Alcohol Effects on Affective Response During Variable and Fixed Duration Threat
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ABSTRACT
Recent research indicates that fear and anxiety are distinct processes with separable neurobiological substrates. Experimental procedures using predictable vs. unpredictable shock administration have been used to elicit fear vs. anxiety, respectively (Grillon et al., 2004). Using these procedures, our lab has demonstrated that alcohol reduces anxiety to unpredictable shock but not fear to predictable shock (Moberg & Curtin, 2009). However, this manipulation of predictability varied both the probability and temporal precision of threat, raising critical questions as to which stimulus characteristics are central to both the elicitation of anxiety and the anxiolytic effects of alcohol.

To disentangle these two characteristics, we developed a novel paradigm to systematically vary temporal occurrence of threat while holding the probability of threat occurrence constant. Intoxicated (0.08% BAC), non-intoxicated, and placebo participants viewed a series of visual cues. Fixed 5s cue presentations were equivalent to predictable shock cues that elicited fear in earlier research. Variable duration cues (5s, 20s, 50s, or 80s) were designed to elicit anxiety due to the temporal uncertainty of the threat occurrence. Startle potentiation (SP) relative to matched cue periods in no-shock blocks provided the primary measure of affective response.

All shock cues produced robust SP. Additionally, two key findings were observed. We first examined affective response during the first 4 seconds of the cue presentation, such that startle probe occurrence was matched between variable and fixed duration blocks. We found that alcohol significantly reduced SP during variable threat duration cues, whereas there was no detectable alcohol effect during fixed threat duration cues. We then examined affective response later during each variable duration cue. We found that alcohol reduced SP during later time points in the longer cues, suggesting that the alcohol effects persist over time.

These results build on evidence suggesting that fear and anxiety are distinct, separable affective responses, and suggest that anxiety can be elicited by altering either threat probability or temporal precision. Underpinning previous findings that alcohol selectively reduces anxiety but not fear, this work has important implications for high rates of comorbidity between anxiety disorders and alcoholism.

BACKGROUND & HYPOTHESIS
- **Startle Reflex**: The startle reflex is used to assess affective response to threat (e.g. electric shock; see Davis et al., 2010). Measurement of the startle reflex is non-invasive, operates outside of consciousness, and can be assessed across species.
- **Fear vs. Anxiety**: Fearous (brief) startle potentiation (SP) is observed when threat is highly predictable, certain, and imminent. These manipulations have been used to model fear in the lab. Sustained SP is observed when threats are more distal, tonic, uncertain, or otherwise unpredictable. These manipulations have been used to model anxiety in the lab.
- **Animal Models**: Animal models have implicated the central nucleus of the amygdala (CeA) in fear whereas the bed nucleus of the stria terminalis (BNST) has been implicated in anxiety.

**Alcohol Effects on Affective Response**
- Moberg and Curtin (2009) demonstrated that alcohol selectively reduced SP to uncertain but not certain threat cues using a manipulation of predictability. This unpredictability manipulation confounded threat probability with threat imminence.
- A recent experiment by our lab (Hefner & Curtin, in prep) has demonstrated that alcohol reduces SP during blocks where threat occurs during 20% of cues but not during blocks on which participants are shocked on every trial.
- The current study aimed to further examine the aspect of threat imminence and whether alcohol equally affects proximal and distal threats.

**Hypothesis**: A moderate dose of alcohol will selectively reduce startle potentiation during stimuli of variable (unpredictable) duration.

METHOD
- **Participants**: 72 social drinking undergraduates
- **Three beverage groups**: Alcohol (target BAC: 0.08%), placebo, and no alcohol
- **General Procedure**: All participants completed a pre-drink baseline startle assessment and a post-drink shock tolerance assessment.
- **Participants viewed blocks of colored square "cue" presentations separated by an inter-trial interval**
  - There were four types of block:
    1. Variable duration shock
    2. Variable duration no shock
    3. Fixed duration shock
    4. Fixed duration no shock

**Analytic Design**
- **Cue Type (within subjects)**: 2 types (Fixed vs. Variable)
- **Beverage Group (between subjects)**: 3 groups: No Alcohol, Placebo, and Alcohol, collapsed into 2 groups: Control (No Alcohol & Placebo) vs. Alcohol

**Startle Potentiation by Beverage Group and Cue Type**
- **Startle response during cues was significantly reduced (p = .021)** and alcohol reduced SP by only 9.54 µV during variable cue blocks, the effect of beverage group was significant (p=.016).
- **The main effect of Beverage group was not significant (p = .075)**.
- **The Beverage group X Cue type interaction was significant (p = .029)**.
- **Within fixed cue blocks, the Beverage group effect is not significant (p = .368)**; alcohol reduced SP by only 9.54 µV.
- **Within variable cue blocks, the Beverage group effect is significant (p = .014)**; alcohol reduced SP by 27.24 µV.
- **There was a main effect of beverage group, (p=.016)**
- **The Beverage group X Probe time (First vs. Later) interaction was not significant (p = .80)**
- **The simple effect of beverage group on startle potentiation for first probe is significant (p = .014)**; alcohol reduced SP by 27.24 µV.
- **The simple effect of beverage group on startle potentiation for the average of 3 later probes is significant (p = .021)**; alcohol reduced SP by 25.81 µV.

**REFERENCES**

Hefner, K.R. & Curtin, J.J. (in prep)

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