



Short Communication

Sex moderates stress reactivity in heavy drinkers

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HIGHLIGHTS

- Study examined stress effects on craving and mood among heavy drinkers.
- Females showed greater stress-induced craving and negative mood than males.
- The relationship between mood and craving was stronger among females.

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ABSTRACT

Psychological stress and alcohol use disorders have a well-known connection. Individual differences in stress reactivity have been an area of interest in alcohol research, particularly given the relationship between craving and stress reactivity to later relapse. The present study examines the role of sex on stress-induced alcohol craving and emotional reactivity using a guided imagery stress paradigm. Participants were 64 non-treatment seeking heavy drinkers from the community who completed a two-session protocol that included two guided imagery exposures, Stress and Neutral. Participants reported their mood and craving before and after each exposure using the Differential Emotions Scale and the Alcohol Urge Questionnaire respectively. Analyses revealed a significant Stress \times Sex \times Trial effect on craving [$F(1,61) = 5.35; p < .05$] after controlling for AUDIT scores [$F(1,61) = 8.16; p < .01$] such that females reported greater increases in craving from baseline to post-imagery during the stress imagery versus the neutral imagery condition, than did males. Mood reactivity analysis showed similar patterns. Specifically, there was a significant Stress \times Sex \times Trial effect on the anxiety subscale of the DES [$F(1,61) = 15.81; p < .001$] such that females reported greater increases in anxiety from baseline to post-imagery during the stress imagery versus the neutral conditions, than did males. These results suggest that female heavy drinkers were more sensitive to the effects of the stress-induction on alcohol craving and mood reactivity than males. If supported by future studies, these initial findings may help advance understanding of the mechanisms of stress and mood regulation as central to alcoholism liability and recovery in females.

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1. Introduction

The link between psychological stress and alcohol use disorders is well established (Pohorecky, 1991). Data from the National Epidemiological Survey on Alcohol and Related Conditions (NESARC) showed that greater number of life stressors were associated with greater levels of frequent heavy drinking (Dawson, Grant, & Ruan, 2005). In laboratory settings, stress induction has been shown to provoke physiological reactivity and lead to subsequent drinking (Thomas, Bacon, Randall, Brady, & See, 2011).

Given the relation of craving and stress reactivity to later relapse (Bottlender & Soyka, 2004; Brown, Vik, Patterson, Grant, & Schuckit, 1995), individual differences in stress reactivity have been an area of interest in alcohol research. Many studies have utilized the Trier Social Stress Task (TSST; Kirschbaum & Pirke, 1993) for laboratory stress induction. However, this paradigm relies on an individual's social and performance anxiety to induce stress. The present study utilized guided imagery (Sinha et al., 2009) to recreate a stressful event unique to the individual, thus boosting external validity relative to the TSST, which has been shown to be effective in drug abusing populations (Fox et al., 2005).

Further, sex is an important consideration in stress reactivity research. A human laboratory study of healthy social drinkers using guided imagery for stress induction found that women showed greater negative emotional response than men and that men's alcohol craving was associated with higher subjective emotional responses (Chaplin, Hong, Bergquist, & Sinha, 2008). The aforementioned study, however,

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showed no sex differences in alcohol craving. In a study of heavy drinkers using the TSST for stress induction, men consumed more alcohol post-stress than women (Nesic & Duka, 2006). Studies of sex differences in alcohol craving have also yielded mixed results. For example, Willner, Field, Pitts, and Reeve (1998) reported that male, but not female, social drinkers showed greater craving for alcohol after consumption of a priming dose of alcohol (i.e., small alcoholic beverage). In a study of cue reactivity, it was found that women were more reactive to alcohol cues than men when in a negative mood state (Rubonis, Colby, Monti, Rohsenow et al., 1994). While the cognitive mechanisms by which individuals may be more vulnerable to stress and/or cue-induced craving remain opaque, recent studies have found that rumination (Caselli, Bortolai, Leoni, Rovetto, & Spada, 2008; Caselli et al., 2010) and desire thinking (Caselli & Spada, 2011) predict drinking status broadly. Rumination, defined as a passive focus on one's symptoms of distress and possible causes and consequences of those symptoms, has been found to be elevated among females (Nolen-Hoeksema & Jackson, 2001). Desire thinking, defined as voluntary cognitive processing involving verbal and imaginal elaboration of a desired target (Caselli & Spada, 2011), may also serve to maintain cue-induced craving. In fact, Kavanagh, Andrade, and May (2004) argue that one's ability to accept the occurrence of craving and reduce the elaboration of desire is an effective strategy to cope. Therefore it is plausible, yet remains untested, that females may experience greater stress and cue-induced craving as a function of elevations in rumination or desire thinking. Interestingly, the aforementioned associations between rumination and drinking status hold even after controlling for co-occurring depressive symptoms (Caselli et al., 2008; Caselli et al., 2010). According to this line of research, individuals with such preservative cognitive styles may hold stressful information in mind longer and perhaps even elaborate on its content, thus leading to greater increases in alcohol craving.

In light of the literature associating sex with stress reactivity and alcohol craving, this study examines the role of sex on stress-induced alcohol craving and emotional reactivity in heavy drinkers. Specifically, this study tests whether gender moderates stress reactivity at the level of both mood reactivity (i.e., positive mood, negative mood, and anxiety) and stress-induced craving for alcohol. This may be especially important given recent evidence that the sex gap in alcohol use may be closing ("Vital signs: Binge," 2013; Keyes, Grant, & Hasin, 2008). Based on the aforementioned studies, it is hypothesized that men will report greater stress-induced alcohol craving than women, and that women will show greater negative emotional response to stress induction than men. Moreover, this study will utilize guided imagery, an ecologically valid approach, to examine this relationship and will control for symptoms of depression and anxiety, which may bias stress-reactivity.

2. Methods

2.1. Participants and procedures

Non-treatment seeking heavy drinkers were recruited from the Los Angeles community (N = 64). Inclusion criteria were: age 18–65 and an Alcohol Use Disorder Identification Test (AUDIT; Saunders, Aasland, Babor, De La Fuente, & Grant, 1993) score of 8 or higher to verify heavy drinking levels. Exclusion criteria included: current or past 30-day treatment for alcohol problems; lifetime diagnosis of schizophrenia, bipolar or psychosis; current, regular use of psychoactive drugs, other than marijuana. Data for this study were culled from a previous investigation of genetic determinants of stress reactivity (Ray, 2011).

Following a telephone screen, participants were invited to complete a two-session protocol. At the first session participants provided written informed consent and completed self-report measures at which time a Breath Alcohol Concentration (BrAC) of 0.00 g/dl was required. Additionally, participants provided information about a recent non-traumatic, stressful, *unresolved* event and a neutral event. Events

were coded as one of four types: interpersonal, medical, achievement, or environmental. The participants then received relaxation training and imaginal exposure training in order to enhance completion of the guided imagery protocol. At the second visit, participants completed two guided imagery exposures, Stress and Neutral, each consisting of 5-minute tape-recorded scripts recounting the events described by participants at the first visit (Sinha, 2009; Sinha, Fuse, Aubin, & O'Malley, 2000). Guided imagery exposures were conducted one hour apart. Experimental conditions were conducted one hour apart and in randomized and counterbalanced order to avoid carryover effects (see Ray, 2011). All procedures were approved by the UCLA Institutional Review Board for Human Research. Participants were compensated \$50 for completing the study.

2.2. Measures

The following measures were administered pre and post neutral and stress exposures during the protocol.

2.2.1. Alcohol Urge Questionnaire (AUQ)

The AUQ, an 8-item scale, was used to assess state levels of alcohol craving using a 7-point Likert scale (Bohn, Krahn, & Staehler, 1995). Observed Cronbach alphas for the AUQ ranged from .92 to .94 across administrations showing excellent reliability.

2.2.2. Differential Emotions Scale (DES)

The DES is 31-item measure of mood, including positive mood, negative mood, and anxiety. Mood items on the DES are rated on a 5-point Likert scale (Sinha et al., 2009). The positive mood subscale had Cronbach alphas ranging from .89 to .93, the negative mood subscale ranged from .76 to .88, and the anxiety subscale ranged from .58 to .73.

2.2.3. Beck Depression Inventory (BDI-II)

The BDI-II is a 21-item measure which assesses for depressive symptoms present over the past two weeks (Beck, Steer, & Brown, 1993). Scores range from 0 to 63 with a total score above 20 indicating moderate to severe depression.

2.2.4. Beck Anxiety Inventory (BAI)

The BAI is a 21-item measure of anxiety symptoms present over the past week (Beck & Steer, 1993). Scores range from 0 to 63 and total scores above 16 are indicative of moderate to severe anxiety.

2.3. Data analysis plan

To test the study hypothesis regarding sex differences on stress reactivity, a series of mixed design analysis of variance (ANOVAs) were conducted in which Imagery (Stress versus Neutral) and Trial (Before and After Imagery) were within-subject factors, Sex was a between-subjects factor, and scores on mood and alcohol craving were the dependent measures. New variables were created to represent differences between post-stress and pre-stress mood, and post-stress and pre-stress craving, in order to examine the relationship between craving and mood during stress induction. Given that there were differences by sex on measures of alcohol use and alcohol problems (i.e., AUDIT), these variables were entered in the models as covariates. Additionally, BAI, BDI-II, and stressor type were added to the models, one at a time, as covariates.

3. Results

3.1. Participant characteristics

The mean age of the sample was 20.75 (SD = 2.64). The majority of the sample was employed part-time or were full-time students

(73.4%), while the remainder of the sample was either employed full-time (7.8%) or unemployed (18.8%). All participants reported they were never married (100%). The ethnic composition of the sample was the following: 73.4% Caucasian, 17.2% Asian, 7.8% African American, and 1.6% Latino. The sample had a mean AUDIT score of 15.61 (SD = 5.49) and reported an average of 11.76 drinking days in the past month (SD = 7.27). The average number of drinks per drinking day in the past month was 5.91 (SD = 2.81).

Males and females did not significantly differ in age. Males and females differed significantly on ethnicity, $\chi^2(3, N = 64) = 14.45$, $p < 0.05$ in that 48% of females versus 88% of males were Caucasian. Males and females differed significantly on AUDIT score, $t(60) = -3.51$, $p < 0.001$, such that males scored higher than females (Mean AUDIT = 12.9 (3.8) vs. 17.1 (5.8)). Additionally, males reported significantly more drinks per episode, $t(60) = -2.34$, $p < .05$ (6.5 vs. 4.8), and higher number of drinking days, $t(60) = -3.43$, $p < 0.01$ (13.8 vs. 7.8), than females. Men and women did not differ on type of stressor experienced ($\chi^2(1, N = 64) = .095$, $p > .05$).

3.2. Stress-induced craving

Analyses revealed a significant Imagery \times Sex \times Trial interaction effect on craving [$F(1,61) = 5.35$; $p < .05$, partial $\eta^2 = 0.081$], after controlling for AUDIT scores [$F(1,61) = 8.16$; $p < .01$], such that females reported greater increases in craving from baseline to post-stress versus the neutral imagery condition, than did males (see Fig. 1). The stress \times sex \times trial interaction remained significant after controlling for BAI [$F(1,33) = 5.57$; $p < .05$], BDI-II [$F(1,60) = 5.51$; $p < .05$], and stressor type [$F(1,60) = 5.30$; $p < .05$]. There was not a main effect of sex on craving [$F(1,61) = 1.44$; $p = .23$]. In addition, the Stress \times Sex interaction was also significant [$F(1,61) = 4.92$; $p < .05$], such that females had greater overall craving in the stress condition.

3.3. Stress-induced mood changes

A similar pattern of results emerged for mood reactivity following the stress-induction paradigm. Specifically, there was a significant Stress \times Sex \times Trial effect on the anxiety subscale of the DES [$F(1,61) = 15.81$; $p < .001$, partial $\eta^2 = 0.206$] such that females reported greater increases in anxiety from baseline to post-imagery during the stress imagery versus the neutral conditions, than did males (see Fig. 2). This effect remained significant after controlling for BAI [$F(1,34) = 13.76$; $p < .001$], BDI-II [$F(1,60) = 14.35$; $p < .001$], and stressor type [$F(1,60) = 15.72$; $p < .001$]. There was also a main effect of sex [$F(1,61) = 5.73$; $p < .05$] and a Stress \times Sex interaction

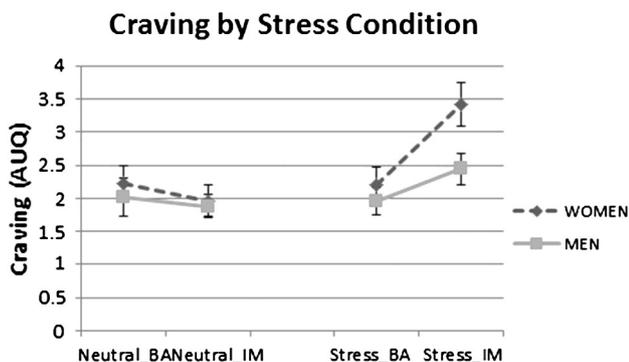


Fig. 1. Mean (and standard error bar) alcohol craving (AUQ score) before and after neutral imagery and before and after stress imagery for males and females. Analyses controlled for AUDIT scores.

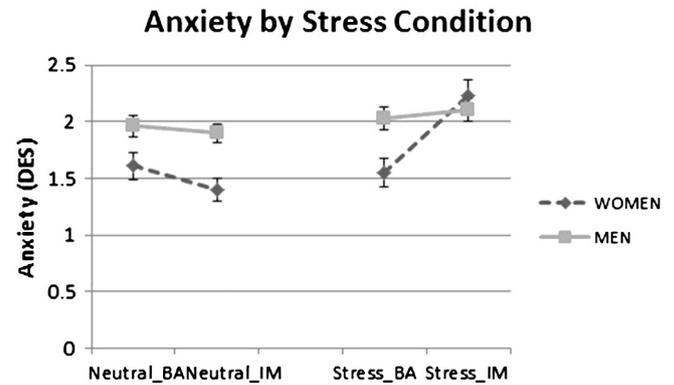


Fig. 2. Mean (and standard error bar) self-reported anxiety (DES score) before and after neutral imagery and before and after stress imagery for males and females. Analyses controlled for AUDIT scores.

[$F(1,61) = 6.73$; $p < .05$] such that females had greater overall anxiety, particularly during the stress imagery condition. No significant relationships were observed for negative mood [$F(1,61) = 2.0$; $p = .16$, partial $\eta^2 = 0.032$] or positive mood [$F(1,61) = 0.45$; $p = .50$, partial $\eta^2 = 0.007$]. The results for negative [$F(1,60) = 2.02$; $p > .05$] and positive [$F(1,60) = .44$; $p > .05$] mood remained unchanged after controlling for stressor type.

3.4. Relation between mood and craving during stress induction

In the full sample, stress-induced anxiety was significantly related to stress-induced craving [$F(1,59) = 21.7$; $p < .0001$]. This result was driven by females, as the association between anxiety and craving was significant in females [$t(21) = 5.45$; $p < .0001$] but not in males [$t(38) = -0.61$; $p > .54$]. Negative mood in response to stress induction was also predictive of higher craving during stress [$F(1,59) = 4.11$; $p < .05$] and this was significant for both males [$t(38) = 2.44$; $p < .02$] and females [$t(21) = 3.82$; $p < .001$]; albeit the magnitude of the relationship was stronger for females. No significant relationship was observed between stress-induced changes in positive mood and stress-induced alcohol craving [$F(1,61) = 1.83$; $p = .22$].

4. Discussion

The results of this study demonstrate that sex moderates stress reactivity in the lab among heavy drinkers. Specifically, we found that females reported greater craving and greater anxiety after stress induction than their male counterparts, suggesting that females were more sensitive to the stress induction than males. Furthermore, stress-induced craving and stress-induced anxiety were associated in females but not in males. Likewise, stress-induced increase in craving was related to the increase in negative mood for women at a higher level than for men. These results suggest that the relationship between stress-induced craving and mood is moderated by sex. In particular, there is a stronger relationship between anxiety and negative mood, following stress induction, in females as compared to males.

The finding that women had greater negative emotional response to the stress paradigm is consistent with Chaplin et al. (2008) results with heavy social drinkers. However, this study differs from Chaplin in that the women in the present study exhibited greater craving than the men. This study also contrasts with Nesci and Duka (2006) and Willner et al. (1998) studies of heavy drinkers that respectively reported higher alcohol consumption and higher craving in male subjects than in females. These studies however, used distinct methodologies, such as the TSST, followed by alcohol self-administration (Nesci & Duka, 2006) and administration of a priming dose of alcohol (Willner et al., 1998). In brief, experimental paradigms seem to converge on greater affective reactivity in females versus males. The present study suggests that in

heavy drinkers, females have stronger associations between stress-induced craving, stress-induced anxiety and negative mood, than males. While the specific mechanism by which females may be more vulnerable to stress-induced craving and negative mood remains unclear, it is plausible that gender differences in rumination may mediate this effect. The present study did not collect data on rumination or desire thinking as cognitive styles, thus it is not possible to examine this hypothesis empirically.

There is some evidence that the sex gap in drinking prevalence is getting smaller (Center for Disease Control, 2013; Keyes et al., 2008) and that the heritability of alcoholism does not differ by sex (Prescott & Kendler, 2000). Moreover, a recent study found that childhood maltreatment and other life stressors were predictive of later stress-related drinking among women (Young-Wolff, Kendler, & Prescott, 2012). These results are consistent with the present findings and suggest a mechanism by which life stressors may predispose females to heavy drinking, namely by triggering negative mood and anxiety, which in turn are associated with greater alcohol craving in females and much less so in males.

In summary, the present study extends the literature on stress-induced craving and mood reactivity by suggesting that females are more reactive to stress, via craving and negative mood, than males. Importantly, the association between stress-induced increases in craving and increases in negative mood/anxiety is stronger in females than in males. These results held after controlling for type of stress as well as current symptoms of depression and anxiety. These findings advance a mechanism by which females may be more vulnerable to heavy drinking than males, thus offering unique avenues for prevention and intervention. This experimental study relied on an ecologically valid stress manipulation task in a sample of heavy drinkers. Limitations of the study include the subclinical nature of the sample comprised of heavy drinkers, which may limit generalizability. In addition, the lack of biomarkers of stress reactivity, such as cortisol or skin conductance, represents a limitation of the present study. Replication in clinical samples and with biomarker verification is warranted to extend the present finding. Exploration of cognitive styles, such as rumination and desire thinking, should also be considered as a plausible mechanism of alcohol craving, which in turn may be moderated by gender.

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Contributors

Dr. Ray designed the study and wrote study protocol. Ms. Hartwell conducted literature searches and wrote the first draft of the manuscript. Both authors conducted statistical analyses and approved the final draft.

Conflict of interest

The authors declare that they have no competing financial interests or conflict of interest relating to the data included in this manuscript. The authors declare that, except for income received from primary employer, no financial support or compensation has been received from any individual or corporate entity relevant to the data in this manuscript. There are no personal financial holdings that could be perceived as constituting a potential conflict of interest for this manuscript.

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