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The Effects of Comorbid Mild Traumatic Brain Injury and Alcohol Use Disorder

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The Effects of Comorbid Mild Traumatic

Brain Injury and Alcohol Use Disorder

by

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THE EFFECTS OF COMORBID MILD TRAUMATIC BRAIN INJURY AND ALCOHOL USE DISORDER

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ABSTRACT

Title: The Effects of Comorbid Mild Traumatic Brain Injury and Alcohol Use Disorder

Objective: Sustaining a mild traumatic brain injury (mTBI) may influence alcohol consumption. The current study investigated the impact of self-reported mTBIs on alcohol use in a sample of individuals with alcohol use disorder (AUD) or a history of seeking treatment.

Participants and Methods: 173 individuals recruited for a neuroimaging/genetic study of alcohol abuse completed the Alcohol Use Disorders Identification Test (AUDIT) to assess consequences of consumption, and the Time Line Follow-back to assess average drinks per drinking day (DPDD). The Rivermead Concussion Scale was completed for each injury reported. The effects of the number of mTBIs (0,1, more than one) were assessed. A more detailed analysis of the effects of mTBI including information on injury recency and severity, was performed for the most recent injury reported.

Results: 60.7% of individuals reported a history of at least one mTBI and some had up to four prior injuries. The number of reported mTBIs did not affect AUDIT scores ($p = .410$) or TLFB-DPDD ($p = .172$). For the most recent injury, a significant interaction effect for remoteness by severity was found for TLFB-DPDD ($p = .010$) but not for AUDIT ($p = .270$).

Conclusions: Individuals with more recent and more severe mTBIs, were found to consume more drinks per drinking day than individuals with more remote and less severe mTBIs. In contrast, it was found that injury severity and injury remoteness were not linked to harmful or hazardous drinking as measured by the AUDIT.

Keywords: Traumatic Brain Injury, Brain Injury, Alcohol Use Disorder

TABLE OF CONTENTS

LIST OF TABLES

Chapter 1

Introduction

There is compelling evidence that a relationship exists between traumatic brain injury (TBI) and substance use (Bombardier et al., 2002; Bjork and Grant, 2009; Olson-Madden et al., 2012). The most commonly reported observations concern the risk of sustaining a TBI and the possible impact of intoxication at the time of injury. Thus, individuals with alcohol and drug intoxication, or with a diagnosis of substance use disorder (SUD) are at an increased risk of being involved in accidents and sustaining a TBI. Further, alcohol intoxication may mediate the biological effects of injury (Bjork and Grant, 2009, Pandit et al., 2014). In contrast, the current report asks a different, yet clinically relevant question: how does a history of mild TBI (mTBI) affect drinking behavior?

mTBI Epidemiology and Symptomatology

TBI is a leading cause of morbidity and mortality among young persons in the United States (Raj et al., 2015). It can lead to diverse cognitive impairments, headaches, pain, and chronic traumatic encephalopathy (CTE), as well as an increased risk for developing an affective disorder. TBI severity can range from mild to severe, with the Centers for Disease Control and Prevention (CDC) reporting that approximately 75% of TBIs meet criteria for mTBI (CDC, 2003).

The current definition of TBI from the CDC is “an injury that disrupts the normal function of the brain. It can be caused by a bump, blow, or jolt to the head or a penetrating head injury” (CDC, 2014, p.2). TBIs occur in several different settings

including combat, sports, falls, and motor vehicle accidents. Researchers note that a link exists between repeated mTBIs in young athletes and significant neurodegeneration many years after the athletes retire from play (Karr et al., 2014). This repeated head trauma can perhaps result in CTE, in which the individual exhibits symptoms beginning with attention and memory problems, headaches, and disorientation and then following with the manifestation of lack of insight and overt dementia in cases of progressive deterioration (McKee et al., 2009). The Defense and Veterans Brain Injury Center estimates that in military populations, over 80% of TBIs occur in non-deployed settings (Johnson et al., 2015). A meta-analysis conducted by Carroll et al (2004) determined that the classification of a mTBI is typically based on one or more of the following: loss of consciousness (LOC) for 30 minutes or less, confusion or disorientation after the injury, post traumatic amnesia (PTA) lasting less than 24 hours, a Glasgow Coma Scale (GCS) score of 13-15 for up to 30 minutes after the injury, and the experience of transient neurological abnormalities. Furthermore, these manifestations cannot be the result of other injuries or psychosocial problems, and they are not caused by a penetrating head injury, or the result of drugs/medications/alcohol (Carroll et al., 2004).

In the majority of mTBI cases, cognitive recovery is typically achieved by three months' post injury (Belanger et al., 2005). Similarly, in older adults' findings indicate that at three months' post injury, the risk of poor cognitive performance is largely accounted for by their predisposition for injury due to older age (Kinsella et al., 2014). Research on cognitive and physical recovery immediately following mTBI, specifically "return to learn" and "return to play" policies, indicates that strict cognitive rest may not be beneficial in the long term for patient recovery, which runs contrary to popular belief

(Buckley et al., 2016). Notably, in a randomized control study examining rest strategies in adolescent patients following acute mTBI, Thomas et al. (2015) found that strict rest did not improve neurocognitive, balance, and symptom outcomes when compared with usual care. For the purpose of this study, strict rest was defined as no work, school, or physical activity for five days followed by a stepwise return to these activities. Furthermore, patients assigned to the strict rest intervention overall reported more symptoms than did those in the control condition (Thomas et al., 2015). Similarly, Buckley et al. (2016) found that when comparing patients in a one day "rest-day" condition with those with no-rest, the no-rest group was asymptomatic significantly sooner than the rest day group.

There appears to be a worse prognosis for those who sustain recurrent TBIs. In a population of deployed military personal it was found than with increasing number of mTBIs participants endorsed significantly higher symptom severities on measures of depression, PTSD, and TBI symptom severity. Further, participants also endorsed an increase in lifetime suicidal thoughts or behaviors following multiple mTBIs (Bryan and Clemans, 2013). An increased risk for clinical depression following recurrent TBIs has also been shown in a sample of retired professional football players (Guskiewicz et al., 2007). For college football players, a dose response relationship appears to be evident between number of TBIs and likelihood of sustaining a subsequent TBI. When compared with football players with no prior history of TBIs, players who had a history of three or more TBIs were three times more likely to sustain a TBI over the following football season. Further, individuals with recurrent TBIs had overall slower TBI symptom recovery compared with individuals with fewer TBIs (Guskiewicz et al., 2003). These

findings raise the question of how to measure overall TBI impact to better quantify the physical, emotional, and cognitive symptoms associated with TBIs. In addition to the number of mTBI incidents, the severity and recency of each injury may also contribute to clinical status.

The prevalence rate of persistent cognitive, physical and emotional symptoms has been documented to range from 7-8% to 10-20% and as high as 33% (Belanger et al., 2005). A meta-analysis (Belanger et al., 2005) concluded that within the first 3 months following a mTBI, individuals experience mild neuropsychological impairment across a number of cognitive domains. More specifically these impairments are most often found in the areas of delayed memory recall and fluency. Following the three-month mark, the meta-analysis provides compelling evidence for little-to-no effect of mTBI on neuropsychological function (Belanger et al., 2005). Another meta-analysis of neuropsychological outcomes following concussions found that the cognitive domain of executive functioning appears to be most sensitive to repeated mTBIs followed by delayed memory (Karr et al., 2014).

The racial groups with the highest rate of death from TBI due to violence were American Indians/Alaskan Natives and African Americans (Hyder et al., 2007). Together these moderating variables point to a number of different factors that further burden this population.

In assessing the relationship between age and TBI incidence, a trimodal distribution was reported by the CDC. In the U.S., males ranging in age from 0 to 4 years old make up the group with the highest rate of TBI emergency department visits, hospitalizations, and death. Females ranging in age from 0 to 4 follow this group. U.S.

males and females between 15 and 19 years of age and males and females over 75 years of age made up the trimodal distribution (Hyder et al., 2017). Of note, older individuals aged 75 years and over comprise the group with the highest proportion of TBI related hospitalizations and deaths. Falls are the leading cause of TBI in this age population. Road traffic incidences are responsible for highest number of hospitalizations due to TBIs and this accounts for about 20% of all TBIs (Hyder et al., 2007).

Alcohol as a risk factor

Alcohol intoxication is a known risk factor for many injuries and the literature suggests that it is frequently associated with head injury (Pandit et al., 2014). Corrigan (1995) was one of the first researchers to compile the literature on substance abuse rates in individuals with TBI. He determined that between one-third and one-half of individuals hospitalized for TBI were under the influence of alcohol at the time of their injury. Further, between 50% and 66% of individuals with a TBI had a history of alcohol use or other drug use. Of note, these results did not come from rehabilitation studies as few had been completed at the time of the review (Corrigan, 1995). Current research suggests that approximately half of all individuals who sustain a TBI are under the influence of alcohol at the time of their injury (Raj et al., 2015). Further, the alcohol literature points to the deleterious effect of sustained alcohol abuse on the brain in cognitive domains (Oscar-Berman and Marinković, 2007). Brain structural abnormalities in gray and white matter are also apparent in neuroimaging studies of individuals with alcohol use disorder (Ruiz et al., 2012; Monnig et al., 2012).

In a Norwegian study of substance use and TBI they found that almost half of the patients were under the influence of intoxicating substances at the time of their admission to the hospital (Andelic et al., 2010). Substance use at the time of hospital admission was found to be more frequent in patients with mTBI due to sports accidents, falls and violence as compared to more severe injuries. Further the patient's pre-injury substance use was found to increase the probability of a more severe injury to the brain, which were often the result of falls and motor vehicle accidents (Andelic et al., 2010).

In a recent study conducted by Raj et al., (2015), the authors examined the effect of positive blood alcohol concentration (BAC) on patient outcomes after a TBI for those patients who were treated in the intensive care unit. The authors did not report the severity of the TBIs in this study. With a sample of just over 400 patients with TBI, the authors utilized two outcome measures, six-month mortality and six-month neurological outcome (as measured by the Glasgow Outcome Scale (GOS) (Raj et al., 2015). The GOS, while being a commonly used scale for assessing outcome after TBI, has a few important limitations. The GOS is usually unstructured, determined after a short interview, and does not follow a specific written protocol. These limitations can result in achieving only a gross understanding of outcome, which is more appropriate for moderate to severe TBI (Wilson et al., 1998). Low BAC (< 2.3%) at the time of hospital admission was shown independently to reduce risk of six-month mortality in this patient population. A trend toward better long-term neurological outcomes was also found in patients with a positive BAC, though this value did not reach significance (Raj et al., 2015). Similarly, a study conducted by Pandit et al., (2014) found that in patients with

TBI, alcohol intoxication was found to be an independent predictor of mortality, and further, that alcohol was associated with higher complication rates.

Alcohol's Possible Neuroprotective Effect: Acute Intoxication

The effect of alcohol intoxication at the time of injury on overall outcome after a TBI has been extensively studied. Unfortunately, no consensus has emerged. Inconsistent findings arise for a number of different reasons (see Li et al., 1997). Evidence from laboratory and animal studies suggests that alcohol may have a neuroprotective effect on the brain following a TBI (Goodman et al., 2013). Goodman et al. (2013) investigated pre-injury alcohol exposure using an animal model. They proposed that ethanol treatment prior to a TBI might deliver neuroprotection by lessening the local neuroinflammatory response to the traumatic injury. Mice were given either ethanol or water and then an hour later the anesthetized mice received either a blunt TBI using a weight drop or a sham injury where the mice were anesthetized but were not subjected to a TBI. The weight drop induced a moderately severe closed head injury that did not lead to an extra-axial hemorrhage or a skull fracture. Both cohorts then completed an acute neurological evaluation via the righting reflex response (RRR) task. In this task, the animal is placed in a supine position immediately after injury and the animal has to right itself to a prone position consecutively three times. The authors found that neurologic recovery as measured by the RRR was slower in the mice treated with ethanol compared with mice treated with water. Mice in the water and TBI condition experienced a fifteen-fold increase in time compared with the water and sham condition. Mice that were subjected

to both the alcohol and TBI condition had a four-fold increase in RRR time compared to the ethanol and sham condition. Mice that were given alcohol prior to the TBI could right themselves faster than mice that were given water prior to the TBI. The authors also assessed posttraumatic systemic inflammatory response. Specifically, they found in mice that were given ethanol pretreatment, there was a significant reduction of serum 1L-6 by ethanol pretreatment. In contrast, after water pre-treatment, a TBI induced an increase of cytokine serum 1L-6 and serum KC levels that peaked at 3 hours post TBI and maintained serum level elevations at 24 hours post TBI. The authors concluded that in their model, ethanol intoxication before a TBI leads to a reduction in the local neuroinflammatory response to an injury. These results provide evidence for the possible neuroprotective effect of alcohol and the authors propose that acutely intoxicated individuals may experience improved clinical outcomes due to the decreased inflammatory and neurologic burden of the TBI (Goodman et al., 2013).

Laboratory and animal studies suggest a few different mechanisms behind alcohol's neuroprotective effect on the brain after injury. These mechanisms include inhibition of the N-methyl-D-aspartate (NMDA) receptor-mediated excitotoxicity (Cebere et al., 2003; Sönmez et al., 2015), attenuation of TBI induced hyperthermia (Taylor et al., 2002), and suppression of the production of pro-inflammatory cytokines released following injury (Gottesfeld et al., 2012). Thus, while alcohol may be a neuroprotective factor, the increased mortality due in part to an increased risk of TBI incidence is an important component to be aware of as well as the time frame of alcohol use (Chen et al., 2012).

History of Abuse

A history of chronic alcohol abuse or alcohol dependence preceding a TBI is associated with a number of poor outcomes including mortality, increased risk for mass lesions, and subsequent injury (Ruff et al., 1990; Kelly et al., 1997). Pre-injury chronic alcohol use is also known to be higher for individuals with TBI when compared to the general population (O'Dell et al., 2012). Approximately one half to two thirds of individuals who have sustained a TBI have a history of prior heavy alcohol use (O'Dell et al., 2012). Further, about half of all individuals in inpatient rehabilitation for a TBI report having a history of alcohol related issues (Bombardier et al., 2002).

Jorge et al. (2005) examined the relationship between alcohol abuse or alcohol dependence and mood disorders in individuals who had sustained TBIs. Their sample consisted of 158 individuals with closed head injuries, 98 of whom were determined to have moderate to severe injuries and 60 who had a mTBI. The participants in their sample were recruited from a hospital and a trauma center. Individuals who developed mood disorders in the year following a TBI were significantly more likely to have had a history of alcohol abuse or alcohol dependence. Further, the authors found that among those that had a history of abuse or dependence, MRI neuroimaging data showed significantly reduced frontal gray matter volumes compared with individuals who did not have a history of abuse or dependence. Neuroimaging also revealed that individuals who resumed alcohol abuse after their TBI showed decreased medial frontal gray matter volumes as well as poorer performance on tasks of executive functioning (Jorge et al., 2005).

Ponsford et al. (2013) examined the relationship between pre-injury alcohol use, post-injury/current alcohol use, and post-injury cognitive functioning. Their study sample consisted of 50 individuals over the age of 18 who had sustained a TBI that ranged from complicated mild to severe. Participants in this sample were recruited to participate in a brief alcohol intervention. The severity rating was based on posttraumatic amnesia (PTA) duration as measured by the Westmead PTA scale. Of those who participated in the study, the mean PTA duration was 13.34 days. Approximately 40% of individuals had a PTA duration between 1 and 7 days, and 53% of participants had a PTA duration between 8 and 28 days. The remaining participants had a PTA duration longer than 28 days (Ponsford et al., 2013). Pre-injury alcohol use was assessed using the Alcohol Use Disorders Identification Test (AUDIT) and post-injury/current alcohol use across a variety of domains. Processing speed and attention were assessed using the Symbol Digit Modalities Test (SDMT) and post-injury cognitive functioning was assessed using the California Verbal Learning Test (CVLT-II) and the Modified Six Elements Test (MSET) (Ponsford et al., 2013). The authors hypothesized that harmful levels of alcohol consumption as measured by the AUDIT in the year prior to the TBI, as well as harmful post-injury levels of alcohol in the month before follow-up, would each be related to poorer measures on cognitive functioning assessments. Results supported the hypotheses. Harmful alcohol use in the year prior to the TBI was found to be associated with slower processing speed on the SDMT as well as poorer memory on the CVLT-II. Further, once the authors controlled for pre-injury drinking, evidence for post-injury alcohol use on the Time-Line Follow-Back (TLFB) was associated with poorer executive functioning on the MSET completed 6 to 9 months post-injury. These conclusions lend support for the

theory that post-injury alcohol consumption may be detrimental to cognition (Ponsford et al., 2013). Though, it should be noted that the results of this study came from a mixed sample in terms of severity, and the specific results for TBI, the most common injury type, were not isolated.

Post-injury Alcohol Use

Studies tend to show that post-injury alcohol and other substance use rates are lower than pre-injury rates for the first year. Post-injury alcohol use is typically assessed using the AUDIT or the TLFB (Ponsford et al., 2007; Ponsford et al., 2013). In accordance with the literature we will measure post-injury alcohol use using the AUDIT and TLFB-DPDD.

Bombardier et al. (2003) examined changes in drinking prior to a TBI compared to one year following the TBI. Participants were recruited from a sample of patients admitted to the hospital with an acute TBI. Their results showed that alcohol-related problems were less frequent post-injury than pre-injury. Further, in their population, abstinence rates increased from 14% to 36% and the proportion of individuals who did not report significant problems related to alcohol increased from 64% to 84%. No significant alcohol problems (or abstinence) were reported in between 13% and 32% of individuals (Bombardier et al., 2003).

Ponsford et al., (2007) examined individuals with premorbid alcohol and drug use who were given rehabilitation after a moderate to severe TBI. Their results showed that 32.4% of individuals in their sample were drinking at high levels prior to the TBI as measured by the AUDIT and 9% of individuals reported a drug problem. This study

utilized a longitudinal approach and measured individuals at one and two-year time points post-injury. Individuals in the study were instructed to abstain from alcohol or drug use for 12 months post-injury, and indeed, results showed a decline in alcohol and drug use in the 12 months post-injury. Of note, only 30% abstained from alcohol in the first year following the injury and 17.4% of individuals were consuming alcohol at a hazardous level. Measures taken at two years post-injury showed a reduction in those abstaining to 21.4% and an increase in hazardous drinking levels to 25.4%. Similarly, drug and alcohol use increased two years post-injury (Ponsford et al., 2007). Adams et al. (2013) found that in individuals who sustained a TBI with loss of consciousness greater than 20 minutes, this was significantly associated with negative drinking related consequences. This finding was independent of binge drinking, combat exposure, posttraumatic stress disorder diagnosis, or demographics (Adams et al., 2013). Clearly, the combination of alcohol use and TBI may lead to a number of negative outcomes.

Moderating variables

It is important to consider factors that may moderate the relationship between substance abuse and mTBI. Males are one and half times more likely than females to sustain a TBI over the course of their lifetime (Hyder et al., 2007). Females sustain approximately one third of all TBIs (Toor et al., 2015). The literature suggests that women with a TBI, when compared with age-matched controls without a TBI, experience more post-partum difficulties, amenorrhea and are more often have fewer children. Furthermore, women who have sustained a TBI when compared with men who have sustained a TBI report experiencing more cognitive, emotional, and somatic difficulties

(Toor et al., 2015). In their study, Toor et al., (2015) examined long-term health outcomes in women who had sustained a moderate or severe TBI and found that women with a TBI had greater odds of being unmarried or partnered after an injury than women who had not sustained a TBI. Women with a TBI were also more likely to be living alone.

Another important moderating factor to look at when examining this body of literature is the research setting. The studies presented thus far occurred in a variety of different research settings including hospital emergency departments (Dikmen et al., 1995), inpatient rehabilitation centers (Ponsford et al., 2007; Jorge et al., 2005), as well as from hospital admissions (Andelic et al. 2010) and intensive care unit admissions (Raj et al., 2015). The variety of research settings may influence participant selection criteria and in turn impact results. Ideally, it is important to collect date from different types of sites to aid in generalizability of findings.

Summary

The literature clearly reveals that shortly after a mTBI an individual experiences physical, cognitive and emotional symptoms. These symptoms seem to be present for up to three months and then remit in the majority of TBI cases; in a small percentage symptoms do not remit and the individual experiences persistent problems. Furthermore, the presence of alcohol at the time of the injury and the presence of alcohol use disorder impacts several domains. Some studies suggest that acute alcohol intoxication is a neuroprotective factor while others argue that the high correlation between alcohol use and TBI is reason enough to show alcohol as detrimental to the post injury recovery. The

literature also supports the theory that post-injury alcohol consumption may be detrimental to cognition. Though post-injury alcohol and other substance use rates in samples with a range of alcohol consumption levels tend to be lower than pre-injury rates for the first year following an injury for individuals with more moderate to severe injuries.

Chapter 2

Methodology

Hypotheses

The current study sought to address relationships between alcohol consumption and alcohol problems and a history of mTBI, within a large existing data set collected via the Mind Research Network (see Claus et al., 2011a). This data set contains results from a study that evaluated alcohol use in heavy drinking, treatment seeking individuals. This large sample is particularly informative because it contains high quality data on alcohol use, as well as detailed mTBI information. Further, the clinical importance of alcohol consumption patterns are greatest in this "heavy drinking" population. We hypothesized that:

1. The number of injuries an individual sustained would be positively correlated with AUDIT scores.
2. The number of injuries an individual sustained would be positively correlated with TLFB-DPDD scores.
3. Among individuals who had sustained an mTBI, specifically, their most recent injury, we hypothesize that more severe and more recent injuries would result in higher AUDIT scores.
4. Among individuals who had sustained an mTBI, specifically, their most recent injury, we hypothesize that more severe and more recent injuries would result in higher TLFB-DPDD scores.

Participants

173 individuals (113 males; 65.3%) between the ages of 21 and 56 participated in the present study (see Claus et al., 2011a). Participants were recruited from the greater Albuquerque metropolitan area via radio advertisements, local print advertisements, and online media advertisements to participate in either of the two alcohol studies. To participate in either the treatment seeking or non-treatment seeking studies, participants had to endorse drinking at least 5 or more drinks per drinking occasion for men and 4 or more for women, for at least five times in the past month. Exclusion criteria were met if participants reported prior severe brain injury or a history of severe alcohol withdrawal. All participants were required to have a breath alcohol concentration of 0.00 tested using a breathalyzer before assessment measures were completed. Further, participants were excluded from the study if they were in need of medical detoxification as defined by a score of eight or higher on the Clinical Institute Withdrawal Assessment of Alcohol Scale, Revised (CIWA-Ar; Sullivan et al., 1989).

Measures

Participants completed a demographic questionnaire.

Alcohol and drug use

Drinking was assessed using the Alcohol Use Disorders Identification Test (AUDIT) (Babor et al., 2001) and Time-Line Follow Back (TLFB). The AUDIT is a 10-item self-report questionnaire that uses a Likert scale and purports to measure harmful alcohol use and/or hazardous drinking in the 12 months prior. Alcohol misuse is operationalized in

terms of dependence, consumption, and alcohol-related problems (Bryce et al., 2014). A maximum possible score of 40 can be earned and each question is scored from 0 to 4. Typically, a cutoff score of 8 or higher is used to identify hazardous levels of drinking (Saunders et al., 1993). The AUDIT has been recommended as a standard screening tool for the purpose of detecting post injury alcohol use in studies of TBI (Bryce et al., 2014). The TLFB was administered to assess for frequency and quantity of alcohol, marijuana, and cigarettes in the 60 days prior (Sobell and Sobell, 1992).

TBI

TBI incidence was reported using the Post-Head Injury Symptoms Questionnaire that was adapted from the Rivermead Post-Concussion Symptoms Questionnaire (King et al., 1995). A TBI was defined via self-report. The Rivermead Concussion Scale was completed for each injury reported, up to four injuries. A TBI "severity index" was calculated for each injury. Specifically, the severity score was calculated by adding the three dichotomous variables: the presence or absence of loss of consciousness, memory problems, or being dazed and disoriented. Therefore, an individual could receive a score ranging from 0 to 3. A score of zero indicated that the participant did not lose consciousness, did not report memory problems, and did not endorse being dazed or disoriented. A score of three indicated that they endorsed all three symptoms.

Remoteness

mTBI "remoteness" was calculated for each injury. Specifically, the remoteness score was calculated by first subtracting age at the time of the most recent injury from age at

time of testing. This value was then recoded into five clinically relevant levels of remoteness, reflecting the fact that most recent injuries are likely to be much more important than remote injuries. Individuals who sustained a mTBI up to one year prior to testing received a score of five, those who sustained an injury two through four years prior received a score of four, injuries five through ten years prior received a score of three, injuries eleven through twenty years prior received a score of two, and injuries twenty-one through forty-eight years prior received a score of one (see Table 3). Therefore, those with more recent injuries, i.e. in the past year, earned higher scores than did those whose injuries were more remote.

Table 1

Injury Remoteness

Years	Remoteness Score	n
0 - 1	5	18
2 - 4	4	11
5 - 10	3	12
11 - 20	2	25
21 - 48	1	38

Data analysis

Data analysis was conducted using IBM SPSS version 23. Descriptive and frequency statistics were calculated to observe the relationship between TLFB-DPDD and AUDIT scores. To evaluate the relationship between number of injuries and alcohol use in the sample we conducted two general linear models with fixed factors of sex and mTBI group (0,1, more than one), with current age as a covariate, and including interactions of sex and age with group. To examine the effects of an individual's most recent injury we

evaluated the importance of severity and remoteness on alcohol use. We conducted two general linear models with fixed factors of sex, remoteness (1,2,3,4,5), and severity (0,1,2,3), with current age as a covariate, and including all two-way interactions. Post hoc analyses were conducted with all substance use variables for all four general linear models.

Chapter 3

Results

Demographics

The demographics of the study group are presented in Table 2. The 172 individuals who participated in the study included more men than women. The majority identified themselves as White, with Latino being the second most prominent group. A large majority of the individuals reported earning their high school diploma/GED or continuing onto to higher education. The average age was 39.38 years (SD = 8.88). A chi square test of independence was performed to examine the relationship between self-identified white vs. minority status and history vs. no history of one or more mTBI. The relationship was non-significant ($X^2=0.0001, p = .99$). The average age of individuals who sustained zero mTBIs was 38.31 years (SD = 8.53) and the average age of individuals who sustained only one mTBI was 39.38 years (SD = 8.88). Further the average age of individuals who sustained more than one mTBI was 41.27 years (SD = 9.07).

Table 2.

Demographics of each mTBI level

	Zero mTBIs		One mTBI		More than one mTBI	
	n	%	n	%	n	%
Sex						
Male	47	69.10	42	56.80	23	76.70
Female	21	30.90	32	43.20	7	23.30
Race						
White	29	42.60	26	35.10	17	56.70
Minority	39	57.40	45	60.80	12	40.00
Black	2	2.90	3	4.10	0	0
Asian	1	1.50	0	0	0	0
Latino	27	39.70	21	28.40	7	23.30
Native	2	2.90	11	14.90	2	6.70
Mixed	7	10.30	10	13.40	3	10.00
Other	0	0.00	3	4.10	1	3.30
Education						
Less than High School	3	4.40	9	12.50	2	6.8
High school or GED	25	36.80	24	33.30	12	41.40
More than High School	40	58.80	39	54.20	15	51.40

Assessment of TBI

60.5% of individuals reported a history of mTBI. Specifically, 68 individuals (39.50%) did not sustain a mTBI; 74 (43.00%) individuals sustained exactly one mTBI; 30 individuals (17.40%) sustained more than one mTBI. Table 3 summarizes the results of the mTBI assessment.

Table 3

mTBI Group

mTBI Group	n	Percentage
Zero mTBIs	68	39.5
One mTBI	74	43.0
More than one mTBI	30	17.4

Substance Abuse

Tables 4 and 5 summarize the results of the alcohol assessments. For those who did not sustain an mTBI, the average AUDIT total score was 22.48 (SD = 7.20), compared with individuals who had sustained one or more mTBIs whose AUDIT total score was 23.79 (SD = 7.28). For individuals with no history of mTBI their AUDIT total scores ranged from 9 to 38 and for those who sustained one or more mTBIs their AUDIT total scores ranged from 7 to 39. Notably, individuals who sustained more than one mTBI endorsed heavier substance use overall when compared with those who sustained only one or zero mTBIs (see Table 4).

Table 4

Substance Use

Number of mTBIs	DPDD	Heavy Drinking Days	Drink Days	Cigarette Days	Marijuana Days
0	8.38 (4.09)	33.23 (19.32)	41.85 (16.30)	27.27 (28.18)	4.16 (11.65)
1	8.95 (4.96)	33.40 (18.44)	41.66 (15.71)	27.60 (28.59)	3.05 (10.47)
> 1	9.15 (4.36)	39.10 (18.97)	47.33 (13.13)	35.60 (28.51)	7.40 (14.01)

Table 5.

AUDIT, Average drinks per drinking day (DPDD), Cigarettes per day, and Marijuana per day as measured by the Time Line Follow Back measure

		No mTBI			One mTBI			More than one mTBI		
Measure		n	Mean	SD	n	Mean	SD	n	Mean	SD
AUDIT Total Score										
	Male	46	22.11	7.00	41	24.10	5.37	23	24.26	7.46
	Female	21	23.29	7.72	30	23.37	8.56	7	22.29	11.34
	Total	67	22.48	7.20	71	23.79	6.85	30	23.80	8.34
TLFB – DPDD*										
	Male	47	8.96	4.14	41	10.04	5.28	23	9.74	4.51
	Female	21	7.08	3.75	32	7.55	4.20	7	7.23	3.47
	Total	68	8.37	4.09	73	8.95	4.96	30	9.16	4.37
Cigarettes Per Day										
	Male	46	28.09	28.51	41	25.22	28.40	23	38.61	27.39
	Female	21	25.81	28.08	32	30.66	29.00	7	25.71	32.07
	Total	67	27.37	28.18	73	27.60	28.59	30	35.60	28.51
Marijuana Per Day										
	Male	46	4.80	11.37	41	2.90	10.05	23	9.61	15.39
	Female	21	2.76	12.43	32	3.25	11.18	7	0.14	0.38
	Total	67	4.16	11.65	73	3.05	10.47	30	7.40	14.01

*TLFB-DPDD = Timeline Follow Back (Average Drinks Per Drinking Day)

To evaluate the relationship between number of injuries and alcohol use in the sample we conducted two general linear models. For the AUDIT scores we conducted a general linear model with fixed factors of sex and mTBI group (0,1, more than one), with current age as a covariate, and including interactions of sex and age with group. This analysis revealed a non-significant effect for number of injuries grouping ($F(2, 168) = .897$, $p = .410$, partial eta squared = .011). Similarly, for DPDD the same general liner model revealed a non-significant effect for number of injuries grouping ($F(2, 171) = 1.783$, $p = .172$, partial eta squared = .022). Further, the interactions of sex by TBI group and age by TBI group were not significant in either analysis.

Though our specific hypotheses concerned AUDIT and DPDD, exploratory analyses were performed with the other main substance use variables. These variables were examined with four GLM analyses, as described above. For Heavy Drinking Days, a general liner model with fixed factors of sex and mTBI number group, and with age as a covariate, indicated a non-significant effect for number of injuries grouping ($F(2,170) = 1.129$, $p = .326$, partial eta squared = .014). Similar results were found for Drink Days ($F(2,171) = .455$, $p = .635$, partial eta squared = .006), Cigarette Days ($F(2,170) = 1.115$, $p = .331$, partial eta squared = .014), and Marijuana Days ($F(2,170) = .845$, $p = .431$, partial eta squared = .010). Further, the interactions of sex by TBI group and age by TBI group were not significant in any of the four analyses.

Most Recent Injury

Looking only at individual's most recent injury we evaluated the relationship between severity and remoteness and alcohol use. Thus, important clinical details

regarding the injury were systematically evaluated. We conducted two general linear models. For the AUDIT scores, we conducted a general linear model with fixed factors of sex, remoteness (1,2,3,4,5), and severity (0,1,2,3), with current age as a covariate, and including all two-way interactions. This analysis revealed non-significant main effects and a non-significant interaction effect for remoteness by severity ($F(12, 101) = 1.25$, $p = .270$, partial eta squared = .187). For DPDD the same general liner model revealed a significant interaction effect for remoteness by severity ($F(12, 103) = 2.46$, $p = .01$, partial eta squared = .306).

To illustrate simply the nature of the significant DPDD interaction we examined means and parameter estimates. Individuals with the highest remoteness and highest severity drink more drinks per drinking day than do individuals with lower remoteness and lower severity. Specifically, for DPDD the mean score was 15.10 (SD = 6.60) for those individuals with highest remoteness and highest severity and the mean score for lowest remoteness and lowest severity was 7.43 (SD = 1.62).

Exploratory analyses were similarly performed with the other main substance use variables. These variables were examined with four GLM analyses, as described above. For Heavy Drinking Days, a general liner model with fixed factors of sex, remoteness, and severity, with current age as a covariate, and including all two-way interactions revealed a non-significant effect for remoteness by severity ($F(12,103) = .764$, $p = .685$, partial eta squared = .120). Similar results were found for Drink Days ($F(12,103) = .670$, $p = .773$, partial eta squared = .107), Cigarette Days ($F(12,103) = .849$, $p = .601$, partial eta squared = .132), and Marijuana Days ($F(12,103) = .695$, $p = .751$, partial eta squared = .011).

Chapter 4

Discussion

The aim of the present study was to examine the relationship between self-reported mTBIs on alcohol use in a sample of heavy drinkers. Drinking was assessed using the AUDIT and the TLFB-DPDD to examine harmful or hazardous alcohol use over the past year and daily alcohol consumption over the last month. mTBI incidence was measured via self-report using the Rivermead Post-Concussion Symptom Questionnaire for each injury reported. Approximately 60% of individuals in this sample reported a history of one or more mTBI. Specifically, 68 individuals did not sustain an mTBI, 74 individuals sustained exactly one mTBI, and 30 individuals sustained more than one mTBI. The number of prior mTBIs did not affect drinking behaviors. However, follow-up results indicated that individuals with more severe and more recent injuries on average consumed more drinks per drinking day as measured by TLFB-DPDD.

A key feature of our first analysis was a focus on the number of prior mTBIs. Other studies have also explored the importance of number of prior injuries on diverse outcome variables, but results are quite mixed. As previously stated, the literature suggests that there appears to be a worse prognosis for those who sustain recurrent TBIs. In military populations, individuals report increased life-time suicidal thoughts or behaviors as well as higher symptom severities on measures of depression, PTSD, and TBI symptom severity (Bryan and Clemans, 2013). Bryan and Clemans (2013) stratified concussion history based on individuals with no prior injuries, one prior TBI, and more than one prior injuries. Notably, lifetime total number of TBI's in this population ranged from zero to nineteen. Concussion symptom severity was examined by computing a

severity score by summing all symptoms to provide a metric of concussion symptom severity. The authors reported higher symptom severities for those with more TBIs. In retired professional athletes, there appears to be a greater risk for clinical depression and slower symptom recovery with increased number of mTBIs (Guskiewicz et al., 2007). Guskiewicz et al (2007) stratified concussion history based on individuals with no injuries, one or two prior TBI's, and three or more prior injuries. Time since injury or time between injury was not reported, instead the authors reported number of years since retirement.

Other research has examined single or recurrent mTBIs in a population of college athletes. The authors found that while all participants were cleared to return to play 10 days post injury, those who sustained a recurrent mTBI were found to have significantly greater difficulties on a balance restoration measure 30 days post injury compared with participants who sustained one mTBI. The authors posit that behavioral symptom resolution may not be indicative of brain injury resolution (Slobounov et al., 2007). It should be noted that in this study the sample size was very small (nine individuals) and recurrent mTBIs occurred within the year following the first mTBI. These findings raise the question of how to best examine the prior mTBI history as a possible predictive measure. This is especially relevant given that studies vary in number of recurrent mTBIs and time between mTBIs. One could argue that number of injuries may be a rather insensitive metric; instead, one could examine severity of each injury and recency of each injury as a more well-rounded measure for analysis.

Another key feature of the current study was the detailed information on current drinking behavior and drinking consequences. Regarding alcohol assessment as measured

by the AUDIT, for those individuals who did not sustain an mTBI, the average AUDIT total score was 22.48, which is possibly indicative of alcohol dependence (Babor et al., 2011). When examining those individuals who had sustained one mTBI, the average AUDIT total score was 23.79 which may also indicate alcohol dependence. A similar average AUDIT total score of 23.80 was found for individuals who sustained more than one mTBI. With regard to DPDD, for those individuals who did not sustain an mTBI, the average DPDD was 8.37. For those individuals who had sustained one mTBI, the average DPDD was 8.95. Similarly, for individuals who sustained more than one mTBI the average DPDD was 9.16.

To evaluate the relationship between number of injuries and alcohol use in the sample we conducted two general linear models. Number of injuries was classified as zero mTBI, one mTBI, or more than one mTBI. For both AUDIT scores and DPDD, these analyses revealed a non-significant effect for the number of injuries variable. The number of mTBIs sustained did not impact the number of drinks per drinking day or harmful or hazardous drinking behavior in this population. Subsequent analyses of our other main substance use variables were similarly non-significant. Specifically, heavy drinking days, drink days, cigarette days, and marijuana days were not found to be impacted by the number of mTBIs, though fewer individuals used these substances, reducing statistical power. These results point to the limitiations of solely assessing number the number of injuries to make inferences about alcohol symptoms following mTBI.

Looking only at individual's most recent mTBI, we evaluated the relationship between severity and remoteness and alcohol use via two general linear models. No

significant effects were found for AUDIT. Therefore, severity and injury remoteness were not predicative of harmful or hazardous drinking. For DPDD, this analysis revealed a significant interaction effect for remoteness by severity. Individuals who sustained *both* a more severe and a more recent injury drank more than did those with more remote and less severe injuries. It is important to note that neither severity or recency showed a main effect, only the interaction was significant.

To further examine the nature of the significant DPDD interaction we examined means and parameter estimates. Individuals with the highest remoteness scores and highest severity scores drink more drinks per drinking day than do individuals with more remote and less severe injuries. Individuals who sustained mTBIs that were *both* more recent and more severe consumed more drinks per drinking day than do those individuals whose mTBIs were more remote and less severe. Given that the time frame for cognitive recovery from mTBI in most cases is three months' post injury with a percentage of individuals requiring a longer recovery time, it may be that more recent injuries that are more severe are more problematic for the individual (Belanger et al., 2005).

The present study demonstrates that an important factor to consider when examining mTBIs is not the number of injuries but rather the clinical details of the injury, specifically how long ago the injury occurred and the severity of the symptoms. Studies that simply make inferences based on the number of injuries an individual sustained may be missing integral pieces of information when discounting the time since injury and the heterogeneity of symptoms in mTBIs.

Wu et al. (2016) conducted a nationwide population based ten-year cohort study in Taiwan on TBI and substance related disorder. They found the overall incidence of

substance related disorders in patients with TBI to be 3.62-fold higher than in control participants. Further, for those individuals who sustained a more severe TBI, they were found to be approximately nine times more likely to have developed a substance related disorder when compared to controls. The authors argued that in their population the presence of a TBI is significantly associated with subsequent risk of developing a substance related disorder (Wu et al., 2016). The authors in this study also maintain that medical professions should be privy to their findings to intervene immediately following TBI.

It is important to have early identification of individuals with alcohol use disorder and hazardous drinking behaviors following TBI. As previously stated, this population is at an increased risk of alcohol use and abuse, as well as additional TBIs, and therefore early intervention and assessment early on could be beneficial (Raj et al., 2015; Pandit et al., 2014).

Limitations

One possible limitation to this study is the absence of information on co-occurring mental health disorders in participants with mTBI. McHugo et al., 2016, found a high rate of TBIs in individuals with co-occurring mental health disorders. The authors contend that cognitive and behavioral symptoms of TBI can mimic symptoms associated with mental illness and therefore it is important to assess for comorbidities in this population (McHugo et al., 2016).

Another possible limitation to this study is participant recall of their TBI history and use of self-report measures. Clearly, hospital records would be preferred, but many

individuals do not go to hospitals following an mTBI. In one study researchers examined the accuracy of adult recall of hospitalized TBI events that occurred between birth and age 25 (McKinlay, Horwood, and Fergusson, 2016). Researchers found a direct relationship between time post injury and TBI recall, with increased recall being associated with decreasing time since the TBI. 95% of individuals who were hospitalized for TBIs between the ages of 15-19 and 20-24 recalled the event at age 25 compared to only 25% of individuals who were hospitalized for TBIs between the ages of 0 and 4 years (McKinlay, Horwood, and Fergusson, 2016). An additional limitation to this study is the lack of a participant condition for individuals with no history of alcohol dependence. Importantly, this sample was biased toward heavy drinking, and therefore these results cannot be generalized to a population that drinks less or consumes other drugs.

Conclusions

Results indicated that individuals with both more severe and more recent injuries on average consumed more drinks per drinking day as measured by TLFB-DPDD. In contrast, it was found that injury severity and injury remoteness were not linked to harmful or hazardous drinking as measured by the AUDIT. These findings argue for the importance of alcohol education at the time mTBI, especially in the case of more severe injuries. Education on the topics of prognosis and expectations following TBI has shown to have a positive on post concussive symptoms (Mittenberg et al., 2001). Further the authors propose that examining both recency and severity may better elucidate the impact of mTBI beyond the mere number of injuries. The findings from this study may be

beneficial to researchers in both the TBI and substance use fields because it helps to illustrate the way in which these clinical issues may be linked.

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