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Review

Alcohol abuse after traumatic brain injury: Experimental and clinical evidence

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ABSTRACT

Brain injury survivors, particularly those injured early in life are very likely to abuse drugs and alcohol later in life. Alcohol abuse following traumatic brain injury (TBI) is associated with poorer rehabilitation outcomes and a greatly increased chance of suffering future head trauma. Thus, substance abuse among persons with brain injury reduces the chances for positive long-term outcomes and greatly increases the societal costs. In this review, we discuss the evidence for modulation of drinking behavior after TBI and the costs of problem drinking after TBI from both a biomedical and economic perspective. Further, we review the existing animal models of drinking after brain injury and consider the potential underlying psychosocial and neurobiological mediators of this phenomenon. In particular, we highlight the potential interactions among TBI, neuroinflammation and alcohol abuse. Substance abuse is a major problem in this vulnerable patient population and a greater understanding of the underlying biology has the potential to greatly improve outcomes.

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1. Introduction

Traumatic brain injury (TBI) is a major public health problem. Annually, in the United States alone approximately 1.7 million people sustain a TBI and this will result in hundreds of thousands of emergency room visits, hospitalizations and as many as 50,000 deaths (Coronado et al., 2012; Faul et al., 2010). Estimates of the total number of TBI are probably low as many patients never seek medical treatment and these numbers do not include the military. The economic cost of TBI is staggering with some estimates ranging into the hundreds of billions of dollars annually (Silver et al., 2011). Further, previous estimates indicated that there are up to five million TBI survivors living in the US (Centers for Disease Control and

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Prevention, 1999; Zaloshnja et al., 2008); however, recent population surveys suggest that as many as 20% to 25% of adults in the general population may have experienced at least one TBI with loss of consciousness sometime in their lifetime (Ilie et al., 2015; Whiteneck et al., 2015).

Alcohol use and misuse are inextricably linked to TBIs, as alcohol intoxication is a proximate cause of an enormous subset of injuries. By some accounts more than half of all TBIs are either directly or indirectly caused by alcohol with large percentages of patients presenting with elevated blood alcohol (Tagliaferri et al., 2006). Importantly, binge drinking, often defined as 5 or more drinks on one occasion, appears to be associated with TBI more than chronic drinking (Centers for Disease Control and Prevention, 1990; Chikritzhs et al., 2001), and produces an odds ratio of 3.4 for sustaining an injury in general, and a greater risk factor for TBIs (Savola et al., 2005). Although abuse of other drugs is a problem among the TBI population, this review will focus on the role of alcohol because of its strong relationship with TBI and because it is the preferred drug of most TBI patients.

TBIs caused by alcohol are mainly falls, moving vehicle crashes and assaults. Nearly all assaulted patients were either intoxicated at the time of assault, or met the diagnostic criteria for an alcohol use disorder (Brismar et al., 1983; Savola et al., 2005). Interestingly, although high blood alcohol is a common finding in all trauma patients it is much more common in head injured patients. For instance, bicycle accidents are more common in intoxicated riders *and* being intoxicated increased the likelihood that a bicycle accident would result in TBIs (Li et al., 2001). Presumably, sober cyclists are able to avoid head injury and in the event of an accident are more likely to present with extremity injuries. The loss of psychomotor control associated with intoxication thus both increases the chances for an accident overall and increases the likelihood that the accident will result in a TBI (Savola et al., 2005).

Critically, alcohol misuse *after* TBI can reduce the efficacy of rehabilitation and increase the chances of developing seizures, mood, and anxiety disorders, as well as greatly increasing the likelihood of subsequent TBIs (Ilie et al., 2014a; Salcido and Costich, 1992; Winqvist et al., 2006). Problem alcohol usage is extremely common both prior to and after TBI. Therefore understanding the independent contributions of TBI to the risk of developing or exacerbating alcohol use disorders has been difficult. In this review, we will evaluate the existing clinical and animal evidence that TBIs, particularly those that occur early in development, increase the lifelong propensity for alcohol abuse and discuss the potential underlying neurobiological mechanisms.

2. Does alcohol abuse increase after TBI?

Although a complete evaluation of this issue is beyond the scope of this review, we will summarize some of the existing evidence for increased problem drinking after TBI in at least a subset of patients particularly those injured early in life. For an excellent in depth review see (Bjork and Grant, 2009). Additionally, as summarized below, drinking after TBI can produce significant negative psychosocial, health and employment consequences, thus the relatively high levels of problem drinking in TBI populations is troubling even if they are not greater than in the general population.

The vast majority of TBI research has focused on the role of alcohol as a cause or risk factor for TBI rather than the other way around. Several unique features of this population complicate epidemiological research into alcohol consumption following TBI. First, there are a very high percentage of patients that are already alcohol abusers before injury (Corrigan, 1995; De Guise et al., 2009). Further, the populations with the highest rates of substance abuse and the highest rates of TBI are partially overlapping. Specifically, young males are both the most likely to suffer a TBI and have the highest rates of substance abuse. Further complicating this issue is that there has been an impression from the clinical literature that more severe injuries are associated with lower rates of substance abuse, however, this likely represents, at least in part, that individuals with the most severe injuries may not have direct physical access to alcohol or drugs and, depending on the degree of disability, might require assistance to administer substances (Taylor et al., 2003). Additionally, patients with the most severe injuries that require prolonged (or permanent) institutional care may also not be allowed to take drugs or alcohol because of environmental restrictions (Taylor et al., 2003). Beyond that there is little evidence that TBI subtypes produce differential alcohol outcomes. There is substantial evidence that alcohol use drops immediately after injury because of a combination of disability, hospitalization and other acute factors (Bombardier et al., 2003; Kreutzer and Harris, 1990; Ponsford et al., 2007). Thus, to get a fuller sense of the relationship between TBI and alcohol abuse, researchers must track patients across time. However, there is strong evidence from clinical studies that tracking TBI patients with substance abuse issues is very difficult and that these individuals are often lost to follow-up and thus could result in skewed results (Corrigan et al., 1997). In any case, there is evidence that despite the large negative costs of drinking after TBI, some proportion of patients still drink heavily and some evidence indicates increased or new problem drinking after TBI.

The Center for Disease Control and Prevention in collaboration with the TBI Model Systems program has published estimates of pre- and post-injury characteristics of the U.S. population over the age of 16 who receive inpatient rehabilitation for a primary diagnosis of TBI. In the year prior to injury, 22.9% have misused alcohol (Cuthbert et al., 2015). By 5 years post-injury, among those discharged from the hospital who are still alive, 14.1% are misusing alcohol (Corrigan et al., 2014). This decline in the percentage may in part be due to persons who misuse having a greater likelihood to die or be lost to follow-up in the first 5 years post-injury; however, it is also due to some proportion of individuals stopping use because of injury-related impairments or reduced access to alcohol because of disability.

Several characteristics of adult TBI patients drinking after injury are clear. First, most studies have reported that alcohol drinking declines precipitously during the first few months after injury and that this represents a window of opportunity for substance abuse treatment/prevention in the TBI population. Second, multiple studies have reported that the rates of alcohol abstinence increase from pre-injury to post-injury indicating that some percentage of patients are heeding their doctor's advice to avoid alcohol. Third, some patients return to drinking heavily over time after injury. Finally, problem drinking before injury is highly predictive of drinking after injury (Bombardier et al., 2003; Dikmen et al., 1995; Kreutzer and Harris, 1990; Ponsford et al., 2007).

There is some suggestion that aspects of substance abuse may be enhanced by TBI in adulthood. For instance, an examination of billing records from a health management organization database revealed a significant difference in the substance abuse rates among patients with a history of psychiatric illness or substance abuse in the year prior to their injury. Patients with no recent pre-injury psychiatric care had an odds ratio of 4.5 for substance abuse in the year following their injuries, before declining over the subsequent 36 months to 1.4 (Fann et al., 2004). Results from the New Haven NIMH Epidemiological Catchment study reported increased drinking behavior after injury, compared to community samples, and increased rates of drug abuse even after controlling for alcohol abuse (Silver et al., 2001). Finally, in a consecutive sample of patients referred to a treatment program for substance abuse after TBI, nearly 20% of patients that had been light drinkers or abstain-