Full length article

Association between problematic alcohol use and reactivity to uncertain threat in two independent samples

Stephanie M. Gorka [a,*], Lynne Lieberman [b], K. Luan Phan [a,b,c,d], Stewart A. Shankman [a,b]

[a] University of Illinois-Chicago, Department of Psychiatry, 1747 West Roosevelt Road, Chicago, IL 60608, United States
[b] University of Illinois-Chicago, Department of Psychology, 1007 West Harrison St. (M/C 285), Chicago, IL 60607, United States
[c] Jesse Brown VA Medical Center, Mental Health Service Line, 820 S. Damen Avenue, Chicago, IL 60612, United States
[d] University of Illinois-Chicago, Department of Anatomy and Cell Biology, and The Graduate Program in Neuroscience, 808 S. Wood Street Chicago, IL 60612,United States

ABSTRACT

Background: Recent laboratory studies have shown that acute alcohol intoxication selectively and effectively dampens aversive responding to uncertain threat. An emerging hypothesis is that individuals who exhibit heightened reactivity to uncertain threat may be especially motivated to use alcohol to dampen their distress, setting the stage for negative reinforcement processes to drive excessive alcohol use. However, no study to date has directly examined whether current problematic drinkers exhibit heightened reactivity to uncertain threat as would be expected.

Methods: The present study was therefore designed to examine the association between current problematic alcohol use and reactivity to uncertain threat during sobriety in two, independent samples. In Study 1 (n = 221) and Study 2 (n = 74), adult participants completed the same well-validated threat-of-shock task which separately probes responses to temporally predictable and unpredictable threat. Startle potentiation was measured as an index of aversive responding. Problematic alcohol use was defined as number of binge episodes within the past 30 days in Study 1 and total scores on a self-report measure of hazardous drinking in Study 2.

Results: As hypothesized, across both studies greater levels of problematic drinking were associated with greater startle potentiation to unpredictable threat. In Study 2, hazardous drinking scores were also positively associated with startle potentiation to predictable threat.

Conclusions: The findings are notably consistent with the notion that heightened reactivity to uncertain threat is an important individual difference factor associated with the onset and/or maintenance of problematic drinking behaviors and may therefore be a novel prevention and intervention target.

© 2016 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Reduction or avoidance of negative affect is a major motive for excessive alcohol use (Koob, 2003, 2013). Alcohol intoxication is thought to bring perceived relief from negative affective states, such as anxiety, thereby negatively reinforcing alcohol consumption and increasing the likelihood of using alcohol in the future (Baker et al., 2004; Khantzian, 1997). Over time, individuals may begin to rely on alcohol as a means of avoidance-based coping which significantly contributes to the onset and worsening of alcohol use disorders (Kassel et al., 2000; Robinson et al., 2011; Schroder and Perrine, 2007). In support of this, survey data indicate

that drinkers use alcohol to ameliorate negative affect (Bibb and Chambless, 1986; Robinson et al., 2009) and believe that alcohol effectively reduces their anxiety (Cox et al., 1993).

Importantly, however, laboratory studies have not consistently demonstrated that alcohol dampens negative affect or stress (Greeley and Oei, 1999; see Curtin and Lang, 2007 for a review), and it has been posited that alcohol may only be stress-dampening for certain individuals under certain conditions. Along these lines, Curtin and colleagues have conducted a series of studies clarifying the conditions by which alcohol is anxiolytic by demonstrating that acute alcohol intoxication dampens aversive reactivity during an uncertain, but not certain, threat/stress (Bradford et al., 2013; Hachiya et al., 2010; Hefner and Curtin, 2012; Moberg and Curtin, 2009). In a seminal paper, using startle potentiation as an index of aversive responding (Bradley et al., 1999), Moberg and Curtin (2009) reported that alcohol intoxication (blood alcohol concen-

tration [BAC] of 0.08%) significantly reduced startle potentiation during cues signaling unpredictable electric shock, but not during cues that signaled predictable shock. Through a series of follow-up studies, it was confirmed that as threat uncertainty increases, so does the magnitude of alcohol's stress-dampening effects and this association is both dose-dependent and generalizable across different forms of threat uncertainty including manipulations in threat timing, probability and severity (Bradford et al., 2013; Hefner and Curtin, 2012; Hefner et al., 2013). Taken together, alcohol selectively and effectively dampens aversive responding to uncertain threat and may therefore target the biological, affective and/or cognitive processes engaged by threat uncertainty.

A large body of rodent and human research indicates that uncertain threat elicits a generalized feeling of apprehension not associated with a clearly identifiable source and heightened, sustained vigilance (labeled *anticipatory anxiety*; Barlow, 2000; Blanchard et al., 1993; Davis, 1998; Herry et al., 2007; Jackson et al., 2015). Meanwhile, predictable or certain threat elicits a phasic response to an identifiable stimulus that is time-locked to the threat (*labeled* fear; Barlow, 2000; Davis et al., 2010). These aversive responses have been shown to be pharmacologically distinct (Grillon et al., 2006, 2011) and mediated by overlapping, but separable, neural circuits (Alvarez et al., 2011; Davis, 2006).

Considering this literature and the findings discussed above alcohol may be especially effective at dampening anticipatory anxiety. This is markedly consistent with early theories suggesting that alcohol intoxication impairs attentional capabilities such as sustaining vigilance and dividing attention (i.e., processes central to anticipatory anxiety; Steele and Josephs, 1990). Given that a major motive for using alcohol is the reduction or avoidance of aversive affective states, an emerging hypothesis is that those who are most sensitive and reactive to uncertain threat, and thus experiencing chronic heightened anticipatory anxiety, are the most motivated to consume alcohol to dampen their distress, setting the stage for negative reinforcement processes to drive excessive, continuous alcohol use. In other words, individuals who excessively use alcohol may experience greater anticipatory anxiety in response to uncertain threat and therefore find alcohol intoxication to be especially reinforcing. Although this points to the possibility that reactivity to uncertain threat is an important individual difference factor that connotes risk for problematic alcohol use, no study to our knowledge has directly examined whether current problematic drinkers do indeed exhibit heightened anticipatory anxiety in response to uncertain threat.

In preliminary support of this hypothesis, however, a recent investigation in a sample of undergraduates found that coping-related drinking motives were positively associated with individual differences in intolerance of uncertainty (a personality construct reflecting the view that uncertainty is distressing and intolerable), even when controlling for broad negative affectivity and anxiety sensitivity – a related personality trait which is known to be associated with problematic drinking (Kraemer et al., 2015). Thus, those who reported that they use alcohol to cope with their distress report a particular sensitivity to uncertainty. Moreover, a prior study by our laboratory found that individuals with current panic disorder (PD) and a *past* diagnosis of alcohol dependence exhibited greater startle potentiation during unpredictable, but not predictable, threat-of-shock relative to healthy controls and individuals with PD-only (Gorka et al., 2013), indicating that those with a history of problematic drinking displayed greater reactivity to uncertain threat relative to those who did not. Together, these findings provide important preliminary evidence to suggest that individuals who engage in excessive, problematic alcohol use exhibit a hyper-sensitivity to uncertain threat; however, this hypothesis remains to be directly tested. Based on prior studies, it is still unclear whether problematic drinking behaviors, rather than

just coping motives, are related to sensitivity to uncertain threat, and whether the findings from Gorka et al. (2013) were driven by the history of problematic drinking/alcohol dependence.

The present study was therefore designed to examine the association between current, problematic alcohol use and reactivity to uncertain threat during sobriety in two, independent samples (Study 1 and Study 2). In both Study 1 and Study 2, participants completed the same well-validated threat-of-shock task designed to probe responses to unpredictable and predictable threat. Startle potentiation was collected as an index of aversive responding. Current problematic alcohol use was assessed via self-reported number of alcohol binge episodes within the past 30 days in Study 1. As both a replication and an extension, in Study 2, participants completed the Alcohol Use Disorders Identification Test (AUDIT; Babor et al., 1989) – a widely used self-report measure that includes information about current drinking frequency and hazardous and problematic drinking patterns. We hypothesized that more binge episodes (Study 1) and higher AUDIT/problematic drinking scores (Study 2) would be associated with greater startle potentiation to unpredictable threat above and beyond current anxiety and depressive symptoms which have both been previously linked to threat reactivity (Grillon et al., 2013; Shankman et al., 2013).

2. Material and methods

2.1. Participants

Study 1 and Study 2 were designed to recruit adult volunteers with a range of psychiatric diagnoses, symptoms and alcohol use problems consistent with the National Institute of Mental Health (NIMH) Research Domain Criteria (RDoC) initiative. All participants were recruited via advertisements posted in the community, local psychiatric clinics, nearby college campuses and in area newspapers/websites. A variety of advertisements were used to target different populations (e.g., healthy controls, heavy drinkers, anxiety disorder patients) in an effort to enroll a diverse sample. Both studies took place at the University of Illinois-Chicago, in different laboratories, and were approved by the university Institutional Review Board. All participants provided written informed consent after review of the protocol. Study 1 and Study 2 required participants to complete a set of laboratory tasks, a battery of questionnaires and a semi-structured clinical interview. Laboratory tasks and questionnaires were administered in a counterbalanced order to eliminate potential order effects. Participants received cash as payment for participation.

As part of the larger aims for Study 1, a total of 161 biological, sibling dyads were recruited to examine familial threat and reward processes. Inclusion criteria for the larger family study included being between the ages of 18 and 30 years old and having at least one biological sibling in the same age range that was also willing and able to participate. Exclusion criteria included a personal or family history of mania or psychosis, a medical or neurological illness that may impact psychophysiological functioning (e.g., epilepsy), an inability to read or write English, a history of serious head trauma, and left-handedness. Of the 292 participants who enrolled and completed the study protocol, 71 were excluded from the study due to technical equipment failure during the startle task ($n = 19$), missing self-report data ($n = 20$), or poor quality startle eyeblink data ($n = 32$; 70% or more of the blinks in any one condition being coded as missing or non-responders or an inability to visually distinguish eyeblink responses from baseline activity). The final sample included 221 individuals (see Table 1).

Study 2 was similarly designed to examine threat processes in adults, but also how these processes change in response to treatment. As such, Study 2 included a subset of treatment seeking