



Alcohol Effects on Affective Response During Variable and Fixed Duration Threat



Laura Y. Hachiya, Christine A. Moberg & John J. Curtin

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 shock 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 duration threat cues, whereas there was no detectable alcohol effect during fixed duration threat 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. Underscoring 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

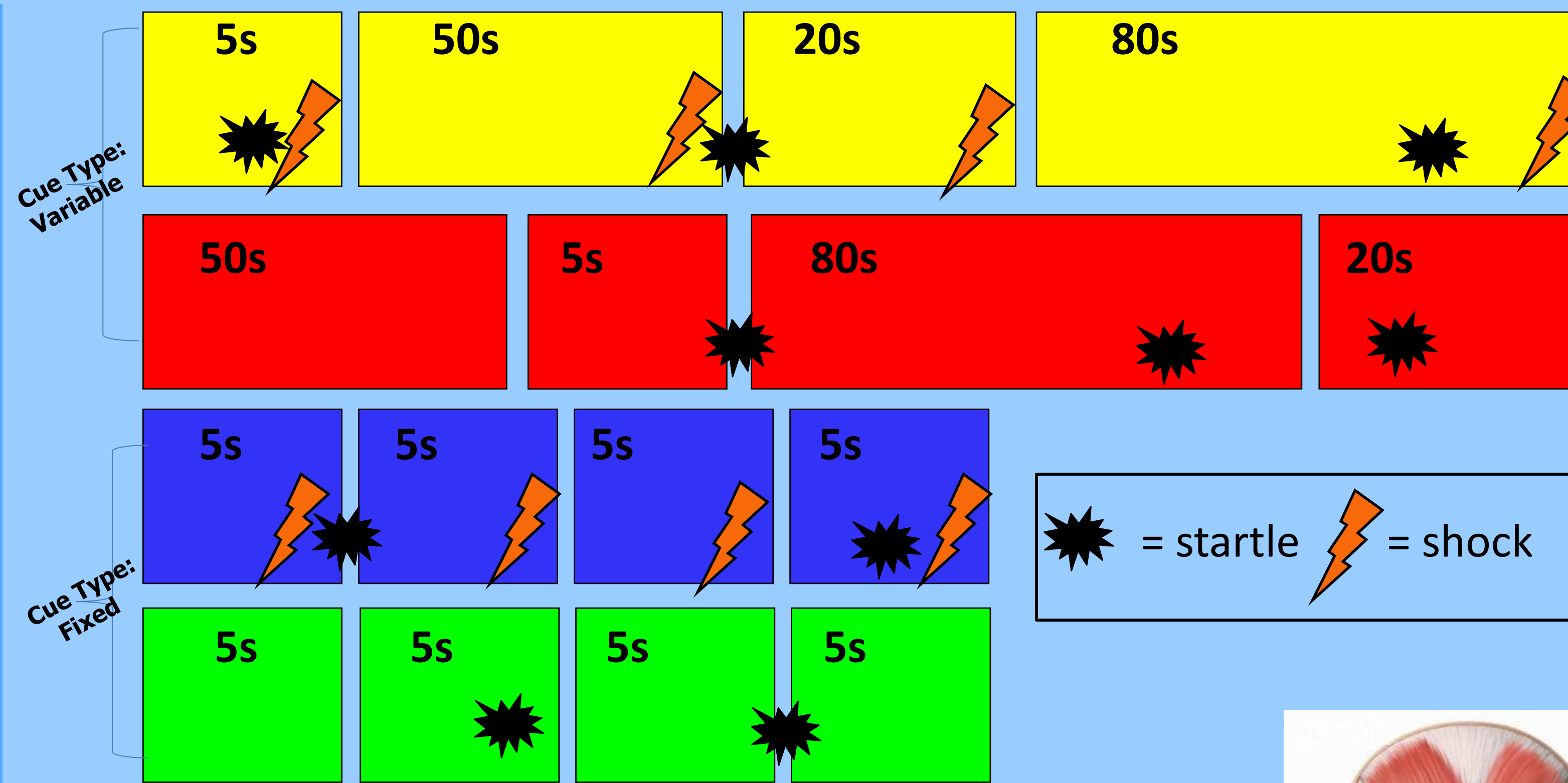
- Phasic (brief) startle potentiation (SP) is observed when threat is highly predictable, certain, and imminent. These manipulations have been used to model **fear** in the lab.
- Sustained SP is observed when threats are more distal, tonic, uncertain, or otherwise unpredictable. These manipulations have been used to model **anxiety** in the lab.
- Animal models 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

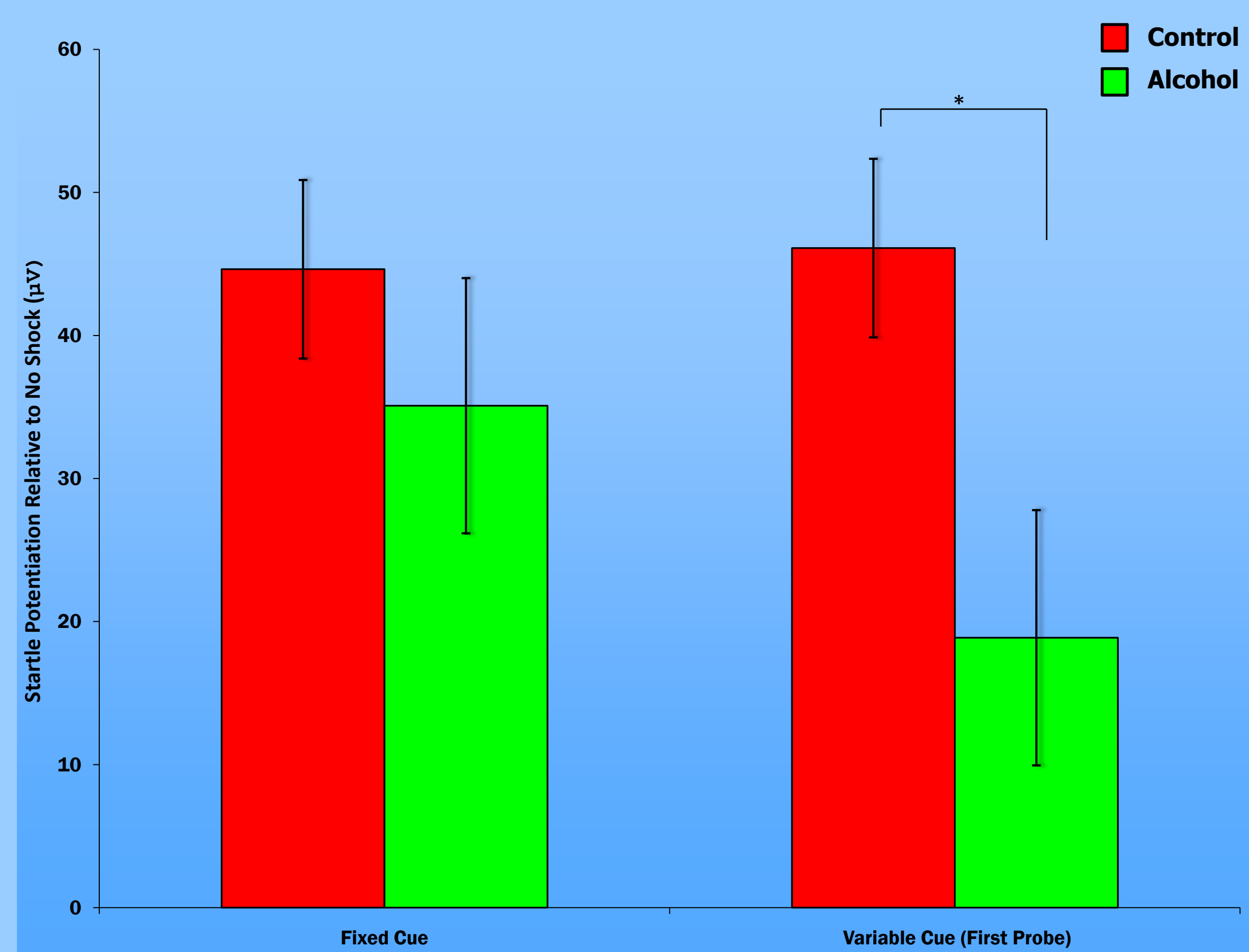
- A moderate dose of alcohol will selectively reduce startle potentiation during stimuli of variable (unpredictable) duration



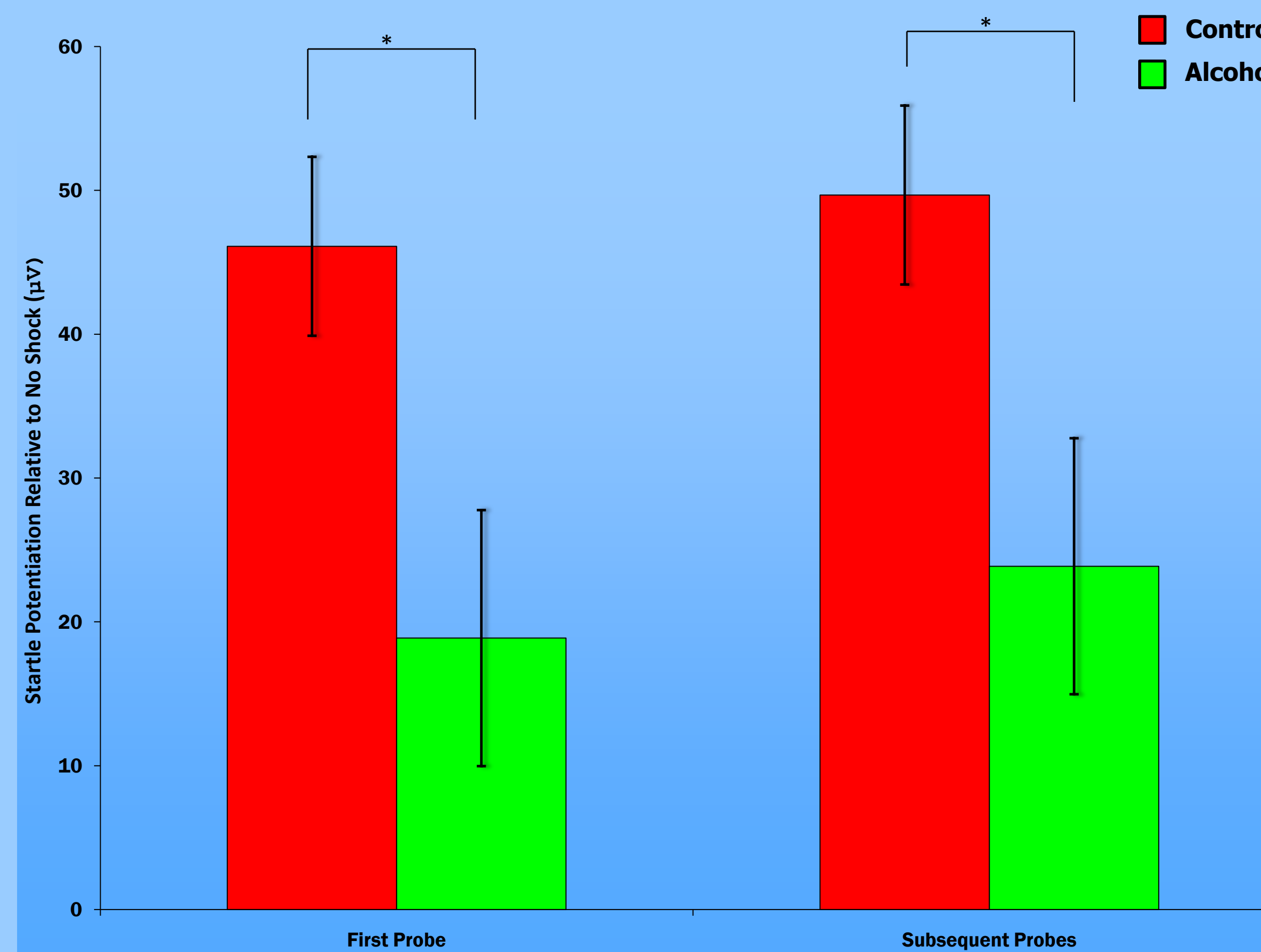
Analytic Design

- **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 Potentiation During Variable Shock Blocks



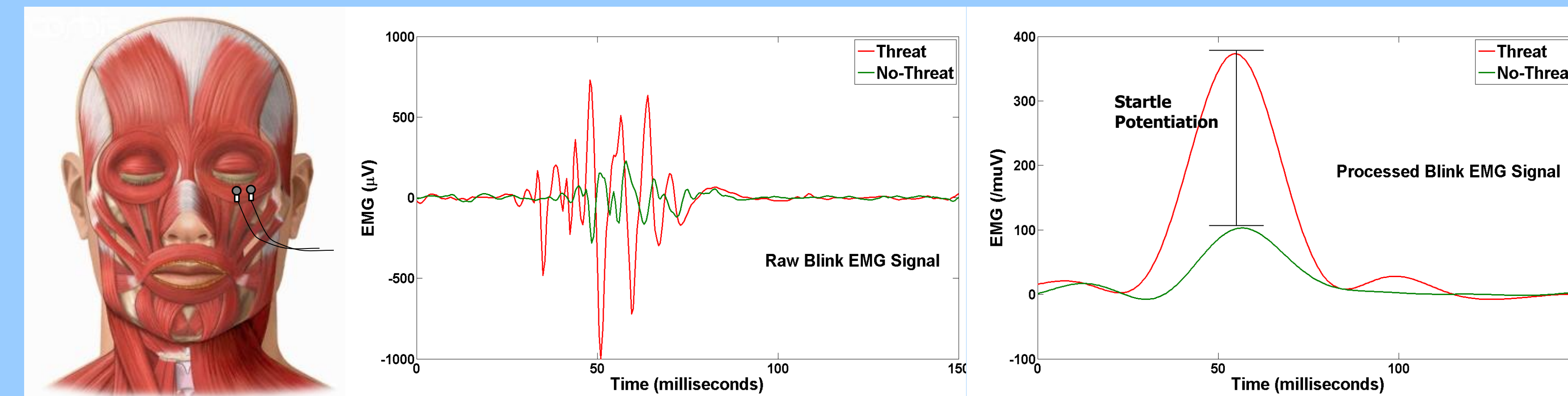
Participants

- 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

METHOD



Measures

- EMG eyeblink startle response to noise probes scored as peak response in 20-120ms post-probe onset
- Potentiation scores are calculated as the startle response to a given probe during a shock block minus startle response magnitude to the corresponding probe during no shock block
- Startle response during cues was significantly potentiated in both fixed shock ($p < .001$) and variable shock ($p < .001$) blocks relative to fixed and variable no shock blocks
- 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** ($p = .388$); 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

INTERPRETATIONS

- We have conceptually **replicated** the finding from Moberg & Curtin (2009) that alcohol selectively reduces startle potentiation during uncertain threat
- We have **extended** those findings by demonstrating alcohol's selective effect using a different manipulation of uncertainty, occurrence in time.
- This study design also allowed us to demonstrate that alcohol dampened participants' startle potentiation over a longer period of time
- Animal models have identified the neural structures responsible for startle response to variable (long) duration cues. The synthesis of the current results with the findings of such preclinical studies may help identify the brain structures which are affected by acute intoxication
- Alcohol's effects on the neurobiological substrates of anxiety may be one target for neuroplastic change supporting alcohol (and other drug) dependence.
- This selective effect may account for the pattern of comorbidity of alcohol use disorders with anxiety disorders.

REFERENCES

- Davis, M., et al. (2010) *Neuropsychopharmacology Reviews*, 35, 105-135.
 Hefner, K.R. & Curtin, J.J. (in prep)
 Moberg, C.A. & Curtin, J.J. (2009). *Journal of Abnormal Psychology*, 118(2), 335-347.

This work was supported by a grant to John Curtin from NIAAA (R01 AA15384) and a grant to Christine Moberg from NIAAA (F31AA018608-01).