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Evaluating Cognitive Changes in Patients Receiving Outpatient Alcohol Treatment

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School of Behavioral Health
in conjunction with the
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Evaluating Cognitive Changes in Patients Receiving Outpatient Alcohol Treatment

by

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A Dissertation submitted in partial satisfaction of
the requirements for the degree
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Each person whose signature appears below certifies that this dissertation in his/her opinion is adequate, in scope and quality, as a dissertation for the degree Doctor of Philosophy.

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ABBREVIATIONS

DSM-5	Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition
NIAAA	National Institute on Alcohol Abuse and Alcoholism
AUD	Alcohol Use Disorder
fMRI	functional Magnetic Resonance Imaging
KS	Korakoff's Syndrome
CBM	Cognitive Bias Modification
LLUBMC	Loma Linda University Behavioral Medicine Center
RBANS	Repeatable Battery for Neuropsychological Status
ANCOVA	Analysis of Covariance

ABSTRACT OF THE DISSERTATION

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by

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Chronic alcohol use has been linked to various physical health concerns, neurological changes, and cognitive deficits. Research has shown that some of these neurologic and cognitive deficits can improve over time following detoxification and abstinence; however, the exact nature or timeline of this recovery process has not been established. The aim of the current study is to identify cognitive deficits and changes present in the alcohol addiction treatment population, the influence of cognitive deficits on treatment completion, and the effect of previous engagement in treatment (which is indicative of previous relapse) on cognitive functioning at both treatment onset and treatment completion. Results suggest that individuals within an intensive outpatient AUD program experienced improvements in language and overall cognitive functioning. Additional variables approaching significance include the subtests of story learning, figure copy, semantic fluency, digit span, coding, and the overall attention index, all of which exhibited small to medium effect sizes. In contrast, impairments in cognitive functioning were not related to treatment drop-out. Finally, previous treatment engagement was not suggestive of worse cognitive functioning. Despite reduced sample size, these results provide some insight into the variability in cognitive functioning within AUD, suggesting that providers may need to consider tailoring treatment for those who

present with various cognitive impairments. Programs that account for memory, executive functioning, and processing speed impairments may assist their patient's in the retention of information presented during treatment, thus improving rehabilitation and increasing subsequent success in sobriety.

CHAPTER ONE

INTRODUCTION

The Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition (DSM-5) specifies that the diagnosis of substance use disorders requires symptoms across four criteria: impaired control, social impairment, risky use, and pharmacological criteria (2013). Individuals with a substance use disorder experience impaired control over substance use, cravings for the substance, failure to fulfill major role obligations, continued use despite physical or psychological problems, use in situations that may be physically hazardous, increased tolerance of the substance, and withdrawal symptoms. Evaluation of rates of abuse and misuse of specific substances reveals that alcohol has the highest rate of abuse among all drugs (National Council on Alcoholism and Drug Dependence, 2015).

According to the National Institute on Alcohol Abuse and Alcoholism (NIAAA), 56.9% of people age 18 or older reported drinking alcohol in the past month, while 24.7% reported engaging in binge drinking, defined as a pattern of drinking that brings blood alcohol concentration levels to 0.008g/dL (e.g., five or more alcoholic drinks for men within two hours, four or more alcoholic drinks for women within two hours) within the past month, and 6.7% reported engaging in heavy drinking, defined as binge drinking on five or more days in the past month in (NIAAA, 2016). In 2015, approximately 16.3 million adults met criteria for an Alcohol Use Disorder (AUD), and 1.5 million adults received treatment for an AUD from a specialized chemical dependency treatment program (NIAAA, 2016). The economic burden of alcohol misuse is considerable, such

that in 2010, it cost the United States $249 billion. Beyond economics, alcohol misuse has resulted in the deaths of 88,000 people in the United States and 3.3 million individuals worldwide in 2012 (NIAAA, 2016).

Physical Health Risks of Alcohol Use

Alcohol misuse has been found to be related to numerous health concerns including, but not limited to, cancer, pancreatitis, and liver disease. Increased risk of developing a diagnosis of pancreatitis is dose-related, such that after a threshold of four drinks per day, the risk of diagnosis increases proportionally to the amount of alcohol consumed (Irving, Samokhavalov, & Rehm, 2012). Additionally, there is a dose-response pattern of the effect of alcohol use on risk of cirrhosis of the liver (Day, 2006). This relationship can be exacerbated by body weight, type II diabetes, and genetic risk factors, which also may be influenced by alcohol misuse. Further evaluation of liver disease indicates that the median survival rate for those with a diagnosis of cirrhosis of the liver is approximately two years with evidence of decompensation and ten years with compensated cirrhosis; however, survival rates improve significantly with abstinence (Day, 2006). In regard to cancer, alcohol has been causally linked to squamous cell-carcinoma of the oral cavity, pharynx, larynx, and esophagus. There is a correlational relationship between alcohol use and colon cancer, liver cancer, and breast cancer, as well as a confounding relationship between lung cancer and alcohol use, such that cigarette use increases during alcohol consumption (Boffetta & Hashibe, 2006).

Alcohol misuse is not only costly at economic and global levels, but also to the individual's physical and neuropsychological health. Research has indicated that there is

a J-shaped relationship between alcohol use and health deficits, such that minimal daily alcohol use may be linked to positive health benefits, while high level consumption is linked with negative health effects (Di Castelnuovo et al., 2006). Specifically, this dose-dependent relationship has indicated that more than one to two drinks per day for women and two to four drinks per day for men increases risk for negative health concerns (Di Castelnuovo et al., 2006; O'Keefe, Bybee, & Lavie, 2007). In addition to the negative impact of chronic misuse of alcohol, those who engage in occasional misuse, such as binge drinking, also suffer from negative health consequences such as cancer, pancreatitis, and liver disease (Day, 2006; Irving, Samokhavalov, & Rehm, 2012; O'Keefe, Bybee, & Lavie, 2007). More specifically, even minimal alcohol consumption has been linked to increased risk of breast cancer in women (Shield, Soerjomataram, & Rehm, 2016). These negative effects are also impacted by alcohol type, such that alcohol consumption, with the exception of wine, is associated with increased risk for liver cirrhosis (Day, 2006).

In contrast to the negative health risks associated with alcohol use, positive benefits of minimal to moderate alcohol use, specifically ethanol rather than particular components of various alcoholic beverages, has been linked to cardiovascular protection (O'Keefe, Bybee, & Lavie, 2007) and reduced risk for cardiovascular dementia (Deng, Li, Wang, Gao, & Chen, 2005; Ganguli, Vander Bilt, Saxton, Shen, & Dodge, 2005; Ruitenberg et al., 2002; Stampfre, Kang, Chen, Cherry, & Grodstein, 2005). Small to moderate amounts of alcohol consumption has been associated with lower risk of myocardial infarction, which is hypothesized to be attributed to the relationship between alcohol and HDL cholesterol, fibrinogen, and insulin sensitivity (Mukamal et al., 2005).

Small to moderate alcohol consumption is also associated with reduced glucose excursion in diabetic patients (Turner, Jenkins, Kerr, Sherwin, & Cavan, 2001), due to ethanol's tendency to suppress the release of fatty acid from adipose tissue (Greenfield et al., 2003). The relationship with alcohol consumption and abdominal weight is also exemplified by a J-shaped relationship, such that those who consume light amounts of alcohol on a daily basis have less abdominal obesity compared to non-drinkers; however, more than two drinks per day is associated with greater abdominal obesity in proportion to the number of drinks consumed per day (Dorn et al., 2003).

Neurological Effects of Chronic Alcohol Use

Alcohol misuse has also been linked to neurologic changes (Bates, Bowden, & Barry, 2002; Crews & Nixon, 2008; Harper, 2009; Oscar-Berman & Marinkovic, 2007; Sullivan & Pfefferbaum, 2005). Evidence of alterations in neurological functioning have been found during intoxication (Crews & Nixon, 2008), periods of binge drinking (Weissenborn & Duka, 2003), for patients who have been long-term alcohol users (Pitel et al., 2007), and even in those who are social drinkers that do not meet the criteria for an AUD (Harper, 2009). Neuroimaging studies have revealed volume loss in the frontal lobes, cerebellar vermis, and anterior hippocampus, as well as increased ventricular and sulcal cerebrospinal fluid (Bates, Bowden, & Barry, 2002; Harper, 2009). Evaluation of MRI and fMRI studies revealed that excessive consumption of alcohol results in patterns of circuitry disruption between the frontocerebellar neuronal nodes and connecting circuitry throughout the brain (Sullivan & Pfefferbaum, 2005). Oscar-Berman and Marinkovic (2007) found up to a 20% decrease in gray matter volume bilaterally in the

dorsolateral frontal cortex, as well as gray matter decrease in the temporal cortex, insula, thalamus, and cerebellum. Research has also found up to 10% decrease in white matter of the corpus callosum in chronic alcohol users (Chanraud et al., 2007; Oscar-Berman & Marinkovic, 2007). Neurological changes have also been found in clinically and socially intact alcohol-dependent individuals, such as alterations of the cerebello-thalamo-cortical pathways, as well as reduction in brain volume in the dorsolateral frontal lobe, temporal cortex, insula, thalamus, and cerebellum (Chanraud et al., 2007).

Further evaluation of neuropsychological functioning indicates that patients with an AUD have significant difficulty when acquiring complex novel information (Pitel et al., 2007). fMRI studies indicate that, for patients with an AUD, there is increased cerebellar activation on tasks primarily considered to be associated with frontal lobe function, despite scoring within normal limits in functioning, which is indicative of a compensatory strategy (Pitel et al., 2007; Sullivan & Pfefferbaum, 2005). While this compensatory strategy may produce results within the normal range, it presents as ineffective and taxing, thus revealing the toll chronic alcohol use takes on the brain. Additional research indicates that higher-order executive functions are utilized to compensate for deficits in basic cognitive domain task performance (Pitel et al., 2007; Scheurich, 2005). More specifically, for recently detoxified men, they utilize frontal executive systems to perform basic visuospatial processes, such as visual perceptual learning and recall, to perform at the same level as normal controls, despite the fact that normal controls utilize more basic processes (Fama, Pfeferbaum, & Sullivan, 2004).

Neuropsychological Effect of Chronic Alcohol Use

Given the neurological changes associated with alcohol use, and specifically the structural and functional changes within the frontal cortices, temporal cortices, and neuronal circuitry throughout the brain, patients' neuropsychological functioning is also negatively influenced (Crews et al., 2005; Duka, Townshend, Collier, & Stephens, 2003; Pitel et al., 2007). The neuropsychological domains that may be affected by functional changes related to alcohol use include visuospatial functioning, learning and memory, executive functioning, language, attention, and processing speed.

Visuospatial Functioning

Alcohol use has been associated with deficits in visuospatial abilities (Crews et al., 2005). Those engaging in moderate to heavy alcohol consumption experience poorer performance in visuospatial functioning compared to healthy controls (Green et al, 2010). Patients with AUD exhibit deficits in visuospatial functioning, including the scanning, construction, and utilization and manipulation of visual information (Beatty et al., 1996). When compared to healthy controls, recently detoxified patients displayed reduced performance in the learning and construction, delayed recall, and even recognition of a complex figure (Dawson & Grant, 2000). Additionally, compared to healthy controls, recently detoxified patients presented with reduced problem-solving skills in organization, perceptual clustering, and constructional accuracy, which likely effects their ability to integrate visuospatial information in a complex design task.

Learning and Memory

The impact of alcohol use and misuse on learning and memory has proven to be variable, based on a number of factors, including type of memory and level of alcohol use. Compared to healthy controls, participants engaging in moderate to heavy alcohol consumption exhibit poorer performances in immediate memory (e.g., list learning and story learning; Sullivan, Harris, & Pfefferbaum, 2010). Alcoholic patients have also been found to exhibit a pattern of moderate impairment across verbal and non-verbal ability and memory (Tivis, Beatty, Nixon, & Parsons, 1995). When evaluating learning and memory beyond list learning, alcohol patients exhibit impairments in their ability to learn complex novel information (Pitel et al., 2007). Patients with severe alcohol misuse resulting in Korsakoff's Syndrome (KS) exhibit variations in memory performances such that they exhibit impairments on tests of explicit memory, particularly those tasks wherein they are not provided cues (Sullivan, Harris, & Pfefferbaum, 2010), but exhibit fewer impairments in verbal and non-verbal tests of implicit memory (Sullivan, Harris, & Pfefferbaum, 2010).

Executive Functioning

Neuropsychological profiles of patients with mild alcoholism are likely to be more sensitive to frontal lobe damage than social drinkers (Duka, Townshend, Collier, & Stephens, 2003). Deficits in executive functioning in chronic alcohol use have been found in cognitive flexibility (Ratti, Bo, Giardini, & Soragna, 2002) and working memory (Sullivan, Harris, & Pfefferbaum, 2010). The impairments have been found to increase with level of alcohol use, such that those with higher levels of alcohol consumption

exhibit greater impairments in perseverative responding, response inhibition, and cognitive flexibility (Houston et al., 2014). The negative effects of heavy drinking are not limited to chronic users, but also effect those who engage in binge drinking or social drinking (Parada et al., 2012; Weissenborn & Duka, 2003). Binge drinkers have been found to exhibit impairments in executive functioning and the ability to retain and manipulate verbal working memory (backward digit span; Parada et al., 2012), while those who engage in acute or social alcohol use also demonstrate impairments in executive functioning (Weissenborn & Duka, 2003).

Language, Attention, and Processing Speed

Results concerning deficits with regard to language, attention, and processing speed are variable. With regard to language, alcoholic participants showed relative sparing in the domain of language functioning (Crews et al., 2005). In terms of attention, over an eight-year period, adolescents and young adults who qualify for a diagnosis of alcohol use disorder exhibit a decline in attentional abilities, with increased decline associated with longer period of use (Tapert, Granholm, Leedy, & Brown, 2002). Patients who have recently completed detoxification exhibit deficits in attention; furthermore, those who resume drinking after detoxification continue to exhibit deficits in attention (Bourke & Grant, 1999). With regard to processing speed, alcohol patients have been found to experience a pattern of moderate impairments in perceptual motor skill (Tivis, Beatty, Nixon, & Parsons, 1995), with heavier drinking being associated with increased slowing in psychomotor speed (Houston et al., 2014). Recently detoxified male alcohol patients also experience deficits in psychomotor processing speed, which is further

exacerbated with resumed alcohol consumption after detoxification (Bourke & Grant, 1999). This pattern continues with older male adults, such that deficits increase with age and older male adults perform significantly worse than their same-age peers on measures of psychomotor processing compared to the discrepancy found in younger males (Bourke & Grant, 1999).

Recovery of Function after Abstinence

Despite the neurological and neuropsychological deficits associated with alcohol use and AUDs, selective functional improvements and some recovery of brain mass have been found as a result of abstinence (Crews et al., 2005). Research has revealed that neurogenesis occurs during abstinence (Crews et al., 2005), and cell proliferation across multiple brain regions has been shown to occur as early as the first day of abstinence (Crews & Nixon, 2008). Nixon, Kim, Potts, He, and Crews (2008), reported cell proliferation throughout the hippocampus and cortex after approximately two days of abstinence, and as the person remains abstinent, there is increased cell proliferation throughout the cortex by 28 days of sobriety. MRI studies have revealed that recovering patients with an AUD show greater white matter volumes in the frontal lobes, greater cortical gray matter in the orbital frontal pole and somatosensory cortex, as well as reduced white matter volume in the frontal lobes, compared to active heavy drinkers (O'Neill, Cardenas, & Meyerhoff, 2001). Notably, frontal lobe changes are potentially reversible with abstinence for several months or years (Moselhy, Georgiou, & Khan, 2001).

As neurological functioning and brain structures recover in abstinence, so too does cognitive function (Mann, Gunther, Stetter, & Ackermann, 1999). Patients who have received outpatient alcohol treatment exhibit improvements in executive functioning, verbal ability, and information processing after six weeks of abstinence; however, due to the small effect size, improvement may not be considered clinically significant (Bates, Voelbel, Buchman, Labouvie, & Barry, 2005). A meta-analysis revealed that cognitive deficits were still present in eleven cognitive domains, including language verbal fluency, processing speed, working memory, attention, executive functioning, verbal learning and memory, and visual learning and memory after just one month of abstinence; however, these deficits were resolved after one year of abstinence, even for participants who began treatment with minimal neuropsychological difficulties (Oscar-Berman & Marinkovic, 2007; Stavro, Pelletier, & Potvin, 2011). Similarly, long-term abstinent males with a previous AUD, who remained abstinent for two years, exhibited similar neuropsychological results compared to healthy controls (Bourke & Grant, 1999). While research has shown some cognitive improvements with long-term periods of abstinence (e.g., six months to a year), results assessing the older veteran population found that within the early stages of recovery (e.g., first two months of abstinence) they still exhibit deficits in verbal and nonverbal learning, with verbal learning being profoundly impaired (e.g., two standard deviations below same-age peers) across the learning trials, despite experiencing a time of abstinence (Bell, Vissicchio, & Weinstein, 2016). These results suggest that cognitive recovery is dependent upon time since abstinence.

Research has been mixed with regard to the cognitive domains that undergo improvement. Mann, Gunther, Stetter, and Ackermann (1999) reported that after

approximately five weeks, the performance discrepancy between control participants and patients engaged in alcohol abstinence was reduced, with the exception for verbal short-term memory. In contrast, Fein, Backhman, Fisher, and Davenport (1990), indicated that impairments in cognitive functioning have been found across the first five months of abstinence, such that half to two-thirds of abstinent alcohol exhibit these impairments; however, these deficits have been found to last for years after detoxification, with visuospatial functioning, psychomotor speed, abstract reasoning, and new learning experiencing the greatest impairments.

The pattern of cognitive impairment in abstinence is impacted influenced by a number factors, including time since detoxification and age of onset of alcohol use (Fein, Bachman, Fisher, & Davenport, 1990). Specifically, those in acute detoxification (zero to two weeks of abstinence), exhibit deficits in attention, concentration, reaction time, motor coordination, motor speed, judgment, problem-solving, learning, and short-term memory (Fein, Bachman, Fisher, & Davenport, 1990). Patients in the intermediate-term of abstinence (two weeks to two months) exhibit persistent deficits in visuospatial processing and problem-solving. In some cases, the ability to learn new verbal material improves within the first two weeks of abstinence; however, it remains impaired after one month. Patients in the stages of long-term abstinence (greater than two months) experience variable results, such that while there are still improvements in cognitive functioning, the level of improvement varies across domain and may still not reach the level of same-age controls. Research is mixed with regard to improvements in long-term abstinence, such that some researchers indicate that cognitive deficits remain after one year of abstinence (Stavro, Pelletier, & Potvin, 2011).

Age of onset of alcohol use has shown to be associated with cognitive impairment, such that those who begin drinking at a mean age of 14 experience significantly more severe impairments than those with a mean age of onset of 23, controlling for number of years of heavy drinking (Fein, Bachman, Fisher, & Davenport, 1990). Within six-months, improvements in episodic memory and executive functioning performances can return to normal; however, this is influenced by length of alcohol misuse, such that those with shorter length of alcohol use and misuse experience greater improvements in episodic memory recovery (Pitel et al., 2009). The reversal in cognitive deficits throughout abstinence and AUD recovery indicates that that the brain may be capable of repair and restructuring throughout adulthood (Crews et al., 2005).

Results indicate that with abstinence, many individuals with significant cognitive deficits exhibit at least a partial recovery from their alcohol-related cognitive impairment (Bates, Buckman, & Nguyen, 2013). Beyond abstinence, cognitive training has been associated with reduced risk for alcohol relapse up to one year after treatment (Verdejo-Garcia, 2016). Specifically, Cognitive Bias Modification (CBM), a treatment aimed at modifying cognitive biases and changing how one thinks and mentally responds to everyday occurrences, has been found to reduce long-term alcohol use (Verdejo-Garcia, 2016). CBM has also been found to significantly reduce medial prefrontal cortex activation, which has been associated with alcohol-approach bias. Additionally, cognitive rehabilitation may assist in the recovery of cognitive functioning when patients are provided domain specific tasks, such as copying figures, decoding rhythmic signals, attending to and interpreting orally presented stories, multi-tasking, visual reasoning, recalling stories, completing crossword puzzles, and developing mnemonic strategies

(Allen, Goldstein, & Seaton, 1997). Cognitive rehabilitation has been linked to improved performance in executive functioning, memory, and other cognitive abilities, which thus influence the behavioral outcomes of treatment, such as abstinence and interpersonal relationships (Bates, Buckman, & Nguyen, 2013).

Factors Related to Treatment Outcome

Neuropsychological functioning is essential for daily functioning and has been found to be related to treatment outcome (Tapert, Ozyurt, Myers, & Brown, 2016). Those who exhibit deficits in verbal learning are likely to experience reduced effectiveness of verbally-based interventions and psychoeducation, thus affecting their long-term recovery (Bell, Vissiccio, & Weinstein, 2016). Research has found that neurocognitive abilities moderate the relationship between coping and treatment outcome, such that those with poorer neurocognitive functioning are likely to have poorer treatment outcomes (Tapert, Ozyurt, Myers, & Brown, 2016). These results are likely due to the fact that alcohol-dependent adults with neuropsychological deficits may have more difficulty utilizing adaptive coping skills (Tapert, Ozyurt, Myers, & Brown, 2016). Additionally, chronic alcohol users also suffer impairments in prospective memory for both short-term and long-term events, which may also influence long-term recovery (Heffernan, Moss, & Ling, 2002). Given the findings that poorer neurocognitive functioning is predictive of poorer treatment outcome, evaluation of cognitive changes within treatment are necessary. It will be essential to determine the neurocognitive status and changes in patients receiving treatment for an AUD to ensure that they have access to the best treatment outcomes possible.

Impact of Relapse on Health and Recovery

It has been noted that relapse rates within a population of alcohol-dependent patients is high, such that up to 85% of the patients will relapse, even years after treatment. (Wiers & Heinz, 2015). Evaluation of neuroimaging suggests that, compared to individuals maintaining abstinence, those who relapse have been found to have relatively smaller volume in the orbitofrontal cortex and medial prefrontal cortex (Wiers & Heins, 2015), as well as altered connectivity responses in the anterior cingulate cortex (Zakiniaeiz, Scheinost, Seo, Sinha, & Constable, 2017). Neuroimaging studies also report structural changes within the amygdala, which is associated with increased craving for alcohol, in those who relapse compared to abstainers (Wiers & Heinz, 2015). Even previous relapses and detoxifications are associated with subsequent relapse behavior, as those with multiple previous detoxifications drink more intensely than patients without previous detoxifications (Malcolm, Roberts, Wang, Myrick, & Anton, 2000). Overall, those with less cortical volume are more likely to drink heavily during relapse (Naqvi & Morgenstern, 2015). This suggests that these patients are drinking significantly more alcohol prior to their abstinence, which may ultimately influence their cognitive functioning.

Given the complexity of recovery, it is notable that relapse can be impacted by a number of factors (e.g., psychosocial, neurological); however, diminished cognitive abilities likely add to the difficulty of maintaining abstinence (Stavro, Pelletier, & Potvin, 2012). Evaluation of neurocognitive functioning suggests that individuals with poorer general cognitive skills and decision-making are at an increased risk for subsequent relapse (Dominguez-Salas, Diaz-Batanero, Lozano-Rojas, & Verdejo-Garcia, 2016).

Beyond overall or general cognitive functioning, research has indicated that specific cognitive domains are also implicated in relapse rates. More specifically, those who have undergone more than one detoxification of alcohol experience increased impairments in visuospatial abilities, learning and memory, attentional problems, and primarily executive functioning (Duka, Townshend, Collier, & Stephens, 2003). Additionally, within the domains of episodic memory and executive functioning, those who relapse not only perform significantly worse than abstainers, but also perform worse than their own baseline performance (Pitel et al., 2009). Working memory (as exhibited by a task such as the n-back task) has also been identified as indicative of subsequent relapse, with poor performance related to increased risk for relapse (Wiers & Heinz, 2015). Individuals who relapse do not show improvements in cognitive functioning or brain volume, as do those who remain abstinent (Pfefferbaum et al., 1995). These studies suggest that previous relapse largely impacts subsequent neurological and cognitive functioning. Given the influence of cognitive functioning on overall recovery and health, it will be important to determine if previous relapse is associated with worse cognitive performance, suggestive of reduced recovery success.

Aims and Hypotheses

The first aim of this study is to evaluate the neurocognitive deficits and changes across treatment for patients receiving intensive outpatient treatment for an AUD. It is hypothesized that patients will exhibit improvements in their cognitive functioning at the end of their alcohol treatment, particularly in the domains of immediate memory, delayed memory, visuospatial functioning, and processing speed. The second aim of this study is

to identify if cognitive deficits present at the beginning of treatment are predictive of treatment completion. It is hypothesized that patients with poorer cognitive performance will have poorer treatment completion rates. The third and final aim of this study is to evaluate the cognitive performance within those who have undergone previous detoxification for AUD. Notably, it is hypothesized that overall cognitive abilities, as well as specific cognitive domains such as attention and memory (i.e., immediate and delayed) will be significantly worse for a those who have experienced previous periods of formal detoxification, across time points (i.e., onset of treatment, completion of treatment).

CHAPTER TWO

METHOD

Participants

Participants were selected from the Loma Linda University Behavioral Medicine Center (LLUBMC), from a pool of patients who completed a seven-day inpatient detoxification program at the LLUBMC and received intensive outpatient chemical dependency treatment strictly for alcohol use disorder. Participants who qualified for enrollment were selected by the chemical dependency director at the LLUBMC. All participants were detoxified and medically stable at outpatient treatment entry. Participants aged 20-89 were included in this study.

The final sample comprises 57 adults seeking intensive outpatient alcohol addiction treatment (age 26 to 64 years, M = 47.39, SD = 10.37; 49.1% female). In the current sample, 43 successfully completed their alcohol treatment, and of those 43, 20 participants (age 26 to 63 years, M = 49.80, SD = 10.84; 55% female) were successfully tested after approximately three weeks of treatment.

Procedures

Participants of the chemical dependency treatment program were recruited for the study within two days of admission to the outpatient program, after completing an inpatient detoxification at the LLUBMC. Upon enrollment in the study, written informed consent was obtained in accordance with the procedures set by the Loma Linda University Institutional Review Board. Participants were then administered the Repeatable Battery for Neuropsychological Status (RBANS), as well as a structured

clinical interview regarding demographic information, as well as health, drug, and legal history. Participants were then re-evaluated approximately three weeks later, at the end of their treatment, to assess for any changes in cognitive functioning.

Measures

The RBANS (Randolph, 1998) is a brief, individually administered assessment battery that assesses the neuropsychological status of adults with neurologic injury or disease. There are 12 subtests of the RBANS: list learning, story memory, figure copy, line orientation, digit span, symbol digit coding, picture naming, semantic fluency, list recall, list recognition, story recall, and figure recall. The 12 subtests assess different areas of cognitive function that result in five indices: immediate memory, visuospatial/constructional, language, attention, and delayed memory. The Immediate Memory Index is composed of list learning and story memory. The Visuospatial Index is composed of figure copy and line orientation. The Language Index is comprised of picture naming and semantic fluency. The Attention index includes the digit span and coding subtests. Finally, the Delayed Memory Index is composed of list recall, list recognition, story recall, and figure recall. A total scale score provides a global measure of neuropsychological functioning. The RBANS utilizes a United States population-based normative standardization, and index scores are scaled using age-based norms. The RBANS has been found to demonstrate sufficient validity and reliability within the clinical populations of dementia (i.e., Alzheimer's, vascular, HIV, Huntington's, Parkinson's), depression, schizophrenia, and traumatic brain injury (Randolph, 2006). External research also indicated that the RBANS demonstrates good validity for patients

within the following clinical populations: end-stage liver disease (Mooney et al., 2007), schizophrenia (Gold, Queern, Iannone, & Buchanan, 1999; Wilk et al., 2004), stroke (Green, Sinclair, Rodgers, Birks, & Lincoln, 2013), and traumatic brain injury (McKay, Casey, Wetheimer, & Fichtenberg 2006).

Analyses

Evaluation of the relationship of the sample demographics (e.g., gender, ethnicity, years of education) and cognitive performance was will be conducted. Evaluation of group differences for treatment completers and non-completers was conducted to determine if differences within demographic variables exist. Lastly, evaluation of the relationship between demographic variables and previous alcohol treatment was conducted. As there were significant differences among groups and cognitive factors, such variables were controlled for in subsequent analyses. Of note, age-adjusted z-scores and index scores were utilized for RBANS data, and thus age was not included as a covariate.

The first aim of this study was to identify the cognitive changes present in patients receiving intensive outpatient treatment. It was hypothesized that participants will show improvements in the domains of immediate memory, delayed memory, visuospatial functioning, and processing speed. Repeated Measures Analysis of Covariance was conducted, comparing within-subject changes, to evaluate the effect of treatment on cognitive functioning (DV) across time points (IV) within RBANS Total Scores, Index Scores, and individual subtests. Should the demographic variables of gender, years of education, and ethnicity show significant relationship with variables of cognitive

performance, they will be controlled within the analyses. Additionally, we calculated Bonferroni Corrections to correct for the elevated risk of Type 1 error. Finally, reported effect sizes (partial eta squared) to determine the strength of any significant differences.

The second aim of this study was to identify if cognitive deficits present at the beginning of treatment are associated with treatment completion. It was hypothesized that participants with more prominent cognitive functioning deficits will have increased rates of treatment dropout. Independent samples *t*-tests were conducted to evaluate if cognitive deficits are related to dropout rates. Specifically, we evaluated each cognitive domain and categorical index to determine if there was a relationship between cognitive performance and subsequent completion of treatment. Analyses were conducted with all participants at the first-time point (n = 57) utilizing Treatment Completion as the independent variable. We conducted 18 independent samples *t*-tests and reporting effect sizes (Cohen's *d*) to determine the strength of these differences. Additionally, Bonferroni correction was utilized to correct for Type I error.

The third aim of this study was to identify if there was a relationship between exposure to previous formal alcohol treatment and cognitive functioning. It was hypothesized that participants with previous formal treatment exposure will exhibit reduced cognitive functioning, specifically within overall cognitive functioning, attention, and memory (immediate and delayed), across time points. Analysis of Covariance (ANCOVA), controlling for ethnicity, years of education, and gender, was conducted to evaluate if those with previous treatment exposure will have reduced cognitive functioning compared to those without previous treatment exposure. Effect sizes (eta squared) was also be reported to indicate the strength of the relationship.

CHAPTER THREE

RESULTS

Evaluation of the relationship between demographics and variables of cognitive performance was conducted. Results of correlation analyses revealed significant relationships between gender, education, and ethnicity, and various indices and individual subtests of cognitive functioning (see Table 1). Thus, these variables were controlled for in the repeated measures analysis used to investigate the first and third aim. Evaluation of demographic differences among treatment completers and non-completers was conducted. Results of Chi-Square analyses did not reveal significant differences among those who did and did not complete treatment for the variables of gender, ethnicity, or education (see Table 2). Additionally, an Independent Samples *t*-test showed that there were no significant differences between completers and non-completers for age (see Table 2). A Pearson Correlation was conducted, revealing no significant relationship between previous rehabilitation experience and demographic variables (years of education, gender, and ethnicity). Finally, there were no significant differences among demographic variables or baseline RBANS scores between the individuals who completed treatment and the second time point of testing compared to those who completed treatment without completing the second time point of testing (see Table 3). Given the lack of significant relationship between demographics variables and those who did and did not complete treatment, no demographic variables were controlled for in the second aim of this study.

Table 1. Pearson Correlations between Demographics and Cognitive Variables at the Start and End of Treatment.

	Start Treatment			End Treatment		
	Gender	Ethnicity	Education	Gender	Ethnicity	Education
Immediate Memory Index	0.19	-0.11	0.41**	-0.25	-0.59**	0.30
List Learning	0.13	-0.04	0.36**	-0.06	-0.50*	0.38
Story Memory	0.26	-0.16	0.40**	-0.21	-0.36	0.05
Visuospatial Index	-0.03	-0.15	-0.40**	-0.41	-0.11	0.12
Figure Copy	-0.02	-0.08	0.37**	-0.42	-0.13	-0.11
Line Orientation	0.01	-0.00	0.20	-0.24	-0.04	0.41
Language Index	0.18	0.09	0.27	-0.39	-0.35	-0.13
Semantic Fluency	0.42**	0.07	0.25	-0.34	-0.22	-0.19
Picture Naming	-0.04	-0.24	0.22	-0.35	-0.73**	0.35
Attention Index	0.31*	0.16	0.21	-0.03	-0.34	-0.17
Digit Span	0.18	0.05	-0.01	-0.35	-0.42	-0.28
Coding	0.41**	0.15	0.27*	0.16	0.07	-0.08
Delayed Memory Index	0.07	-0.18	0.36**	-0.02	-0.35	0.54*
List Recall	0.24	-0.07	0.30*	0.05	-0.15	0.53*
List Recognition	-0.02	-0.33*	0.17	-0.11	-0.59**	0.33
Story Recall	0.23	0.03	0.33*	-0.01	0.09	0.36
Figure Recall	0.07	0.01	0.34**	-0.06	0.02	0.13
Total Scale	0.24	-0.07	0.49**	-0.34	-0.43	0.16

*$p < .05$. **$p < .01$.

Table 2. Chi-Square and Independent Samples *t*-test Evaluating Group Differences (Treatment Completion vs. Non-Completion) in Demographic Variables.

	t	*p*	*d*
Age	-1.08	0.28	0.45
	X^2	*p*	Φ
Gender	3.14	0.07	0.24
Ethnicity	1.26	0.53	0.15
Education	6.01	0.20	0.33

Table 3. Independent Samples *t*-test Evaluating Differences in Demographic and RBANS Baseline Variables for Within Treatment Completers (Second Testing vs. Non-Second Testing).

	t	*p*	*d*	Post-Hoc Power
Age	-0.61	0.54	0.19	0.09
Gender	-0.24	0.81	0.07	0.06
Education	-1.69	0.10	0.52	0.38
Immediate Memory Index	-0.12	0.91	0.04	0.05
List Learning	-0.37	0.71	0.11	0.06
Story Memory	0.25	0.80	0.08	0.10
Visuospatial Index	0.20	0.84	0.06	0.08
Figure Copy	1.71	0.10	0.52	0.38
Line Orientation	-0.99	0.33	0.31	0.17
Language Index	-0.60	0.55	0.19	0.09
Semantic Fluency	-0.06	0.96	0.02	0.05
Picture Naming	-0.72	-0.48	0.23	0.11
Attention Index	0.71	0.48	0.22	0.11
Digit Span	1.21	0.23	0.38	0.23
Coding	0.84	0.40	0.26	0.13
Delayed Memory Index	0.65	0.52	0.20	0.10
List Recall	-0.41	0.69	0.12	0.07
List Recognition	0.99	0.33	0.30	0.16
Story Recall	-0.18	0.86	0.06	0.05
Figure Recall	-0.27	0.79	0.08	0.06
Total Scale	0.41	0.68	0.13	0.07

Evaluation of the RBANS variables (subtests and indices) across both time points revealed that the following variables failed tests of normality: line orientation (treatment onset), picture naming (across time points), list recognition (across time points), and the immediate memory index (post treatment). Subsequently, the variables were transformed using a Log transformation ($\log(X_i)$) in an attempt to overcome problems of outliers, skewness, and kurtosis. The transformations successfully rectified problems with line orientation, list recognition, and list recognition; however, the variables of picture naming (across time points), and immediate memory index (post treatment) continued to

demonstrate difficulties with skewness and kurtosis. Subsequently, the Square Root and Reciprocal Transformations were applied to the remaining variables, revealing that they continued to deviate from a comparable normal distribution. As such, picture naming and immediate memory were not utilized in the evaluation of cognitive changes across treatment. Of note, there did not appear to be any significant outliers impacting the remaining variables of interest, therefore no participants were deleted from these results.

To evaluate the cognitive changes within patients receiving intensive outpatient treatment, 16 Repeated Measures Analysis of Covariance were conducted, one for each domain and index (with the exception of the variables that failed tests of normality), controlling for gender, years of education, and ethnicity. Note, age was not controlled for as we utilized age-adjusted normative data for the cognitive variables. Results indicated that the intensive outpatient treatment had a statistically significant effect on cognitive functioning on the indices of Language, $F(1, 19) = 14.94$, $p = 0.04$, $\eta_p^2 = 0.48$, Attention, $F(1,19) = 8.49$, $p = 0.01$, $\eta_p^2 = 0.35$, the individual subtests of Story Learning $F(1, 19) = 10.09$, $p = 0.006$, $\eta_p^2 = 0.39$, Figure Copy $F(1, 19) = 7.10$, $p = 0.02$, $\eta_p^2 = 0.31$, Digit Span, $F(1,19) = 4.33$, $p = 0.05$, $\eta_p^2 = 0.21$, and Coding, $F(1,19) = 56.37$, $p = 0.02$, $\eta_p^2 = 0.29$, as well as the overall Total Scale $F(1,19) = 17.01$, $p = 0.001$, $\eta_p^2 = 0.52$. The effect sizes of these analyses were found to indicate medium to large effects, suggesting that the variables evaluated explain 21-52% of the variance in changes of cognitive functioning (see Table 4). Post-hoc power analyses noted that the significant variables had 50-97% chance of detecting a true difference. Given the minimal sample size utilized in this study, a Bonferroni Correction was conducted to correct for the possibility of Type I error, yielding an alpha value of 0.003. Subsequent review of the results suggested that

there was still a significant effect of intensive outpatient treatment on the Language Index and Total Scale (see Table 4), while the individual subtests of Story Learning (p = 0.006) and Semantic Fluency (p = .004) were approaching significance. Notably, a Wilcoxon Signed-Rank Test was conducted to evaluate the changes in cognitive functioning for the variables that failed the tests of normality. Results indicated that the intensive outpatient treatment program did not elicit a statistically significant change in the Immediate Memory Index (p = 0.12) or the Picture Making subtest (p = 1.00) for those enlisted a AUD treatment program.

Table 4. Repeated Measures Analysis of Covariance Evaluating Effect of Intensive Outpatient Treatment on Cognitive Functioning, Controlling for Gender, Education, and Ethnicity.

	Start Treatment *M (SD)*	End Treatment *M (SD)*	*F* (*p*-value)	η_p^2	Post-Hoc Power
Immediate Memory Index [b]	--	--	--	--	--
List Learning	-0.4 (1.2)	0.1 (0.8)	3.15 (0.09)	0.16	0.39
Story Learning	-0.3 (1.1)	0.2 (0.6)	10.09 (0.006*)	0.39	0.85
Visuospatial Index	**85.6 (15.9)**	**92.9 (17.9)**	**0.63 (0.44)**	**0.04**	**0.12**
Figure Copy	-2.3 (1.9)	-1.6 (1.9)	7.10 (0.02*)	0.31	0.71
Line Orientation [a]	0.3 (0.2)	0.3 (0.2)	2.65 (0.12)	0.14	0.21
Language Index	**98.0 (12.1)**	**97.8 (12.4)**	**14.94 (0.001**)**	**0.48**	**0.95**
Picture Naming [b]	--	--	--	--	--
Semantic Fluency	0.0 (1.2)	-0.0 (1.2)	11.529 (.004*)	0.42	0.89
Attention Index	**94.7 (12.5)**	**102.5 (11.9)**	**8.49 (0.01*)**	**0.35**	**0.78**
Digit Span	-0.2 (0.9)	0.0 (1.0)	4.33 (0.05*)	0.21	0.50
Coding	-0.4 (0.9)	0.2 (1.2)	6.37 (0.02*)	0.29	0.66
Delayed Memory Index	**93.2 (14.9)**	**99.8 (12.3)**	**0.08 (0.78)**	**0.01**	**0.06**
List Recall	-0.3 (1.4)	0.0 (1.1)	0.01 (0.94)	0.00	0.05
List Recognition [a]	0.2 (0.3)	0.2 (0.2)	0.57 (0.46)	0.03	0.07
Story Recall	-0.2 (1.3)	0.3 (0.7)	1.64 (0.22)	0.09	0.23
Figure Recall	-0.6 (1.1)	0.1 (1.2)	0.30 (0.59)	0.02	0.08
Total Scale Index	**90.5 (10.8)**	**98.2 (11.5)**	**17.01 (0.001**)**	**0.52**	**0.97**

[a] Log Transformation applied to denoted variable.
[b] Log Transformation applied to denoted variable and found to be unsuccessful. Variable excluded from subsequent analysis.
*$p < .05$. ** $p < .003$ based on Bonferroni Correction.

To evaluate whether completers and non-completers demonstrated different levels of cognitive functioning at baseline, 16 Independent Samples *t*-tests were conducted. Results revealed that the poor performances on the Attention Index at baseline ($t[55] = -2.00$, $p = 0.05$, $d = -0.54$; see Table 3) was related to subsequent treatment completion. Evaluation of the effect size for the Attention Index, revealed that those who did not

complete treatment had a medium magnitude of effect (54%) for reduced attention. Post-hoc power analyses suggested that there was a 41% chance that results capture a true difference. Of note, while none of the individual subtests were related to subsequent treatment completion, Coding (t[55] = -1.72, p = 0.09, d = -0.46) and Digit span (t[55] = -1.86, p = 0.07, d = -0.50) showed a slight trend toward significance (see Table 4). In contrast, when evaluating these results utilizing the Bonferroni Correction ($\alpha = 0.003$), calculated by dividing the number of tests analyzed by 0.05, results revealed that none of the cognitive domains or indices were related to treatment completion (see Table 5 and Table 6). A Mann-Whitney U Test was conducted to evaluate if there were significant differences between treatment completers and non-completers at baseline for the variables that failed tests of normality; there was no statistically significant differences for the Immediate Memory Index (p = 0.22) or the Picture Naming subtest (p = 0.50).

Table 5. Independent Samples *t*-Test Comparing Cognitive Performance in Cognitive Domains among Those Who Did and Did Not Complete Treatment.

	Treatment Completion	Mean	SD	*t*	*df*	*p*	Cohen's *d*	Post-Hoc Power
Immediate Memory Index [a]		--	--	--	--	--	--	--
Visuospatial Index	Yes	85.9	17.1	0.3	55	0.77	0.08	0.06
	No	87.4	16.5					
Language Index	Yes	96.0	11.9	-0.2	55	0.82	-0.06	0.05
	No	95.2	10.4					
Attention Index	Yes	97.3	15.7	-2.0	55	0.05*	-0.54	0.41
	No	87.1	18.8					
Delayed Memory	Yes	93.9	13.3	-1.5	55	0.14	-0.41	0.26
Index	No	87.2	17.0					
Total Scale	Yes	90.8	12.5	-1.4	55	0.15	-0.40	0.25
Index	No	84.9	15.4					

[a] Log Transformation applied to denoted variable and found unsuccessful. Log Transformation applied to denoted variable and found to be unsuccessful. Variable precluded from subsequent analysis.

*p < .05. ** p < .003 based on Bonferroni correction.

Table 6. Independent Samples *t*-Test Comparing Performances in Individual Subtests among Those Who Did and Did Not Complete Treatment.

	Treatment Completion	Mean	SD	*t*	*df*	*p*	Cohen's *d*	Post-Hoc Power
List Learning	Yes	-0.5	1.1	-1.0	55	0.32	-0.27	0.14
	No	-0.9	-0.5					
Story Memory	Yes	-0.2	1.0	-0.9	55	0.37	-0.24	0.12
	No	-0.6	1.3					
Figure Copy	Yes	-1.8	1.8	0.4	55	0.72	0.10	0.06
	No	-1.6	1.8					
Line Orientation [a]	Yes	0.4	0.2	-0.1	55	0.91	-0.03	0.05
	No	0.3	0.2					
Picture Naming [b]	--	--	--	--	--	--	--	--
	--	--	--					
Semantic Fluency	Yes	-0.1	1.3	-0.9	55	0.37	-0.24	0.12
	No	-0.4	1.1					
Digit Span	Yes	0.1	1.1	-1.9	55	0.07	-0.50	0.36
	No	-0.5	1.0					
Coding	Yes	-0.2	1.2	-1.7	55	0.09	-0.46	0.31
	No	-0.8	1.4					
List Recall	Yes	-0.4	1.1	-0.0	55	0.97	-0.01	0.05
	No	-0.4	1.1					
List Recognition [a]	Yes	0.2	0.2	1.5	55	0.15	0.39	0.24
	No	0.3	0.3					
Story Recall	Yes	-0.3	1.2	-1.1	55	0.27	-0.30	0.16
	No	-0.7	1.5					
Figure Recall	Yes	-0.7	1.0	-0.5	55	0.60	0.28	0.15
	No	-0.9	1.4					

[a] Log Transformation applied to denoted variable.
[b] Log Transformation applied to denoted variable and found to be unsuccessful. Variable precluded from subsequent analysis.
*$p < .01$. **$p < .003$ based on Bonferroni Correction.

Subtest and Index scores were transformed into dichotomous variables (i.e., categorized as impaired [z <= -1.38] or intact [z => -1.37]). Subsequently, three Binary Logistic Regressions were conducted, ensuring independence of observations (i.e., immediate and delayed domains, overall indices), evaluating effects of baseline cognitive functioning on treatment completion. The data was reviewed and met all assumptions

necessary to conduct binary logistic regressions. The binary logistic regression model was statistically significant for the total scale, $X^2(1) = 2.884$, $p < 0.05$. In contrast, the individual indices and subtests remained statistically non-significant (see Table 7). Of note, when these results were evaluated utilizing the Bonferroni Correction ($\alpha = 0.0028$), none of the variables was statistically significant, suggesting that baseline cognitive performance was not associated with treatment completion.

Table 7. Results of Binary Logistic Regression Predicting Treatment Completion from Performance on Individual Subtests and Overall Indices.

				95% CI	
	Wald	OR	*p*-value	Lower	Upper
Immediate Memory Index	**0.18**	**1.40**	**0.67**	**-2.34**	**3.28**
List Learning	0.01	1.10	0.91	-35.64	2.45
Story Memory	0.49	0.39	0.48	-76.50	23.41
Visuospatial Index	**0.59**	**0.59**	**0.44**	**-3.47**	**1.09**
Figure Copy	0.38	0.87	0.85	-19.97	1.62
Line Orientation	1.77	0.13	0.18	-70.47	1.05
Language Index	**0.12**	**0.65**	**0.73**	**-22.21**	**3.10**
Semantic Fluency	0.32	1.72	0.57	-22.55	35.74
Picture Naming	0.96	2.78	0.33	-19.48	36.68
Attention Index	**0.58**	**1.84**	**0.45**	**-2.34**	**3.28**
Digit Span	0.37	1.86	0.54	-40.04	39.42
Coding	1.93	4.49	0.17	-22.28	72.71
Delayed Memory Index	**-0.02**	**-0.14**	**1.00**	**3.48**	**2.19**
List Recall	0.00	0.97	0.98	-20.75	2.17
List Recognition	0.42	0.83	0.84	-20.88	1.89
Story Recall	2.38	3.13	0.12	-0.35	3.06
Figure Recall	2.20	2.71	0.14	-0.62	3.20
Total Scale	**3.94**	**3.86**	**0.04***	**-0.23**	**2.88**

*$p < .05$. **$p < .0028$ based on Bonferroni correction.

In order to determine if engaging in previous alcohol treatment, indicative of multiple relapses, influences cognitive functioning, two ANCOVAs were computed. Results revealed that when controlling for gender, years of education, and ethnicity,

previous treatment enrollment, indicative of previous relapse, was not significantly associated with subsequent cognitive impairments for any subtests or indices (see Table 8 and Table 9). A Mann-Whitney U Test also revealed that previous relapse was not significantly associated with cognitive impairments for the Immediate Memory Index ($p = 0.76$) or the Picture Naming subtest ($p = 0.46$).

Table 8. Analysis of Covariance (ANCOVA) Testing Mean Differences in Baseline Cognitive Functioning Between Individuals Who Did and Did Not Attend Previous Alcohol Treatment, Controlling for Ethnicity, Education, and Gender.

	Previous Treatment					
	Yes (n = 30)	No (n = 27)				
	M (SD)	*M (SD)*	$F(1, 55)$	p-value	Partial η^2	Post-Hoc Power
Immediate Memory Index [b]	--	--	--	--	--	--
List Learning	-0.41 (1.16)	-0.87 (1.10)	0.05	0.83	0.00	0.05
Story Memory	-0.40 (1.26)	-0.27 (0.86)	0.13	0.72	0.01	0.12
Visuospatial Index	**88.10 (18.31)**	**84.19 (15.11)**	**0.89**	**0.36**	**0.06**	**0.47**
Figure Copy	-1.64 (1.89)	-1.90 (1.60)	0.12	0.74	0.01	0.12
Line Orientation [a]	0.32 (0.22)	0.37 (0.21)	0.05	0.83	0.00	0.05
Language Index	**97.32 (9.44)**	**94.15 (13.38)**	**0.77**	**0.39**	**0.05**	**0.40**
Semantic Fluency	-0.01 (1.27)	-0.34 (1.24)	0.07	0.80	0.01	0.12
Picture Naming [b]	--	--	--	--	--	--
Attention Index	**94.47 (17.83)**	**95.19 (16.22)**	**1.41**	**0.25**	**0.09**	**0.64**
Digit Span	-0.11 (1.20)	-0.07 (1.06)	0.89	0.36	0.06	0.47
Coding	-0.44 (1.19)	-0.25 (1.34)	0.52	0.28	0.03	0.26
Delayed Memory Index	**94.50 (14.93)**	**89.70 (13.70)**	**0.32**	**0.58**	**0.02**	**0.18**
List Recall	-0.63 (1.22)	-0.53 (1.04)	1.06	0.18	0.12	0.78
List Recognition [a]	0.17 (0.25)	0.24 (0.25)	0.02	0.90	0.00	0.05
Story Recall	-0.52 (1.39)	-0.29 (1.15)	0.80	0.39	0.05	0.40
Figure Recall	-0.63 (1.22)	-0.89 (0.99)	0.62	0.44	0.04	0.33
Total Scale	**91.27 (14.73)**	**87.26 (11.63)**	**0.24**	**0.63**	**0.02**	**0.18**

[a] Log Transformation applied to denoted variable.

[b] Log Transformation applied to denoted variable and found to be unsuccessful. Variable precluded from subsequent analysis.

Table 9. Results of ANCOVAs Testing Mean Differences in Post-treatment Cognitive Functioning between Individuals who Did and Did Not Attend Previous Alcohol Treatment, Controlling for Ethnicity, Education, and Gender.

	Previous Treatment					
	Yes (n = 9)	No (n = 11)				
	M (SD)	*M (SD)*	$F(1, 18)$	p-value	Partial η^2	Post-Hoc Power
Immediate Memory Index [b]	--	--	--	--	--	--
List Learning	-0.05 (0.79)	0.21 (0.78)	1.54	0.23	0.09	0.26
Story Memory	0.18 (0.51)	0.19 (0.66)	0.09	0.77	0.01	0.07
Visuospatial Index	**92.33 (18.36)**	**93.36 (18.40)**	**0.00**	**0.95**	**0.00**	**0.05**
Figure Copy	-1.64 (2.11)	-1.50 (1.94)	0.02	0.88	0.00	0.05
Line Orientation [a]	0.29 (0.12)	0.29 (1.99)	0.55	0.47	0.04	0.14
Language Index	**97.56 (10.17)**	**97.91 (14.41)**	**0.07**	**0.79**	**0.01**	**0.07**
Semantic Fluency	-0.13 (1.06)	0.09 (1.42)	0.26	0.62	0.02	0.09
Picture Naming [b]	--	--	--	--	--	--
Attention Index	**104.00 (11.81)**	**101.18 (12.34)**	**0.05**	**0.86**	**0.00**	**0.05**
Digit Span	0.06 (1.14)	0.01(0.96)	0.04	0.84	0.00	0.05
Coding	0.43 (1.17)	0.00 (1.17)	0.59	0.45	0.04	0.14
Delayed Memory Index	**99.78 (15.41)**	**99.73 (9.84)**	**0.03**	**0.86**	**0.00**	**0.05**
List Recall	-0.15 (1.51)	0.15 (0.63)	0.47	0.50	0.03	0.11
List Recognition [a]	0.22 (0.20)	0.26 (0.28)	0.00	0.98	0.00	0.05
Story Recall	0.29 (0.52)	0.31 (0.80)	0.01	0.94	0.00	0.05
Figure Recall	-1.17 (1.52)	0.24 (0.88)	0.43	0.52	0.03	0.11
Total Scale	**98.11 (10.09)**	**98.27 (13.06)**	**0.07**	**0.80**	**0.00**	**0.05**

[a] Log Transformation applied to denoted variable.

[b] Log Transformation applied to denoted variable and found to be unsuccessful. Variable precluded from subsequent analysis.

CHAPTER FOUR

DISCUSSION

Alcohol consumption, and certainly AUD, has been found to be significantly related to subsequent cognitive impairments. Recovery from AUD has also been associated with improvements in cognitive functioning. Our hypothesis that patients receiving intensive outpatient treatment for an AUD would experience improvements in cognitive function was partially supported by the current study results. Specifically, the overall Total Scale on the RBANS improved by the end of treatment. Further, the Language Index score also improved at follow-up, though this was not hypothesized. Additional scores in the Index of Attention, and the subtests of Story Learning, Figure Copy, Semantic Fluency, Digit Span, and Coding were no longer significant after correction for multiple comparisons. However, given the small power and the utilization of Bonferroni correction, these results may reflect a Type II error, or retaining the null hypothesis when it should be rejected. This can be assessed by interpreting the effect sizes of these variables, to evaluate if the improvement in scores is due to a statistical relationship, or by chance. The effect sizes for the variables in question show that they explain 21-52% of the variance in the analyses, suggesting that these values may be significant (prior to correction) beyond the influence of chance. Additionally, a retroactive power analysis suggested that there was insufficient power to detect true changes in List Learning, Visuospatial index, Line orientation, Delayed Recall, List Recall, List Recognition, Story Recall, and Figure Recall. Therefore, increasing power may uncover increased improvements in cognitive functioning, across subtests and

domains, after successful completion of outpatient treatment. Importantly, increasing the sample size may provide additional power to detect if truly significant effect exists.

Improvements in cognitive functioning with abstinence have been found to be largely variable depending on factors of length of abstinence and patient demographics (e.g., age, SES, Veteran Affairs). Specifically, within the first two weeks of abstinence, impairments remain within all cognitive domains (Fein, Bachman, Fisher, & Davenport, 1990), while at five weeks of abstinence, there are improvements in all domains with the exception of verbal short-term memory (Mann, Gunther, Stetter, Ackeramann, 1999). Within the first two months of detoxification, impairments within visuospatial processing (Fein, Backman, Fisher, & Davenport, 1990) and verbal learning remained (Bell, Vissicchio, & Weinstein, 2016). Furthermore, it has been noted that many individuals exhibit at least partial recovery from their impairments (Bates, Buckman, & Nguyen, 2013). Notably, our results represent some variation compared to that of other studies, in that by the end of approximately three weeks, our sample was showing improvements on Language and overall cognitive functioning.

Our second hypothesis that baseline cognitive deficits would be more severe for those who dropped out of treatment compared to treatment completers was not supported, as the baseline cognitive differences were not significant after correcting for multiple comparisons. However, the effect size for the Index of Attention, suggests there may be a relationship beyond that of chance that was not detected due to insufficient power. This effect size suggests that those who previously dropped out of treatment had poorer performance on measures of Attention. When the sample was dichotomized into groups

of impaired and intact cognitive functioning across all indices, results were similarly insignificant after applying a Bonferroni correction.

Our final hypothesis that previous AUD treatment, indicative of previous relapse, would be associated with poor cognitive functioning across treatment (beginning and end of treatment) was not supported. Research has indicated that cognitive impairments will reappear with relapse (Dominguez-Salas, Diaz-Batanero, Lozano-Rojas, & Verdejo-Garcia, 2016; Duka, Townshend, Collier, & Stephens, 2003; Pitel et al., 2009), and may even be worse than the patients' own baseline level of performance (Pitel et al., 2009). Notably, the sample utilized resulted in low power, based on post-hoc power analyses, reducing our ability to determine if the engagement in previous treatment multiple times reduces cognitive functioning beyond that of consistent alcohol use.

After correcting for multiple comparisons, findings suggest that patients engaged in intensive outpatient treatment for an AUD will experience general improvements in language and overall cognitive functioning within the three weeks of treatment or sobriety, but may not experience significant changes in other specific domains of cognition, such as memory or attention. This corroborates previous research by Fein, Bachman, Fisher, and Davenport (1990) indicating that regardless of the intensity of treatment, patients may require a greater period of sobriety to experience improvements in cognitive functioning. Additionally, given the low power available, it is difficult to determine if these results suggest that cognitive impairments are related to patient's tendency to prematurely drop-out of treatment. Finally, given the negative affect of numerous alcohol relapses, it is important to evaluate cognitive functioning in patients experiencing difficulties in their recovery. The results in this study were not suggestive of

worse cognitive functioning when compared to other patients engaging in their first treatment program. Again, given the reduced power utilized in this study, it is difficult to determine if it is recurrent struggles with AUD, or an AUD in and of itself, that are related to cognitive impairments.

It must be noted that there are some limitations to this study. The small number of participants raises some questions with regard to power and significance, and prevents true results from being extrapolated. Additionally, the assessment battery selected for this study, while time efficient and appropriately brief to fit within the daily patient schedule in treatment, exhibits a potential weakness for utilization in the AUD population. Particularly, it does not contain a measure of executive functioning, which has been found to be significantly influenced by significant alcohol use. Additionally, while the RBANS has been found to have good validity and reliability, particularly as a screening battery for dementia (Green, Sinclair, Rodgers, Birks, & Lincoln, 2013; Gold, Queern, Iannone, & Buchanan, 1999; McKay, Casey, Wetheimer, & Fichtenberg 2006; Mooney et al., 2007; Wilk et al., 2004), it may not be viable for the unique pattern of cognitive performances exhibited within the AUD population. The AUD cognitive and neurological profile are not suggestive of permanent neurological damage (e.g., Traumatic brain injury, stroke, or neurodegenerative disease), which the RBANS has been found to have sufficient power to identify. Finally, this research fails to track individuals following the completion of their treatment, and thus misses the potential for subsequent recovery of their cognitive functioning in the long-term.

Overall, there were improvements in language and global cognitive functioning for those who completed the intensive outpatient alcohol program. With increased sample

size, additional cognitive domains and subtests (e.g., attention, story learning, figure copy, semantic fluency, digit span, coding) may have displayed significant effects. Nevertheless, the current study does suggest that intensive outpatient alcohol program can help ameliorate at least some of the cognitive consequences associated with alcohol use disorder.

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