8-4	(2-7-5-8-6-2-5-8-4)		
	2	7-1-3-9-4-2-5-6-8	(7-1-3-9-4-2-5-6-8)		
= # of Digits Fwd			**Digits Forward Score:**		

B-2. Digit Span (WAIS-III)

Digits Backward: ***"Now I am going to say some more numbers. But this time when I stop, I want you to say them backward. For example, if I say 7-1-9, what would you say?"*** If participant responds correctly (9-1-7), say: ***"That's right."*** and proceed to trail 1 of digits 2. However, if the participant responds incorrectly say: ***"No, you would say 9-1-7. I said 7-1-9, so to say it backward, you would say 9-1-7. Now try these numbers. Remember you are to say them backward: 3-4-8."*** Do not provide any assistance on this example or any of the items. Whether or not the participants responds correctly (8-4-3), proceed to trial 1 of digits 2 on Digits Backward.

DIGITS BACKWARD					
Digits	Trial	Item	Response	Trial Score	Item Score (0,1,or 2)
2	1	2-4	(4-2)		
	2	5-7	(7-5)		
3	1	6-2-9	(9-2-6)		
	2	4-1-5	(5-1-4)		
4	1	3-2-7-9	(9-7-2-3)		
	2	4-9-6-8	(8-6-9-4)		
5	1	1-5-2-8-6	(6-8-2-5-1)		
	2	6-1-8-4-3	(3-4-8-1-6)		
6	1	5-3-9-4-1-8	(8-1-4-9-3-5)		
	2	7-2-4-8-5-6	(6-5-8-4-2-7)		
7	1	8-1-2-9-3-6-5	(5-6-3-9-2-1-8)		
	2	4-7-3-9-1-2-8	(8-2-1-9-3-7-4)		
8	1	9-4-3-7-6-2-5-8	(8-5-2-6-7-3-4-9)		
	2	7-2-8-1-9-6-5-3	(3-5-6-9-1-8-2-7)		
= # of Digits Bwd			**Digits Backward Score:**		

Digits Forward Score ____+Digits Backward Score ____ = Digit Span Score ____ (max 30)

B-3. WMS-III – Logical Memory

Instructions read to participant: "I am going to read you a story. Please listen carefully because when I am finished with the story, I want you to tell the story back to me as best you can remember. Do you have any questions?"

Story A: Anna Thompson of South Boston, employed as a cook in a school cafeteria, reported at the police station that she had been held up on State Street the night before and robbed of 56 dollars. She had four small children, the rent was due, and they had not eaten for two days. The police, touched by the woman's story, took up a collection for her.

Anna	____ (Anna or variant)	
Thompson	____ (must be Thompson)	
of South	____ (South-any context)	
Boston	____ (Boston-any context)	____ (main char. is female)
employed	____ (she had a job)	
as a cook	____ (cook or some form of the word)	
in a school	____ (must say school)	
cafeteria	____ (must say cafeteria)	____ (main char. employed)
reported	____ (formal stmt. made to an authority)	
at the police	____ (police-any context)	
station	____ (station-any context; word denoting pol.stn.)	
that she had been held up	____ (indic. of being held up-i.e., gunpt.,knife)	
on State Street	____ (State Street-any context)	
the night before	____ (indication of the previous night)	
and robbed	____ (indication that robbery took place)	
of 56 dollars.	____ (accept any amount between $50 and $59)	____ (reported she was robbed)
She had four	____ (must say 4; and indic. that kids were hers)	
small children,	____ (children or synonym)	____ (main char. had children)
the rent was due,	____ (indication that rent was due)	
and they had not eaten	____ (indic. that kids/family were without food)	
for two days.	____ (2 days, or equivalent)	____ (char.'s were in need)
The police	____ (1 or more members of pol. dept.)	
touched by the woman's story	____ (story evoked sympathy)	____ (pol felt sympathy for her)
took up a collection	____ (indication that $ was collected)	
for her.	____ (indication that it was for her or her kids)	____ (pol responded to her need)

Story A – Recall = ____ Thematic Unit Score = ____

After a 30 minute delay, read the following to the participant: "Do you remember the story that I read to you previously? I want you to tell the story back to me as best you can remember. Do you have any questions?" NOTE: DO NOT READ THE STORY TO THE PARTICIPANT, JUST GET THEIR DELAYED RECALL.

Story A: Anna Thompson of South Boston, employed as a cook in a school cafeteria, reported at the police station that she had been held up on State Street the night before and robbed of 56 dollars. She had four small children, the rent was due, and they had not eaten for two days. The police, touched by the woman's story, took up a collection for her.

Anna	____ (Anna or variant)	
Thompson	____ (must be Thompson)	
of South	____ (South-any context)	
Boston	____ (Boston-any context)	____ (main char. is female)
employed	____ (she had a job)	
as a cook	____ (cook or some form of the word)	
in a school	____ (must say school)	
cafeteria	____ (must say cafeteria)	____ (main char. employed)
reported	____ (formal stmt. made to an authority)	
at the police	____ (police-any context)	
station	____ (station-any context; word denoting pol.stn.)	
that she had been held up	____ (indic. of being held up-i.e., gunpt.,knife)	
on State Street	____ (State Street-any context)	
the night before	____ (indication of the previous night)	
and robbed	____ (indication that robbery took place)	
of 56 dollars.	____ (accept any amount between $50 and $59)	____ (reported she was robbed)
She had four	____ (must say 4; and indic. that kids were hers)	
small children,	____ (children or synonym)	____ (main char. had children)
the rent was due,	____ (indication that rent was due)	
and they had not eaten	____ (indic. that kids/family were without food)	
for two days.	____ (2 days, or equivalent)	____ (char.'s were in need)
The police	____ (1 or more members of pol. dept.)	
touched by the woman's story	____ (story evoked sympathy)	____ (pol felt sympathy for her)
took up a collection	____ (indication that $ was collected)	
for her.	____ (indication that it was for her or her kids)	____ (pol responded to her need)

Story A – Recall = ____ Thematic Unit Score = ____

Instructions read to participant: "I am going to read you another story. Again, please listen carefully because when I am finished with the story, I want you to tell the story back to me as best you can remember. Do you have any questions?"

Story B: At 6:00 on Monday evening, Joe Garcia, of San Francisco was watching television as he dressed to go out. A weather bulletin interrupted the program to warn that thunderstorms would move into the area within the next 2 to 3 hours and remain until morning. The announcer said the storm could bring hail and up to 4 inches of rain and cause the temperature to drop by 15 degrees. Joe decided to stay home. He took off his coat and sat down to watch old movies.

At 6:00	____ (must say '6:00')	
on Monday	____ (must say Monday)	
evening	____ (evening-in any context)	
Joe	____ (Joe or variant)	
Garcia	____ (must say Garcia)	
of San Francisco	____ (must say San Francisco)	____ (main char. is a male)
was watching television	____ (indic. he was watching/listening to TV)	
as he dressed	____ (indic. he was getting dressed)	____ (char. was prepar. to leave)
to go out.	____ (indic. he was going out)	
A weather bulletin	____ (indic. of weather announcement)	____ (indic. of weath. announcemt)
interrupted	____ (indic. of a break in reg. program)	
to warn that thunderstorms	____ (indic. that there was a storm warning)	
would move into the area.	____ (indic. that the storm was coming)	____ (indic of storm moving in)
within the next 2 to 3 hours	____ (equivalent of 2-3 hours)	
and remain until morning.	____ (indic. that storm would stay till morning)	____ (indic. of storm duration
The announcer said	____ (indic. that s/o was reporting about storm)	
the storm could bring hail,	____ (indic. that hail was possible)	
and up to 4 inches	____ (must say 4 inches)	
of rain	____ (must say rain)	
and cause the temp. to drop	____ (indic. that temp. would drop)	
by 15 degrees.	____ (must say a relative decrease of 15 degr.)	____ (indic. of storm's activity)
Joe decided to stay home.	____ (indic. he decided to stay home)	____ (char. decided to stay in)
He took off his coat	____ (indic. he took off outer clothing)	

and sat down to watch old movies.	____ (indic. he was sitting down) ____ (must indicate viewing movies)	____ (char.would watch movie/TV)

Story B – Recall = ____ Thematic Unit Score = ____

During the following day's telephone consult, read the following to the participant: "Do you remember the story that I read to you previously? I want you to tell the story back to me as best you can remember. Do you have any questions?" NOTE: DO NOT READ THE STORY TO THE PARTICIPANT, JUST GET THEIR DELAYED RECALL.

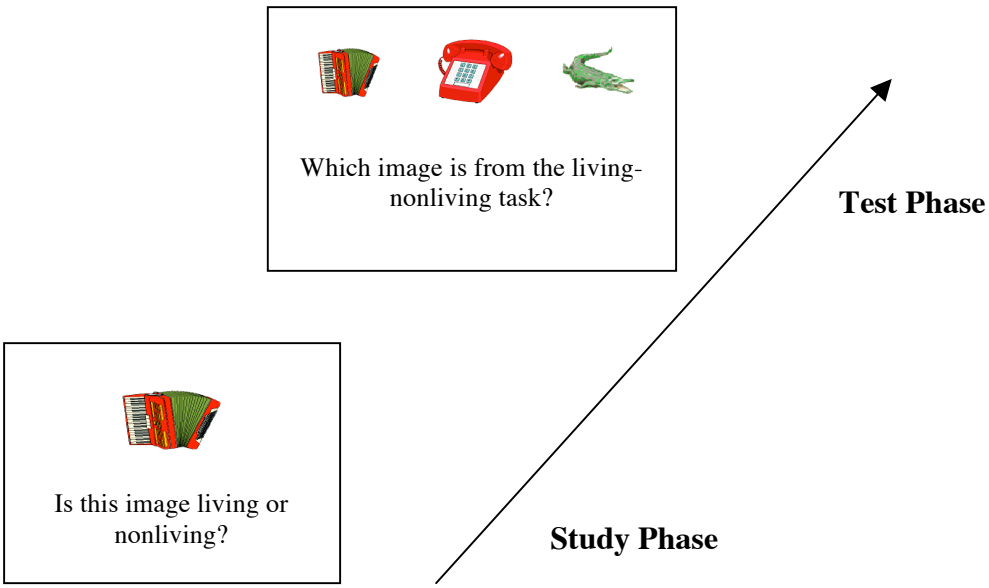
Story B: At 6:00 on Monday evening, Joe Garcia, of San Francisco was watching television as he dressed to go out. A weather bulletin interrupted the program to warn that thunderstorms would move into the area within the next 2 to 3 hours and remain until morning. The announcer said the storm could bring hail and up to 4 inches of rain and cause the temperature to drop by 15 degrees. Joe decided to stay home. He took off his coat and sat down to watch old movies.

At 6:00	____ (must say '6:00')	
on Monday	____ (must say Monday)	
Evening	____ (evening-in any context)	
Joe	____ (Joe or variant)	
Garcia	____ (must say Garcia)	____ (main char. is a male)
of San Francisco	____ (must say San Francisco)	
was watching television	____ (indic. he was watching/listening to TV)	
as he dressed	____ (indic. he was getting dressed)	____ (char. was prepar. to leave)
to go out.	____ (indic. he was going out)	
A weather bulletin	____ (indic. of weather announcement)	____ (indic. of weath. announcemt)
interrupted	____ (indic. of a break in reg. program)	
to warn that thunderstorms	____ (indic. that there was a storm warning)	
would move into the area.	____ (indic. that the storm was coming)	____ (indic of storm moving in)
within the next 2 to 3 hours	____ (equivalent of 2-3 hours)	
and remain until morning.	____ (indic. that storm would stay till morning)	____ (indic. of storm duration
The announcer said	____ (indic. that s/o was reporting about storm)	
the storm could bring hail,	____ (indic. that hail was possible)	
and up to 4 inches	____ (must say 4 inches)	
of rain	____ (must say rain)	
and cause the temp. to drop	____ (indic. that temp. would drop)	____ (indic. of storm's activity)
by 15 degrees.	____ (must say a relative decrease of 15 degr.)	
Joe decided to stay home.	____ (indic. he decided to stay home)	____ (char. decided to stay in)
He took off his coat	____ (indic. he took off outer clothing)	

and sat down	____ (indic. he was sitting down)	
to watch old movies.	____ (must indicate viewing movies)	____ (char.would watch movie/TV)

Story B – Recall = ____ Thematic Unit Score = ____

B-7. Source Memory Task



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