DEFENSE AND VETERANS BRAIN INJURY CENTER

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RESEARCH REVIEW ON MISUSE AND ABUSE OF ALCOHOL AFTER TRAUMATIC BRAIN INJURY

ABSTRACT

Alcohol-related problems are reported by 5% to 12% of previously deployed US military personnel (Jacobson et al., 2008). Over 300,000 diagnosed traumatic brain injuries (TBIs) have been reported between 2000 and 2015 (Defense and Veterans Brain Injury Center, 2016). This review summarizes and describes relevant scientific literature addressing alcohol use disorder (AUD) after traumatic brain injury (TBI). Data from both civilian and military or veteran studies are conflicting regarding the impact of TBI on subsequent risk of alcohol misuse or abuse, although alcohol use is typically lower during the first year after injury than prior to injury (Bombardier, Temkin, Machamer, & Dikmen, 2003; Dikmen, Machamer, Donovan, Winn, & Temkin, 1995; Horner et al., 2005; Pagulayan, Temkin, Machamer, & Dikmen, 2016; Ponsford, Whelan-Goodinson, & Bahar-Fuchs, 2007; Whelan-Goodinson, Ponsford, Johnston, & Grant, 2009). Among military and veteran populations, some studies suggest that the risk of AUD is increased after military-related TBI (Johnson, Eick-Cost, Jeffries, Russell, & Otto, 2015; Miller et al., 2013), although results are not consistent (Heltemes, Dougherty, MacGregor, & Galarneau, 2011). Post-traumatic stress disorder (PTSD) and combat exposure are also associated with alcohol misuse (Adams et al., 2016; Kelley et al., 2012; Polusny et al., 2011). Alcohol misuse is associated with negative medical, employment, and social consequences, regardless of TBI history (Adams, Larson, Corrigan, Ritter, & Williams, 2013; National Institute of Alcohol Abuse and Alcoholism, 2016). In the existing literature, information on AUD history or pre-injury alcohol use is often unavailable. Further research with appropriate control groups, study designs that prevent data loss from attrition, detailed TBI and addiction disorder history, larger sample sizes, and statistical adjustment for confounding factors will provide more evidence regarding AUD after TBI.

INTRODUCTION

TBI is characterized by at least one of the following five clinical signs: decrease or loss of consciousness (LOC), post-traumatic amnesia, alteration of consciousness or mental state, neurological deficits, or intracranial lesion (Department of Veterans Affairs and Department of Defense, 2016). The Department of Defense categorizes TBIs into mild, moderate, or severe based on results from structural imaging (computed tomography), duration of loss of consciousness (LOC), duration of alteration of consciousness (AOC), duration of post-traumatic amnesia (PTA), and Glasgow Coma Scale (GCS) score (Assistant Secretary of Defense, 2015). In published studies, TBI severity is often defined by one variable such as GCS or LOC without regard to duration of PTA or structural findings. The vast majority of TBIs are mild (mTBI) (Defense and Veterans Brain Injury Center, 2016; Faul, Xu, Wald, & Coronado, 2010).

Evidence suggests that alcohol can interfere with recovery from TBI (Corrigan & Cole, 2008; West, 2011). Alcohol can exacerbate the functional limitations and vestibular, somatic, and behavioral/emotional symptoms experienced after TBI (West, 2011). Alcohol abuse or alcohol-related index injury increase the risk of post-traumatic seizure by lowering the seizure threshold and interfering with the action of anti-seizure medications (De Reuck, 2011; Vaaramo,

Puljula, Tetri, Juvela, & Hillbom, 2014). With these risks, it is important to understand the prevalence and risk factors for alcohol abuse and misuse after TBI.

Alcohol abuse and misuse are defined by the Diagnostic and Statistics Manuals (DSM) published by the American Psychological Association. The current diagnostic criteria defined by the 5th edition (DSM-V) is different than the diagnostic criteria used in many of the studies here, from the 4th edition (DSM-IV) (American Psychiatric Association, 1994). The DSM-V defines Alcohol Use Disorder (AUD) as the presence of two of 11 diagnostic criteria within a 12-month period (shown below) (American Psychiatric Association, 2013). The main difference between the two editions is that the 4th edition defined two separate disorders, alcohol abuse and alcohol dependence. Alcohol dependence was defined by criteria including tolerance and withdrawal, while alcohol abuse was defined by similar, partially overlapping criteria that did not include tolerance and withdrawal (American Psychiatric Association, 1994). For purposes of this review, all alcohol-related diagnoses based on DSM-IV or DSM-V criteria are treated as interchangeable.

DSM-V Criteria for Alcohol Use Disorder (AUD)

A problematic pattern of alcohol use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:

1. Alcohol is often taken in larger amounts or over a longer period than was intended.

2. There is a persistent desire or unsuccessful efforts to cut down or control alcohol use.

3. A great deal of time is spent in activities necessary to obtain alcohol, use alcohol, or recover from its effects.

4. Craving, or a strong desire or urge to use alcohol.

5. Recurrent alcohol use resulting in a failure to fulfill major role obligations at work, school, or home.

6. Continued alcohol use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of alcohol.

7. Important social, occupational, or recreational activities are given up or reduced because of alcohol use.

8. Recurrent alcohol use in situations in which it is physically hazardous.

9. Alcohol use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by alcohol.

10. Tolerance, as defined by either of the following:

a. A need for markedly increased amounts of alcohol to achieve intoxication or desired effect.

> b. A markedly diminished effect with continued use of the same amount of alcohol.
>
> 11. Withdrawal, as manifested by either of the following:
>
> a. The characteristic withdrawal syndrome for alcohol (refer to Criteria A and B of the criteria set for alcohol withdrawal, pp. 499–500).
>
> b. Alcohol (or a closely related substance, such as a benzodiazepine) is taken to relieve or avoid withdrawal symptoms (American Psychiatric Association, 2013).

The studies discussed in this review include several alcohol use outcomes: AUD diagnoses (Johnson et al., 2015; Miles, Graham, & Teng, 2015; Miller et al., 2013), self-reported heavy use (Adams, Larson, Corrigan, Horgan, & Williams, 2012; Chase et al., 2012; Horner et al., 2005), and self-reported misuse (Bogner, French, Lange, & Corrigan, 2015), that may or may not meet the full diagnostic criteria for a use disorder. Outcomes of interest also include frequency of binge drinking (Adams et al., 2012; Chase et al., 2012; Horner et al., 2005) and consumption category (Bombardier et al., 2003; Horner et al., 2005; Pagulayan et al., 2016).

Researchers often measure alcohol consumption-related problems using self-report scales. The Alcohol Use Disorders Identification Test (AUDIT) is a 10-item scale that measures alcohol use frequency and quantity, signs of physical dependence and dysfunction associated with alcohol use (Ponsford et al., 2007; World Health Organization, 2001). The Short Michigan Alcoholism Screening Test (SMAST) is a 13-item scale that measures behavioral and functional outcomes related to alcohol misuse (Bombardier et al., 2003; Dikmen et al., 1995; Selzer, Vinokur, & van Rooijen, 1975).

Table 1.

Definitions of alcohol consumption categories (Bombardier et al., 2003).

Quantity	None or < 1 drink	1 to 2 drinks	3 to 4 drinks	5 + drinks
Frequency				
< 1 time/week or none	Abstinent	Light	Moderate	Heavy
1 to 2 times/week	Abstinent	Light	Moderate	Heavy
3 to 4 times/week	Abstinent	Moderate	Moderate	Heavy
5 to 6 times/week	Abstinent	Moderate	Heavy	Heavy
7 + times/week	Abstinent	Heavy	Heavy	Heavy

SCOPE AND METHOD

This research review focuses on alcohol misuse and abuse after TBI. Discussion of the negative social, behavioral, medical, and functional consequences of alcohol abuse and misuse is limited to studies in which TBI is a primary variable. The biological effects of alcohol on the

brain in the context of TBI history are beyond the scope of this review, as is a discussion of the risks of light or moderate alcohol use after TBI. All levels of TBI severity are discussed.

The articles included here were found on PubMed using the search string "((traumatic brain injury[Title/Abstract]) OR (concussion[Title/Abstract]))" combined with substance-related terms using the Boolean operator AND. Substance-related terms included alcohol, alcoholism, drinking, substance, and these terms were required to appear in the article title or abstract. Study reports were excluded if the dependent variable was: intoxication at time of injury; pre-injury substance misuse or abuse; non-alcohol substance; injury mechanism; neuroimaging findings; or criminal arrest, criminal offense, or aggressive behavior. Study reports on the effect of alcohol at tie of injury or during the acute phase of injury recovery were excluded. Other exclusion criteria were: participants were criminal offenders or prison inmates; participants were adolescents; injury sustained during childhood or adolescence; TBI status data are not presented; substance misuse/abuse data are not presented; observational study with fewer than 50 cases; intervention study; editorial or scoping review; case report/series; or animal study. Approximately 500 articles published between 1992 and 2016 were evaluated for inclusion at the title and abstract level. The abstracts of 163 articles were examined, and approximately 60 were evaluated at the full text level. A high number of excluded articles (at least 50) focused on intoxication at time of injury.

PREVALENCE OF ALCOHOL ABUSE OR MISUSE AFTER TBI

Abundant evidence from civilian studies indicates that 37 to 51% of TBI patients are intoxicated with alcohol at the time of injury, and a similar percent have a pre-TBI history of alcohol misuse (Parry-Jones, Vaughan, & Miles Cox, 2006). Overall, several civilian studies show a temporary decline in alcohol use and problems in the first year post-injury (Bombardier et al., 2003; Dikmen et al., 1995; Horner et al., 2005; Pagulayan et al., 2016; Ponsford et al., 2007; Whelan-Goodinson et al., 2009). Some individuals return to drinking in the months and years after TBI, as shown in civilian longitudinal studies (Bombardier et al., 2003; Dikmen et al., 1995; Jorge et al., 2005; Pagulayan et al., 2016). Aside from these well-supported observations, evidence is not consistent on the question of whether the risk of AUD or alcohol misuse increases after TBI.

This section presents data on the prevalence and risk of misuse or abuse of alcohol after TBI. Studies with at least 50% of participants with mTBI are considered as mTBI studies below, as are studies that provide no information on TBI severity. The literature search produced 24 studies (18 controlled, six uncontrolled) that provided quantitative information about alcohol use and misuse after TBI. The controlled studies compared subjects with TBI history to those without TBI history, and the uncontrolled studies compared the alcohol use or misuse of subjects with TBI either to pre-injury use or misuse levels, or to use or misuse levels reported for the general population. A number of methodological differences among these 24 studies are examined below.

Study design

The breakdown of the 18 controlled and six uncontrolled studies in terms of study design and overall conclusion is shown in Tables 1 and 2. Half of the controlled studies showed increased alcohol use or misuse in those with TBI history as compared to those without TBI

history, and half found either no increase in risk of misuse or abuse, or decreased use in those with TBI. The remaining six studies were uncontrolled. None of the six uncontrolled studies reported an increase in alcohol use between pre-injury and post-injury.

Table 2.

Controlled studies with data on alcohol misuse after TBI

Study Characteristic	Studies with increase in misuse or abuse observed after TBI	Studies with no increase in misuse or abuse observed after TBI	Total
Longitudinal controlled studies	0	5 (Bogner et al., 2015; Kelley et al., 2012; Polusny et al., 2011; Ponsford et al., 2007; Tait, Anstey, & Butterworth, 2010)	5
Cross-sectional controlled studies	4 (Adams et al., 2012; Adams et al., 2016; Hanson et al., 2016; Rona et al., 2012)	2 (Allen, Stewart, Cusimano, & Asbridge, 2016; Ettenhofer, Reinhardt, & Barry, 2013)	6
Retrospective controlled studies	5 (Armed Forces Health Surveillance, 2013; Grossbard et al., 2016; Johnson et al., 2015; Miller et al., 2013; Wu et al., 2016)	2 (Heltemes et al., 2011; Miles et al., 2015)	7
Total	9	9	18

Table 3.

Uncontrolled studies with data on alcohol misuse after TBI

Study Characteristic	Studies with increase in misuse or abuse observed after TBI	Studies with no increase in misuse or abuse observed after TBI	Total
Longitudinal uncontrolled studies	0	4 (Bombardier et al., 2003; Dikmen et al., 1995; Jorge et al., 2005; Pagulayan et al., 2016)	4
Cross-sectional uncontrolled studies	1 (Horner et al., 2005)	0	1
Retrospective uncontrolled studies	1 (Chase et al., 2012)	0	1
Total	2	5	7

The reasons for the conflicting results of the controlled studies are not clear, but differences in study design, population, and outcomes may account for some of the differences. Most retrospective studies (six of eight) or cross-sectional (five of eight) studies do show an increase in alcohol misuse or abuse risk for those with TBI compared to those without. All the prospective longitudinal studies (n = 9) in this set of 24 show no increase in alcohol misuse or abuse risk after TBI, compared to either pre-injury use (for the four uncontrolled studies) or compared to misuse and abuse risk among those without TBI (for the five controlled studies). The longitudinal studies have participant retention rates ranging from 51% to 90%. It is possible

those who develop or relapse into drinking problems are more likely to drop out of a study than those who do not, and the reported results of these studies are systematically biased.

Among the uncontrolled studies, pre-injury consumption was compared to consumption at follow-up. Five of the six studies conducted assessments at 1 year post-injury (Bombardier et al., 2003; Dikmen et al., 1995; Horner et al., 2005; Jorge et al., 2005; Pagulayan et al., 2016). Time since injury ranged from 1 month (in two studies that had a second assessment at 1 year post-injury (Bombardier et al., 2003; Dikmen et al., 1995)) to a mean of 16 years (Chase et al., 2012). Overall, these studies showed a decrease in alcohol consumption immediately after injury, followed by a slow return to drinking among some of the participants, although average consumption levels stay below the self-reported pre-injury levels in most of these studies. A limitation of these studies is that pre-injury drinking levels were assessed by recall, which may have introduced error and bias.

Two uncontrolled studies compared the alcohol use of individuals with moderate or severe TBI history to the alcohol use of the general population in the state, and found that persons with TBI have higher rates of binge drinking (Chase et al., 2012; Horner et al., 2005). These comparisons should be interpreted with caution, since neither study matched the general state population data to the sample based on age or other demographic factors, with the exception that Chase et al. matched based on gender (Chase et al., 2012).

Injury Severity

The breakdown of studies by TBI severity is shown in Table 4. Both studies with moderate or severe TBI patients and those with mostly mild TBI (includes studies that provided no information on severity) have mixed results. Eliminating the uncontrolled studies did not provide additional clarity.

Table 4.

Controlled studies with data on alcohol misuse after TBI, divided by TBI severity, participant population, and presence of a no TBI control group

	Studies showing increase in misuse or abuse observed after TBI	Studies showing no increase in misuse or abuse observed after TBI
Military/Veteran controlled studies		
Moderate/severe TBI	0	0
Mild TBI or any severity	8 (Adams et al., 2012; Adams et al., 2016; Armed Forces Health Surveillance, 2013; Grossbard et al., 2016; Hanson et al., 2016; Johnson et al., 2015; Miller et al., 2013; Rona et al., 2012)	5 (Bogner et al., 2015; Heltemes et al., 2011; Kelley et al., 2012; Miles et al., 2015; Polusny et al., 2011)
Civilian controlled studies		
Moderate/severe TBI	0	1 (Ponsford et al., 2007)
Mild TBI or any severity	1 (Wu et al., 2016)	3 (Allen et al., 2016; Ettenhofer et al., 2013; Tait et al., 2010)
Civilian uncontrolled studies		
Moderate/severe TBI	2 (Chase et al., 2012; Horner et al., 2005)	2 (Jorge et al., 2005; Pagulayan et al., 2016)

Mild TBI or any severity	0	2 (Bombardier et al., 2003; Dikmen et al., 1995)

Participant population

Military and veteran studies

Among the 13 studies conducted with military or veteran populations, all examined populations with mild TBI or TBI of unspecified severity. The military studies were retrospective (n = 6), cross-sectional (n = 4), and longitudinal (n = 3), and all had no-TBI control groups. An increased risk of alcohol misuse or abuse after TBI was reported in 8 of these. Eight of the 13 studies used statistical methods to adjust for demographic and other factors (Adams et al., 2012; Adams et al., 2016; Adams et al., 2013; Heltemes et al., 2011; Johnson et al., 2015; Miles et al., 2015; Miller et al., 2013; Rona et al., 2012). Four studies excluded persons with prior alcohol misuse or abuse (Hanson et al., 2016; Heltemes et al., 2011; Johnson et al., 2015; Miller et al., 2013). Five had any exclusion criteria related to prior TBI (Armed Forces Health Surveillance, 2013; Hanson et al., 2016; Johnson et al., 2015; Miller et al., 2013; Polusny et al., 2011).

Three retrospective studies of service members are noteworthy. These were controlled studies that used statistical adjustment to account for demographics (two of the three also accounted for mental health conditions) and excluded persons with prior TBI or addiction-related disorder.

Johnson et al. compared a cohort of service members who were diagnosed with a TBI (n = 53,817) to a random sample of control service members (n = 151,776) with any other diagnosis during the same time period (Johnson et al., 2015). At 1 year post-injury, an AUD diagnosis was 1.5 times (95% CI, 1.4 to 1.6) more likely among those with TBI history as compared to those without TBI history. Statistical adjustment accounted for gender, age, rank, occupation, service branch, TBI severity, PTSD diagnosis (prior or follow-up), and other mental health diagnosis during follow-up.

Miller et al. examined medical records of 5,066 active duty U.S. airmen who sustained mTBI and 44,733 active duty airmen who sustained other injuries during a 7-year period (Miller et al., 2013). The risk of new-onset AUD in the mTBI group was 1.70 times higher (95% CI 1.31 to 2.21) than the control group when assessed at least 3 months after injury. During the period 1 to 3 months after TBI, the risk of new-onset AUD was even more elevated, 2.66 times higher (95% CI 1.86 to 3.81) in the mTBI group than the control group. These results were adjusted for demographic factors and mental health conditions.

Heltemes et al. compared AUD diagnoses among 3,123 male U.S. service members who sustained combat injuries between 2004 and 2007, with 45% constituting the TBI group and the remainder constituting the other-injury group (Heltemes et al., 2011). No significant difference was observed in the rate of AUD diagnosis between the TBI and other-injury group (6.1% and 4.9%, respectively) during the 3-year surveillance period. These results were adjusted for age, but other variables did not meet criteria for confounding and were not included in the model.

Civilian studies

The studies with civilian populations that met inclusion criteria were retrospective (n = 2, one uncontrolled), cross-sectional (n = 4, two uncontrolled), and longitudinal (n = 6, four uncontrolled). Most of these studies (9 of 12) found no increase in risk of alcohol abuse or misuse after TBI.

Five studies examined civilians with moderate or severe TBI. Three longitudinal studies showed that use and problem use was lower 1 year after TBI as compared to before injury (Jorge et al., 2005; Pagulayan et al., 2016; Ponsford et al., 2007). Average alcohol use increased somewhat over the next 2 to 4 years, but remained lower than pre-injury levels (Pagulayan et al., 2016; Ponsford et al., 2007). These studies had retention rates ranging from 51% to 66%. One study that recruited a community control group found that alcohol use and problem use were not significantly different for the TBI participants (Ponsford et al., 2007). The other four studies were uncontrolled, although two found that the frequency of binge drinking among participants with TBI history was higher than that in the general state population (Chase et al., 2012; Horner et al., 2005). None of these five studies were adjusted for potentially confounding factors, and none excluded persons with prior TBI or pre-injury alcohol abuse.

Three controlled civilian studies conducted statistical controls in their analysis. The earliest was a community cohort study by Tait et al. that assessed brain injury and alcohol use at baseline and after four years (Tait et al., 2010). The authors collected prospective longitudinal data on 6,093 participants (those with prior moderate or severe TBI were excluded). During the 4-year period, 56 individuals sustained an mTBI and 44 sustained a moderate TBI (defined as any TBI requiring hospital admission). TBI was not significantly associated with risk of new-onset hazardous/harmful drinking. Given the small number of TBI cases, this study may have been underpowered to assess the relative risk of hazardous drinking for those with and without TBI.

Wu et al. conducted a population-based case-control study to determine whether TBI contributes to risk of subsequent SUD diagnosis (Wu et al., 2016). Individuals with TBI history in a Taiwanese national health database (n = 19,109) were matched 1:1 for age and sex with controls without TBI history. After adjusting for demographic variables, those with TBI were more than three times more likely than controls to receive a subsequent SUD diagnosis. The risk of SUD after an injury requiring surgical intervention (a proxy for severity) was higher than after a more mild injury that did not require a surgical intervention.

Allen et al. used data from a Canadian population health survey to determine the relationship between alcohol use and TBI history among 339 respondents who reported sustaining a TBI in the past 12 months and a random sample of non-injured respondents (n = 10,627). After adjustment for education and income, those with recent TBI history were not found to be more likely to drink or more likely to binge drink than non-injured respondents (Allen et al., 2016).

Two studies of civilians with TBI examined how severity affected alcohol use (Dikmen et al., 1995; Pagulayan et al., 2016). Post-injury alcohol use is lower among those who sustained more severe injuries (lower GCS or more severe classification) compared to those who sustained more mild injuries (Dikmen et al., 1995; Pagulayan et al., 2016).

Study Outcome

The most common outcome among the 24 studies was AUD diagnosis (eight studies, including one that used a combined AUD/SUD outcome, and two that used a research diagnosis based on DSM diagnostic criteria), followed by AUDIT scores (six studies), and binge drinking frequency (five studies). The studies that relied on AUD/SUD diagnoses were mostly with military/veteran populations (six of eight) mostly retrospective (six of eight) and were split in terms of results. Four studies found that TBI history increased the risk of subsequent AUD/SUD diagnosis as compared to non-TBI controls, four studies found a decreased risk of AUD diagnosis, and one study only reported on relapse in participants with prior AUD.

Among the six studies that used an outcome based on AUDIT scores, score interpretations varied. Two studies classified that a score of 9 or more indicated misuse (Hanson et al., 2016; Ponsford et al., 2007), one study held scores of 5 or more as misuse (Grossbard et al., 2016), and one study classified scores of 16 or more as misuse (Rona et al., 2012). One study reported average numerical scores rather that a dichotomized outcome (Polusny et al., 2011), and one study used consumption categories based on AUDIT responses (Tait et al., 2010). Three of the studies found increased risk of misuse or increased use after TBI, two found no difference between TBI and non-TBI participants in AUDIT outcomes, and one uncontrolled study found a significant decrease in AUDIT scores at one year post-injury.

Of the three controlled studies for which binge drinking was a primary outcome, two found increased risk of binge drinking among those with TBI history as compared to those without (Adams et al., 2012; Adams et al., 2016). Two additional uncontrolled studies showed that binge drinking was more frequent among those with TBI history than among the general population (Chase et al., 2012; Horner et al., 2005). Most (four of five) of these studies were cross-sectional and one was retrospective. The two military studies were controlled and found an increased risk of binge drinking after TBI (Adams et al., 2012; Adams et al., 2016), while the three civilian studies had mixed results (Allen et al., 2016; Chase et al., 2012; Horner et al., 2005).

Five studies had other outcomes including Short Michigan Alcoholism Screening Test (SMAST), alcohol consumption categories, alcohol use behaviors, and frequency of alcohol use. All five found decreased or no change in use or misuse (Bombardier et al., 2003; Dikmen et al., 1995; Ettenhofer et al., 2013; Kelley et al., 2012; Pagulayan et al., 2016). Three studies were uncontrolled and showed decreased misuse after TBI (Bombardier et al., 2003; Dikmen et al., 1995; Pagulayan et al., 2016). Two studies compared TBI persons with non-TBI persons and found no increase in misuse or frequency of use (Ettenhofer et al., 2013; Kelley et al., 2012).

Summary

Results are conflicting on the question of whether TBI increases risk of subsequent alcohol abuse. Conflicting findings cannot be explained by a single feature of the studies. An analysis of the study design, subject population, exclusion criteria, outcome type, injury severity, level of statistical adjustment, and exclusion criteria of these 24 studies produced no clear pattern that can explain the discrepancies. Significant evidence supports the hypothesis that after TBI, most civilians decrease alcohol intake for a period of months to years, but some return to

drinking (Bombardier et al., 2003; Dikmen et al., 1995; Jorge et al., 2005; Pagulayan et al., 2016).

IMPACT OF ALCOHOL ABUSE OR MISUSE AFTER TBI

By definition, alcohol use disorder is associated with negative social, behavioral, medical, or functional outcomes (American Psychiatric Association, 2013), and many alcohol abuse assessment tools use the presence or frequency of such problems as a proxy for AUD severity (Bombardier et al., 2003). That alcohol misuse and abuse has social, behavioral, medical, or functional consequences is well-established and beyond the scope of this review (National Institute of Alcohol Abuse and Alcoholism, 2016). This section reports on such consequences in military and veteran populations in which TBI history is reported, and on consequences in civilian studies where TBI history is considered as a primary variable. The largest study in this group provided detailed information on medical, military, and social consequences of alcohol misuse. Three studies addressed the question of whether alcohol use or misuse increases post-concussive symptoms.

Survey data analyzed by Adams et al. showed that TBI with LOC greater than 20 minutes was associated with greater risk of negative alcohol-related consequences, but TBI without LOC or TBI with a shorter duration of LOC were not (Adams et al., 2013). Service members (n = 3,350) who had returned from a combat deployment 6 to 12 months prior provided self-reported data on alcohol use and medical, military, and social consequences of use (Adams et al., 2013). Those who sustained a TBI during their most recent deployment (n = 256) were divided into three groups based on duration of LOC: no LOC (n = 150), LOC less than 20 minutes (n = 72), and LOC greater than 20 minutes (n = 34). After adjustment for demographics, combat exposure, PTSD, depression, suicidal ideation, and/or frequent binge drinking, those with TBI without LOC or with LOC less than 20 minutes did not show increased risk of negative drinking-related consequences. Only those with TBI with LOC greater than 20 minutes had significantly increased risk of negative social, medical, or military consequences. These findings were consistent across several levels of adjustment (Adams et al., 2013).

Three studies were found that addressed the question of whether alcohol use or misuse increases post-concussive symptoms among those with and without TBI history. None of these studies found that alcohol use or abuse had an additive effect on post-concussive symptom severity among those with TBI. However, a comprehensive literature search on this question has not been performed. The earliest of the three studies was published by Allen et al., who investigated neuropsychological deficits associated with TBI (Allen, Goldstein, Caponigro, & Donohue, 2009). Results from male veterans referred for neuropsychological testing (n = 103) during a neurological or neuropsychiatric hospitalization indicated that TBI is associated with neuropsychological deficits regardless of alcoholism status. The TBI and TBI plus alcoholism groups did not differ on neuropsychological outcomes. No data regarding severity of TBI or alcoholism were provided, and the temporal relationship between alcoholism onset and TBI was not reported. In another study of veterans, Cernich et al. retrospectively examined 287 OEF/OIF veterans who screened positive for TBI at an urban VA medical center (Cernich, Chandler, Scherdell, & Kurtz, 2012). The 101 (35%) veterans who screened positive for alcohol abuse did not report more post-concussive symptoms than those who screened negative. The third study of alcohol and post-concussive symptoms found was conducted on undergraduate students with (n

= 256) and without (n = 2,771) mTBI history. Results showed that mTBI status was not related to cognitive, affective, or overall post-concussive symptoms. Symptom outcomes were related to frequency of alcohol use, which did not differ significantly between the mTBI and non-mTBI groups (Ettenhofer et al., 2013). In Allen et al., the variable primarily associated with post-concussive symptoms was TBI, while in Ettenhofer et al., TBI had no effect, but alcohol use affected post-concussive symptoms. The difference may relate to the participants' ages, consumption levels, or time since injury. Overall, existing evidence is insufficient to determine whether alcohol use or abuse increases post-concussive symptoms after TBI.

Although findings from the prison inmate population may not be broadly applicable, results published by Corrigan et al. with incarcerated individuals have shown that lifetime TBI history factors can impact risk of substance abuse disorder as well as other outcomes (Corrigan, Bogner, & Holloman, 2012). These findings demonstrate the complexity and heterogeneity of the TBI patient population, which presents ongoing challenges for researchers and clinicians.

RISK FACTORS FOR ALCOHOL ABUSE OR MISUSE

In the general population, alcohol dependence is more common among men than women, according to National Institutes of Alcohol Abuse and Alcoholism data. Among men, alcohol dependence risk is highest among those 18 to 24 years of age, and among women, the risk is highest among those 25 to 34 years of age (*Module 1: Epidemiology of Alcohol Problems in the United States*, 2005). These demographic patterns were consistent among the populations discussed below. Evidence has also shown genetic influences in alcohol abuse risk (Edenberg & Foroud, 2013), but no studies addressing the interaction of genetics and TBI on alcohol abuse risk were found. The below sections summarize literature that provides details on factors that impact risk of alcohol abuse and misuse among veterans and service members with and without TBI history.

Correlates of alcohol abuse in military mTBI groups

Three studies of service members with mTBI showed that PTSD and positive expectations regarding alcohol consumption were associated with increased alcohol use. Kelley et al. studied 319 combat brigade service members 1 month prior to deployment and 1 month after returning (Kelley et al., 2012). Alcohol-related outcomes were not significantly different post-deployment as compared to pre-deployment. Service members were divided into four groups based on post-deployment PTSD and TBI screening instrument results: control, TBI, PTSD, and PTSD plus TBI. The control group had lower combat exposure and lower post-deployment anxiety scores than all other groups. The PTSD and PTSD plus TBI groups had increased depression scores as compared to the control and TBI groups. Higher frequency of drinking, more alcoholic drinks per day, felt need to cut down drinking, and used more alcohol than intended were all reported by more service members with PTSD or PTSD plus TBI than by control service members. Drunk driving was reported by more service members with PTSD plus TBI than by control service members.

Polusny et al. surveyed 953 US National Guard soldiers for mTBI history, PTSD symptoms, and psychological health outcomes 1 month before returning from Iraq and 1 year after returning (Polusny et al., 2011). Participants were divided into four groups based on mTBI and PTSD status. The four groups differed on a number of characteristics, including those with

mTBI or mTBI plus PTSD were far more likely to have been injured in a blast than control participants or those with PTSD only. Those with PTSD or mTBI plus PTSD and had higher depression symptom scores. AUDIT scores showed a trend with control participants having significantly lower scores than all other groups, followed by those with mTBI only, those with PTSD only, and the highest AUDIT scores were among those with mTBI plus PTSD. Differences between the AUDIT scores between those with mTBI, PTSD, and mTBI plus PTSD were not significant. This study demonstrates that PTSD increases alcohol misuse and abuse risk to an extent that is similar to or greater than that of mTBI.

Bogner et al. found that service members with misuse had significantly more positive beliefs about the social and physical pleasure associated with alcohol, as measured by the Alcohol Expectancy Questionnaire (AEQ-III) (Bogner et al., 2015).

Correlates of alcohol abuse in military and veteran populations

Four publications with three cohorts of service member or veterans were found that addressed the contribution of TBI as compared to other factors in predicting alcohol misuse or abuse. In two of these cohorts, TBI status contributed to risk of alcohol abuse (Adams et al., 2012; Adams et al., 2016; Travis Seidl, Pastorek, Troyanskaya, & Scheibel, 2015). All three studies that considered PTSD status or symptoms found an association with alcohol misuse (Adams et al., 2012; Adams et al., 2016; Cook et al., 2015). Combat exposure was positively associated with alcohol misuse in two publications based on one cohort (Adams et al., 2012; Adams et al., 2016).

Adams et al. examined survey data from 7,155 service members who had returned from a combat deployment within the previous 12 months (Adams et al., 2012). Binge drinking, TBI history, combat exposure, and other variables were surveyed. In regression models, TBI status, male gender, high combat exposure, positive PTSD screen, positive depression screen, and suicidal ideation within the past year were all associated with an increased risk of frequent binge drinking. Serving in the Air Force, self-identified Black or other non-Hispanic race, married (or living as married) status, and senior enlisted or higher rank were all associated with a decreased risk of frequent binge drinking.

A subsequent analysis of data from the same survey included 6,824 service members who had been on a combat deployment in the last 12 months (Adams et al., 2016). Binge drinking data (defined as above) and AUDIT scores were examined for relationships to TBI and PTSD. In bivariate analysis, days of binge drinking were significantly associated with more severe TBI level (TBI levels were: no LOC, LOC less than 20 minutes, or LOC greater than 20 minutes), positive PTSD screen, high lifetime combat exposure, and lower enlisted rank. A path analysis was also performed to determine the impact of various predictors on binge drinking. All four predictors contributed to binge drinking days, with combat exposure having a marginally higher effect than PTSD screen, followed by TBI level, and lower enlisted rank.

In a sample of 80 trauma-exposed OEF/OIF veterans with chronic pain, 75% had current or history of PTSD, and 56% screened positive for TBI history. Participants were recruited to a longitudinal study at a Veterans Affairs health care center, and evaluated for behavioral health outcomes at enrollment and after 1 year. At baseline, alcohol-related problems were assessed with the Rutgers Alcohol Problem Index (RAPI). In a bivariate correlation analysis, alcohol-

related problems were not correlated with TBI, but they were correlated with PTSD symptom scores and disability scores. After 1 year, alcohol-related problems were not a predictor of disability scores (Cook et al., 2015).

Travis Seidl et al. conducted a study of impulsiveness with 72 OEF/OIF veterans with deployment-related mTBI history and 55 control veterans (Travis Seidl et al., 2015). The mTBI group showed significantly higher AUDIT scores (average 7.0, SD 6.4) than the control group (average 3.7, SD 3.8). Regression analysis showed a significant positive relationship between alcohol-related problems and non-planning impulsiveness as measured by self-report scale. No significant differences in impulsiveness were observed between the mTBI and control groups.

CONCLUSION

This research review summarizes recent and relevant scientific literature on AUD after TBI. Some evidence regarding civilian TBI indicates that alcohol use and misuse often declines in the year after TBI, especially after moderate or severe TBI (Bombardier et al., 2003; Dikmen et al., 1995; Horner et al., 2005; Pagulayan et al., 2016; Ponsford et al., 2007; Whelan-Goodinson et al., 2009). However, the long-term impact of TBI on risk of AUD or alcohol misuse is unclear. Additional controlled studies are needed, with sample sizes large enough to enable statistical adjustment for demographic and other factors. Prospective studies with administrative follow-up data collection would enable longitudinal studies that were not significantly impacted by participant attrition.

Among military and veteran populations, findings were similarly inconsistent, but some suggested that risk of AUD is increased after TBI. Among service members with mTBI, PTSD (Adams et al., 2012; Adams et al., 2016) and positive expectations regarding alcohol consumption (Bogner et al., 2015) were associated with increased alcohol use. In studies of military and veteran populations that included those without TBI history, TBI status did not consistently contribute to additional risk for alcohol abuse. PTSD status or symptoms and combat exposure were consistently associated with alcohol misuse than TBI status (Cook et al., 2015), and in three studies, the effect of PTSD on alcohol use or misuse was larger than the effect of TBI (Adams et al., 2016; Kelley et al., 2012; Polusny et al., 2011).

Alcohol misuse is associated with negative medical, military, and social consequences among service members, regardless of TBI history (Adams et al., 2013). Data from military and civilian populations suggest that alcohol misuse may not increase post-concussive symptoms among those with TBI history more than it increases those symptoms among those without TBI (Allen et al., 2009; Cernich et al., 2012; Ettenhofer et al., 2013).

The literature search revealed several research gaps. No studies on military or veteran populations with moderate severe TBI were found. Most military/veteran studies did not account for AUD history or pre-injury alcohol use. Controlling for pre-morbid AUD and alcohol misuse is complicated by the significant proportion of civilian TBI patients with prior alcohol problems (Parry-Jones et al., 2006). A number of civilian studies had high participant attrition or lacked control groups. Further research with longer follow-up periods, non-TBI control groups, and specific populations (co-morbidities, specific injury severity, specific genetic variants) will provide more evidence regarding risks and interventions.

ABBREVIATIONS

AEQ-III, Alcohol Expectancy Questionnaire; AOC, alteration of consciousness; AUD, alcohol use disorder; AUDIT, Alcohol Use Disorders Identification Test; DoD, Department of Defense; DSM-IV, Diagnostics and Statistics Manual, 4th edition; DSM-V, Diagnostics and Statistics Manual, 5th edition; GCS, Glasgow Coma Scale; LOC, loss of consciousness; mTBI, mild traumatic brain injury; n, number in participant group; OEF/OIF, Operation Enduring Freedom/Operation Iraqi Freedom; PTA, post-traumatic amnesia; PTSD, Posttraumatic stress disorder; SMAST, Short Michigan Alcoholism Screening Test; SUD, substance use disorder; TBI, traumatic brain injury; VA, Department of Veterans Affairs.

REFERENCES

Adams, R. S., Larson, M. J., Corrigan, J. D., Horgan, C. M., & Williams, T. V. (2012). Frequent binge drinking after combat-acquired traumatic brain injury among active duty military personnel with a past year combat deployment. *J Head Trauma Rehabil, 27*(5), 349-360. doi: 10.1097/HTR.0b013e318268db94

Adams, R. S., Larson, M. J., Corrigan, J. D., Ritter, G. A., Horgan, C. M., Bray, R. M., & Williams, T. V. (2016). Combat-Acquired Traumatic Brain Injury, Posttraumatic Stress Disorder, and Their Relative Associations With Postdeployment Binge Drinking. *J Head Trauma Rehabil, 31*(1), 13-22. doi: 10.1097/HTR.0000000000000082

Adams, R. S., Larson, M. J., Corrigan, J. D., Ritter, G. A., & Williams, T. V. (2013). Traumatic brain injury among U.S. active duty military personnel and negative drinking-related consequences. *Subst Use Misuse, 48*(10), 821-836. doi: 10.3109/10826084.2013.797995

Allen, D. N., Goldstein, G., Caponigro, J. M., & Donohue, B. (2009). The effects of alcoholism comorbidity on neurocognitive function following traumatic brain injury. *Appl Neuropsychol, 16*(3), 186-192. doi: 10.1080/09084280903098687

Allen, S., Stewart, S. H., Cusimano, M., & Asbridge, M. (2016). Examining the Relationship Between Traumatic Brain Injury and Substance Use Outcomes in the Canadian Population. *Subst Use Misuse, 51*(12), 1577-1586. doi: 10.1080/10826084.2016.1188955

American Psychiatric Association. (1994). *Diagnostic and Statistical Manual of Mental Disorders* (4th (DSM-IV) ed.). Washington, DC: American Psychiatric Association. Retrieved from http://www.psychiatryonline.com/DSMPDF/dsm-iv.pdf

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders* (5 (DSM-5) ed.). Washington, DC: American Psychiatric Association. Retrieved from http://dsm.psychiatryonline.org/doi/full/10.1176/appi.books.9780890425596.dsm16

Armed Forces Health Surveillance, C. (2013). Incident diagnoses of common symptoms ("sequelae") following traumatic brain injury, active component, U.S. Armed Forces, 2000-2012. *MSMR, 20*(6), 9-13.

Assistant Secretary of Defense. (2015). *Traumatic brain injury: Updated definition and reporting.* Washington, DC.

Bogner, J., French, L. M., Lange, R. T., & Corrigan, J. D. (2015). Pilot study of traumatic brain injury and alcohol misuse among service members. *Brain Inj, 29*(7-8), 905-914. doi: 10.3109/02699052.2015.1005136

Bombardier, C. H., Temkin, N. R., Machamer, J., & Dikmen, S. S. (2003). The natural history of drinking and alcohol-related problems after traumatic brain injury. *Arch Phys Med Rehabil, 84*(2), 185-191. doi: 10.1053/apmr.2003.50002

Cernich, A. N., Chandler, L., Scherdell, T., & Kurtz, S. (2012). Assessment of co-occurring disorders in veterans diagnosed with traumatic brain injury. *J Head Trauma Rehabil, 27*(4), 253-260. doi: 10.1097/HTR.0b013e3182585cd5

Chase, S., Ratcliff, G., Vernich, L., Al-Sukhni, E., Yasseen, B., & Colantonio, A. (2012). Preventive health practices and behavioral risk factors in women surviving traumatic brain injury. *Health Care Women Int, 33*(7), 631-645. doi: 10.1080/07399332.2012.673652

Cook, A. J., Meyer, E. C., Evans, L. D., Vowles, K. E., Klocek, J. W., Kimbrel, N. A., . . . Morissette, S. B. (2015). Chronic pain acceptance incrementally predicts disability in polytrauma-exposed veterans at baseline and 1-year follow-up. *Behav Res Ther, 73*, 25-32. doi: 10.1016/j.brat.2015.07.003

Corrigan, J. D., Bogner, J., & Holloman, C. (2012). Lifetime history of traumatic brain injury among persons with substance use disorders. *Brain Inj, 26*(2), 139-150. doi: 10.3109/02699052.2011.648705

Corrigan, J. D., & Cole, T. B. (2008). Substance use disorders and clinical management of traumatic brain injury and posttraumatic stress disorder. *JAMA, 300*(6), 720-721. doi: 10.1001/jama.300.6.720

De Reuck, J. (2011). Risk factors for late-onset seizures related to cerebral contusions in adults with a moderate traumatic brain injury. *Clin Neurol Neurosurg, 113*(6), 469-471. doi: 10.1016/j.clineuro.2011.02.004

Defense and Veterans Brain Injury Center. (2016). *DoD Worldwide Numbers for TBI.* Silver Spring, MD Retrieved from http://dvbic.dcoe.mil/dod-worldwide-numbers-tbi.

Department of Veterans Affairs and Department of Defense. (2016). *Management of Concussion-mild Traumatic Brain Injury (mTBI).* Washington, DC Retrieved from http://www.healthquality.va.gov/guidelines/Rehab/mtbi/.

Dikmen, S. S., Machamer, J. E., Donovan, D. M., Winn, H. R., & Temkin, N. R. (1995). Alcohol use before and after traumatic head injury. *Ann Emerg Med, 26*(2), 167-176.

Edenberg, H. J., & Foroud, T. (2013). Genetics and alcoholism. *Nat Rev Gastroenterol Hepatol, 10*(8), 487-494. doi: 10.1038/nrgastro.2013.86

Ettenhofer, M. L., Reinhardt, L. E., & Barry, D. M. (2013). Predictors of neurobehavioral symptoms in a university population: a multivariate approach using a postconcussive symptom questionnaire. *J Int Neuropsychol Soc, 19*(9), 977-985. doi: 10.1017/S1355617713000763

Faul, M., Xu, L., Wald, M., & Coronado, V. G. (2010). Traumatic Brain Injury in the United States: Emergency Department Visits, Hospitalizations and Deaths 2002–2006. Centers for Disease Control and Prevention, Atlanta, GA. Retrieved from http://www.cdc.gov/traumaticbraininjury/pdf/blue_book.pdf

Grossbard, J., Malte, C. A., Lapham, G., Pagulayan, K., Turner, A. P., Rubinsky, A. D., . . . Hawkins, E. J. (2016). Prevalence of Alcohol Misuse and Follow-Up Care in a National Sample of OEF/OIF VA Patients With and Without TBI. *Psychiatr Serv*, appips201500290. doi: 10.1176/appi.ps.201500290

Hanson, K. L., Schiehser, D. M., Clark, A. L., Sorg, S. F., Kim, R. T., Jacobson, M. W., . . . Delano-Wood, L. (2016). Problem alcohol use in veterans with mild traumatic brain injury: Associations with cognitive performance and psychiatric symptoms. *J Clin Exp Neuropsychol, 38*(10), 1115-1130. doi: 10.1080/13803395.2016.1198468

Heltemes, K. J., Dougherty, A. L., MacGregor, A. J., & Galarneau, M. R. (2011). Alcohol abuse disorders among U.S. service members with mild traumatic brain injury. *Mil Med, 176*(2), 147-150.

Horner, M. D., Ferguson, P. L., Selassie, A. W., Labbate, L. A., Kniele, K., & Corrigan, J. D. (2005). Patterns of alcohol use 1 year after traumatic brain injury: a population-based, epidemiological study. *J Int Neuropsychol Soc, 11*(3), 322-330. doi: 10.1017/S135561770505037X

Jacobson, I. G., Ryan, M. A., Hooper, T. I., Smith, T. C., Amoroso, P. J., Boyko, E. J., . . . Bell, N. S. (2008). Alcohol use and alcohol-related problems before and after military combat deployment. *JAMA, 300*(6), 663-675. doi: 10.1001/jama.300.6.663

Johnson, L. A., Eick-Cost, A., Jeffries, V., Russell, K., & Otto, J. L. (2015). Risk of alcohol use disorder or other drug use disorder among U.S. Service members following traumatic brain injury, 2008-2011. *Mil Med, 180*(2), 208-215. doi: 10.7205/MILMED-D-14-00268

Jorge, R. E., Starkstein, S. E., Arndt, S., Moser, D., Crespo-Facorro, B., & Robinson, R. G. (2005). Alcohol misuse and mood disorders following traumatic brain injury. *Arch Gen Psychiatry, 62*(7), 742-749. doi: 10.1001/archpsyc.62.7.742

Kelley, A. M., Athy, J. R., Cho, T. H., Erickson, B., King, M., & Cruz, P. (2012). Risk propensity and health risk behaviors in U.S. army soldiers with and without psychological disturbances across the deployment cycle. *J Psychiatr Res, 46*(5), 582-589. doi: 10.1016/j.jpsychires.2012.01.017

Miles, S. R., Graham, D. P., & Teng, E. J. (2015). Examining the influence of mild traumatic brain injury and posttraumatic stress disorder on alcohol use disorder in OEF/OIF veterans. *Mil Med, 180*(1), 45-52. doi: 10.7205/MILMED-D-14-00187

Miller, S. C., Baktash, S. H., Webb, T. S., Whitehead, C. R., Maynard, C., Wells, T. S., . . . Gore, R. K. (2013). Risk for addiction-related disorders following mild traumatic brain injury in a large cohort of active-duty U.S. airmen. *Am J Psychiatry, 170*(4), 383-390. doi: 10.1176/appi.ajp.2012.12010126

Module 1: Epidemiology of Alcohol Problems in the United States. (2005). Bethesda, MD: National Institute of Alcohol Abuse and Alcoholism Retrieved from https://pubs.niaaa.nih.gov/publications/social/module1epidemiology/module1.html.

National Institute of Alcohol Abuse and Alcoholism. (2016). *Alcohol Facts and Statistics.* Bethesda, MD Retrieved from https://www.niaaa.nih.gov/alcohol-health/overview-alcohol-consumption/alcohol-facts-and-statistics.

Pagulayan, K. F., Temkin, N. R., Machamer, J. E., & Dikmen, S. S. (2016). Patterns of Alcohol Use after Traumatic Brain Injury. *J Neurotrauma*. doi: 10.1089/neu.2015.4071

Parry-Jones, B. L., Vaughan, F. L., & Miles Cox, W. (2006). Traumatic brain injury and substance misuse: a systematic review of prevalence and outcomes research (1994-2004). *Neuropsychol Rehabil, 16*(5), 537-560. doi: 10.1080/09602010500231875

Polusny, M. A., Kehle, S. M., Nelson, N. W., Erbes, C. R., Arbisi, P. A., & Thuras, P. (2011). Longitudinal effects of mild traumatic brain injury and posttraumatic stress disorder comorbidity on postdeployment outcomes in national guard soldiers deployed to Iraq. *Arch Gen Psychiatry, 68*(1), 79-89. doi: 10.1001/archgenpsychiatry.2010.172

Ponsford, J., Whelan-Goodinson, R., & Bahar-Fuchs, A. (2007). Alcohol and drug use following traumatic brain injury: a prospective study. *Brain Inj, 21*(13-14), 1385-1392. doi: 10.1080/02699050701796960

Rona, R. J., Jones, M., Fear, N. T., Hull, L., Murphy, D., Machell, L., . . . Wessely, S. (2012). Mild traumatic brain injury in UK military personnel returning from Afghanistan and Iraq: cohort and cross-sectional analyses. *J Head Trauma Rehabil, 27*(1), 33-44. doi: 10.1097/HTR.0b013e318212f814

Selzer, M. L., Vinokur, A., & van Rooijen, L. (1975). A self-administered Short Michigan Alcoholism Screening Test (SMAST). *J Stud Alcohol, 36*(1), 117-126.

Tait, R. J., Anstey, K. J., & Butterworth, P. (2010). Incidence of self-reported brain injury and the relationship with substance abuse: findings from a longitudinal community survey. *BMC Public Health, 10*, 171. doi: 10.1186/1471-2458-10-171

Travis Seidl, J. N., Pastorek, N. J., Troyanskaya, M., & Scheibel, R. S. (2015). Neuropsychological and behavioral correlates of impulsiveness in veterans with and without mild traumatic brain injury. *J Clin Exp Neuropsychol, 37*(1), 84-91. doi: 10.1080/13803395.2014.989817

Vaaramo, K., Puljula, J., Tetri, S., Juvela, S., & Hillbom, M. (2014). Predictors of new-onset seizures: a 10-year follow-up of head trauma subjects with and without traumatic brain injury. *J Neurol Neurosurg Psychiatry, 85*(6), 598-602. doi: 10.1136/jnnp-2012-304457

West, S. L. (2011). Substance use among persons with traumatic brain injury: a review. *NeuroRehabilitation, 29*(1), 1-8. doi: 10.3233/NRE-2011-0671

Whelan-Goodinson, R., Ponsford, J., Johnston, L., & Grant, F. (2009). Psychiatric disorders following traumatic brain injury: their nature and frequency. *J Head Trauma Rehabil, 24*(5), 324-332. doi: 10.1097/HTR.0b013e3181a712aa

World Health Organization. (2001). *AUDIT - The Alcohol Use Disorders Identification Test: Guidelines for Use in Primary Care, 2nd Edition.* Retrieved from http://www.who.int/substance_abuse/publications/alcohol/en/.

Wu, C. H., Tsai, T. H., Su, Y. F., Zhang, Z. H., Liu, W., Wu, M. K., . . . Lin, C. L. (2016). Traumatic Brain Injury and Substance Related Disorder: A 10-Year Nationwide Cohort Study in Taiwan. *Neural Plast, 2016*, 8030676. doi: 10.1155/2016/8030676