ABSTRACT
The stress reducing properties of alcohol are well known and occasionally pursued by all drinkers. However, individuals who drink primarily for stress reduction are at increased risk for developing alcohol use disorders. Moreover, stress exposure is a powerful precipitant for relapse to alcohol use among dependent users. Thus understanding the mechanisms underlying alcohol’s effect on stress is critical for understanding both social and problematic alcohol use.

Research with both animals (Sullivan et al., 2004; Walker & Davis, 1997) and humans (Grillon et al., 2006; Hoge & Curtin, 2006) has synthesized precise laboratory manipulations of stress with sensitive measurement procedures to parse stress response into fear and anxiety through the manipulation of threat contingencies. Specifically, research has suggested that contingent vs. non-contingent aversive stimuli elicit fear vs. anxiety, respectively. The primary aim of this study was to test if alcohol would reduce anxiety in response to non-contingent shocks but would not affect fear response to contingent shocks. Intoxicated (BAC=0.08%) and non-intoxicated participants viewed a series of colored squares separated by a variable inter-trial interval (ITI) in three conditions. In the first condition, electric shocks were contingently paired with square presentation such that shocks were administered during every square. In the second condition, shocks were administered non-contingently (i.e., during both squares and ITI). In the third condition, no shocks were administered.

Alcohol selectively reduced startle potentiation during the blocks of non-contingent shocks but did not attenuate startle potentiation in response to contingent shock administration. These results suggest that alcohol has selective effects on anxiety but not fear. This anxiety/fear effect may be a mechanism underlying alcohol’s reinforcing effects in social drinkers. Moreover, synthesis with extant data suggests that the neural substrate of this anxiety effect may be a target for neuropsychiatric change supporting addicted use in alcohol dependent individuals.

BACKGROUND & HYPOTHESES
- Individuals who drink to reduce stress are at increased risk for developing alcohol use disorders; stress is a powerful precipitant of relapse in abstinent dependent users.
- Alcohol challenge research using fear-potentiated startle (FPS) has begun to clarify when and how alcohol reduces stress.
- Moderate doses of alcohol do not reduce FPS to simple, punctate threats that elicit fear (Curtin et al., 2001).
- Precise experimental methods to elicit fear vs. anxiety in humans have been developed (Grillon et al., 2006).
- Preclinical research suggests that the neurobiological substrates of fear vs. anxiety may be dissociable (Walker et al., 2003).
- Preclinical research has suggested alcohol selectively impairs conditioning to context but not to specific threat cues (Mello et al., 1996).
- In humans, anxiolytic drugs (e.g., alprazolam, diazepam) have larger effects on response to anxiety vs. fear manipulations (Baas et al., 2002; Grillon et al., 2006).
- Hypothesis: A moderate dose of alcohol will selectively reduce anxiety but not fear.

METHOD
Participants
- 64 healthy social drinkers
- Two beverage groups: Alcohol (target BAC: 0.08%) and placebo.

General Procedure
- All participants completed a pre-drink baseline startle assessment and a post-drink emergence of tolerance assessment.
- Participants viewed blocks of 6s colored square “cue” presentations separated by an inter-trial interval (range 19-23s).
- Shock contingency was manipulated within subjects across three block types
  - No Shocks: No shocks administered
  - Predictable Shocks: Shocks administered during every red square cue
  - Unpredictable Shocks: Shocks administered during both blue cues and ITI

Block Orders: PUNUNP or UNPNPU

Measures
- EMG eyblink startle response to noise probes was measured during both cue presentation and ITIs in all blocks. Scored as peak response in 20-120ms post-probe onset. Analyses of both raw startle response and potentiated startle (vs. no shock blocks) were conducted.

DISCUSSION/FUTURE DIRECTIONS
- Precise manipulations of eliciting stimuli (e.g., shock-cue contingencies) and startle response measurement may provide a method to parse fear vs. anxiety, which, as animal research indicates, have dissociable neural substrates.
- Both manipulations succeeded in potentiating startle, but these data suggest a selective effect of moderate doses of alcohol on anxiety but not fear.
- This observation may help resolve the heterogeneity of findings regarding alcohol’s “stress response dampening” effects. The data highlight the importance of carefully considering the emotion-eliciting stimuli used in research, with specific attention to intensity, timing, predictability, and complexity.
- The selective effect may help explain the pattern of co-morbidity of alcohol use disorders with anxiety disorders.
- Alcohol’s effects on the neurobiological substrates of anxiety may be one target for neuropsychiatric change supporting alcohol (and other drug) dependence. Future work should consider this possibility by examining differential startle response potentiation in withdrawn dependent users.

RESULTS
- The main effect of Beverage group was significant (p < .001).
- The main effect of Block type was significant (p < .001). Startle response during cues was significantly potentiated in both predictable (p < .001) and unpredictable (p < .001) blocks relative to no shock blocks.
- The Beverage group X Block type interaction was significant (p = .04).
- The simple effect of Beverage group was NOT significant during predictable blocks (p = .020).
- The simple effect of Beverage group was significant during unpredictable blocks (p = .013).

Beverage group
- Alcohol
- Placebo

Shocks (N)
- No Shocks (N)
- Predictable Shocks (P)
- Unpredictable Shocks (U)

Startle probe Electric shock

MANIPULATION CHECK
- The Block type X Condition (cue vs. ITI) interaction was significant (p < .001).
- The Condition effect was significant in predictable blocks (p < .001).
- The Condition effect was NOT significant in unpredictable blocks (p = .903).
- Startle response during cues was significantly higher in predictable (p < .001) and unpredictable blocks (p < .001) than in no shock blocks.

Startle Response
- The main effect of Beverage group was significant (p < .001).
- The main effect of Block type was significant (p < .001). Startle response during cues was significantly potentiated in both predictable (p < .001) and unpredictable (p < .001) blocks relative to no shock blocks.
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Alcohol Selectively Affects Anxiety But Not Fear
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