

Alcohol Effects on Affective Response During Variable and Fixed Duration Threat

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

khefner@wisc.edu

ABSTRACT

Recent research indicates that fear and anxiety are distinct processes with separable neurobiological substrates. Predictable vs. unpredictable shock administration procedures have been used to elicit fear vs. anxiety, respectively, and we have recently demonstrated that alcohol reduces anxiety to unpredictable shock but not fear to predictable shock. However, previous manipulations of predictability have varied both the probability and temporal precision of shock threat, leaving looming questions as to which stimulus characteristics are central to both the elicitation of anxiety and the anxiolytic effects of alcohol. We developed a novel paradigm to systematically vary temporal presentation of threat while holding probability of threat 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 eliciting fear in earlier research. Variable duration cues (5, 20, 50 or 80s) were designed to elicit anxiety due to the temporal uncertainty of threat. Startle potentiation relative to matched cue periods in no-shock blocks provided the primary measure of affective response.

All shock cues produced robust startle potentiation. Alcohol reduced startle potentiation during the first 4s of cue presentation in variable but not fixed duration threat cues. Alcohol also reduced startle potentiation during later time points in the longer variable duration cues, suggesting that these alcohol "stress dampening" effects persist over time.

This work builds on evidence suggesting that fear and anxiety are discrete affective responses, and indicates that temporal uncertainty as well as probabilistic presentation of threat can elicit anxiety. Underscoring previous findings regarding alcohol's selective effects on anxiety, this work has implications for comorbidity between anxiety disorders and alcoholism.

BACKGROUND & HYPOTHESES

Alcohol Effects on Affective Response

- Stress-response dampening (SRD), or alcohol's tendency to reduce negative emotions such as anxiety is a motivation for drinking alcohol that is associated with problematic use.
- Previous work indicates that alcohol selectively reduces anxiety to uncertain (vs. certain) threat as measured by the **acoustic startle response** (Moberg & Curtin, 2009).

The Startle Response: Fear vs. Anxiety

- The startle reflex can be used to assess affective response to threat (e.g., electric shock).
- Recent animal research has differentiated between phasic and sustained startle potentiation (SP) and has implicated distinct, corresponding neurobiological substrates (e.g., Davis et al., 2010) of these effects.
- Phasic (brief) SP is observed to highly predictable, certain, imminent threat. Such manipulations have been used to model **fear** in the human laboratory.
- Sustained SP is observed when threats are distal, tonic ambiguous, or otherwise uncertain. Such threats are considered to model human anxiety.
- Animal models have implicated the central nucleus of the amygdala (CeA) in **fear** and the bed nucleus of the stria terminalis (BNST) in **anxiety**, respectively.

The Present Study

- Our earlier manipulation of uncertainty confounded threat probability with threat imminence (Moberg & Curtin, 2009).
- Other recent work (Hefner & Curtin, in press) precisely assessed probability effects, demonstrating that alcohol reduces SP monotonically, with greater reductions in SP as threat probability decreases.
- The current study aimed to further examine the aspect of threat imminence and alcohol's effect on SP during proximal vs. distal threats.

Hypothesis: A moderate dose of alcohol will selectively reduce startle potentiation during variable duration shock blocks (designed to elicit anxiety).

REFERENCES

Bradford DE, Kaye JT & Curtin JJ. Poster presented at: *Society for Psychophysiology Research 51st Annual Meeting*, 2011 Oct 14-19. Boston, MA. Davis M, et al. (2010) *Neuropsychopharmacology Reviews*, 35, 105-135. Gloria R & Curtin JJ. (2009). *Society for Psychophysiology Research 49th Annual Meeting*. Published Abstract. Hefner KR & Curtin JJ. (in press). *Journal of Psychopharmacology*. Moberg CA & Curtin JJ. (2009). *Journal of Abnormal Psychology*, 118(2), 335-347.

METHOD

Participants

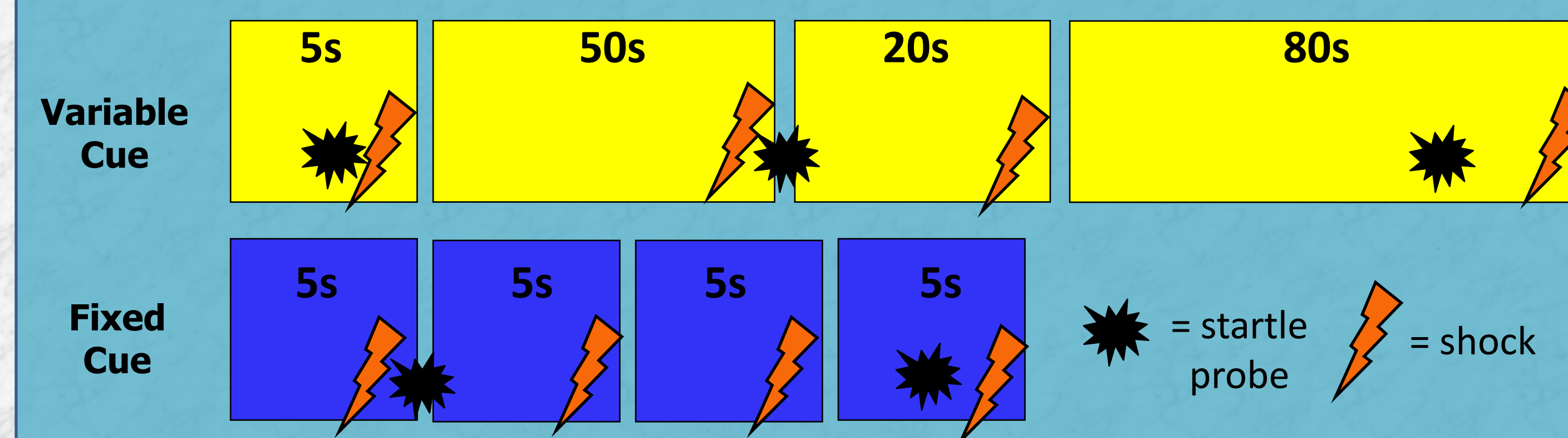
- 72 social drinking undergraduates
- Three beverage groups: Alcohol (target BAC: 0.08%), placebo, and no alcohol

General Procedure

- All participants completed a pre-drink baseline startle assessment and a post-beverage manipulation shock tolerance assessment
- Participants viewed blocks of colored square "cue" presentations separated by an inter-trial interval

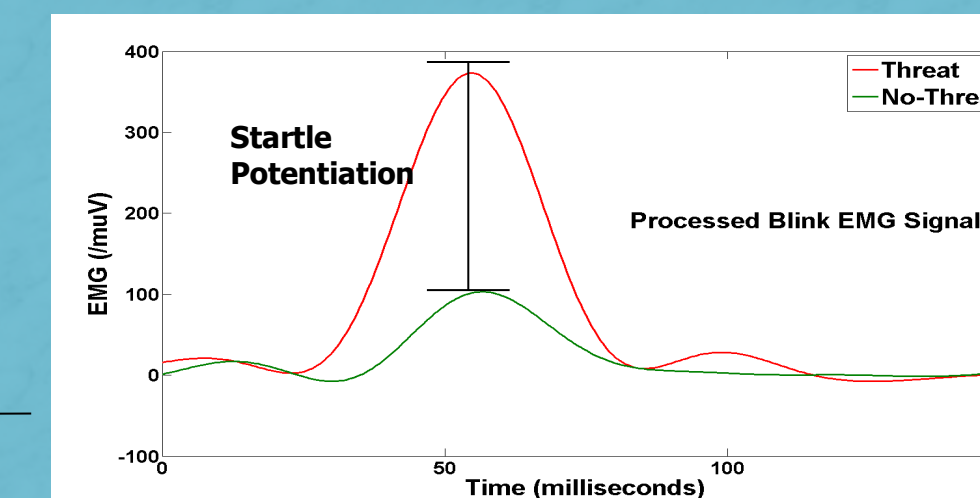
Two types of shock blocks were used and compared to corresponding no shock blocks

- Variable duration shock block
- Fixed duration shock block



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 corresponding no shock block

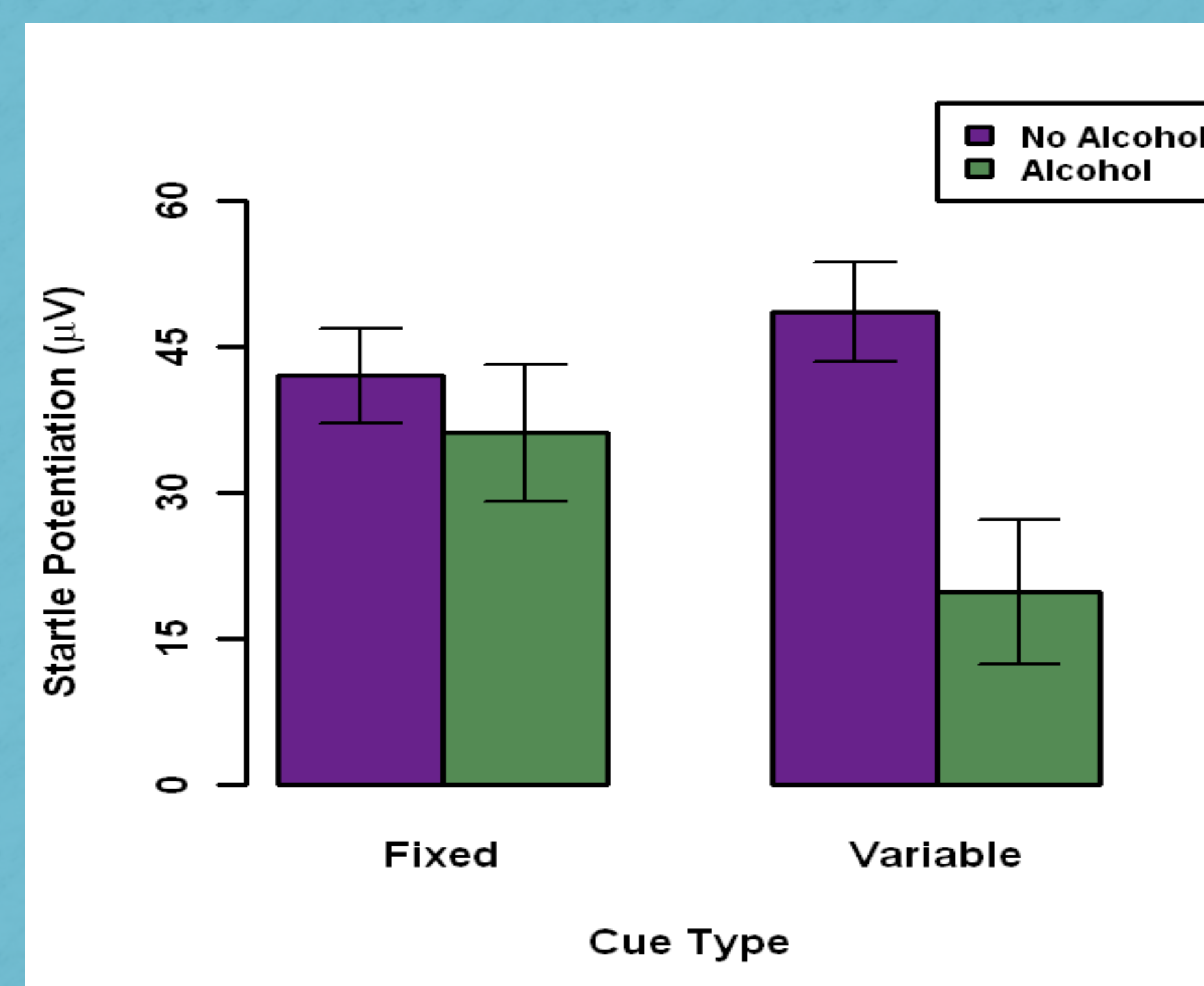


Analytic Design

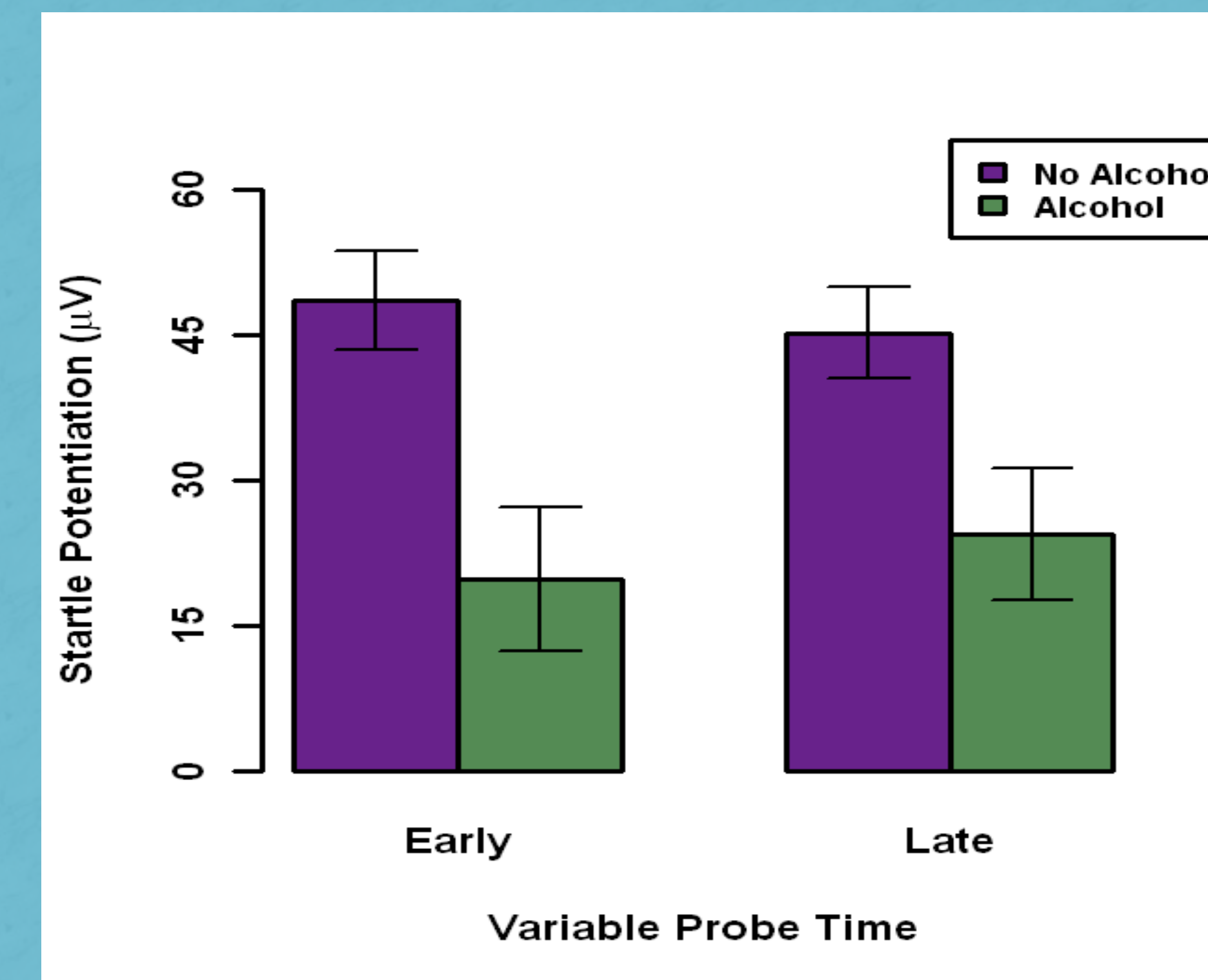
- **Cue Type (within subjects):** 2 types (Fixed vs. Variable)
- **Beverage Group (between subjects):** 3 groups: No Alcohol, Placebo, and Alcohol, collapsed into 2 groups: Control (No Alcohol & Placebo) vs. Alcohol
- Data were analyzed in a GLM with between-subjects regressors of Beverage Group (Alcohol vs. No Alcohol/Placebo) and repeated measures of Cue Type (Fixed vs. Variable). Baseline startle & Sex were included as covariates.

RESULTS

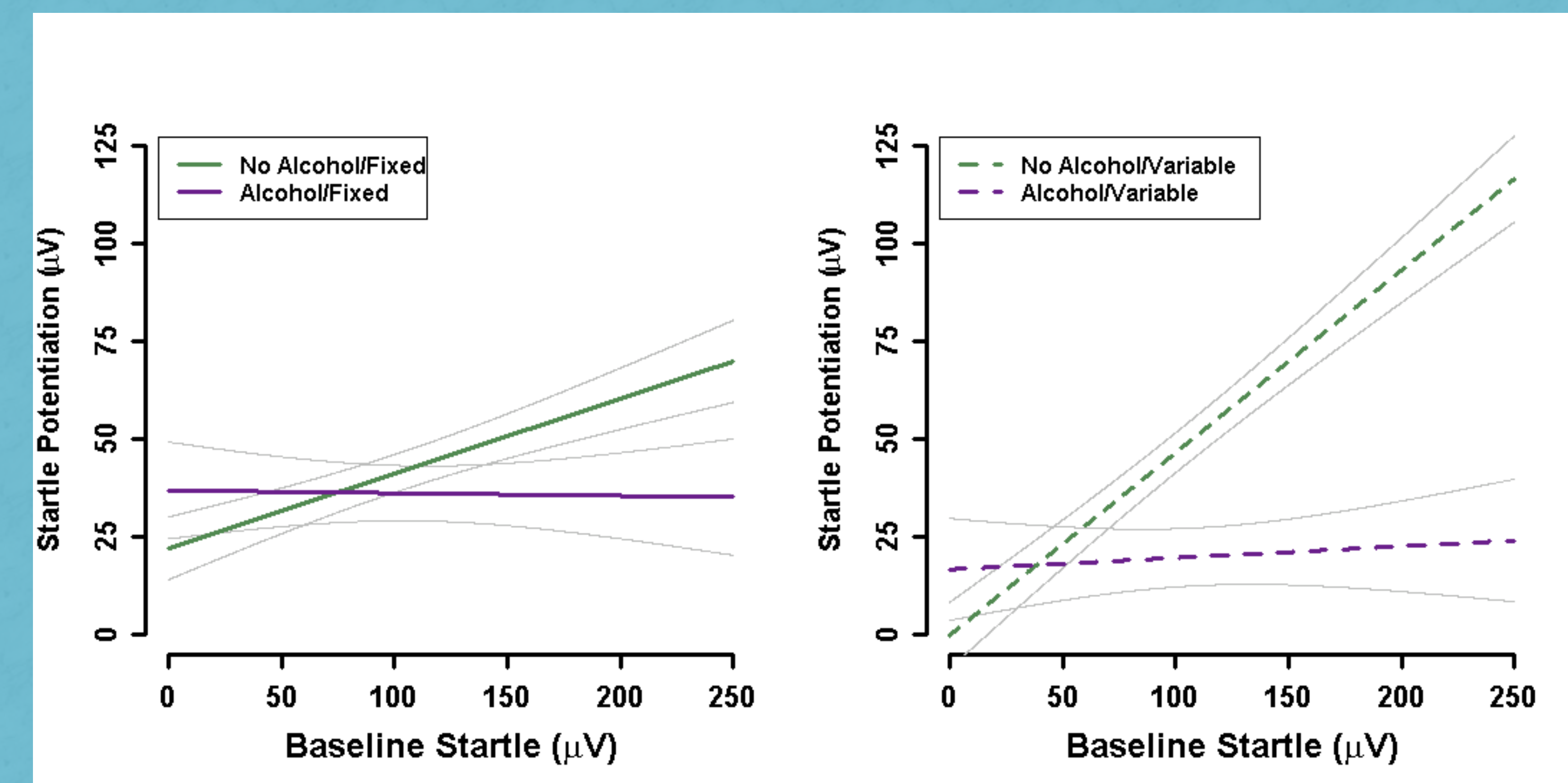
- The **main effect of Beverage group** was significant, $t(63) = -2.23, p = .029$
- The **Beverage group X Cue type** interaction was significant, $t(63) = 2.81, p = .007$
 - Within fixed cue blocks, the **Beverage group** effect is **not** significant, $t(63) = -.69, p = .496$
 - Within variable cue blocks, the **Beverage group** effect is **significant**, $t(63) = -3.2, p = .002$



RESULTS, Continued



- The **Beverage group X Probe time** (Early vs. 3 Later) interaction was not significant, $t(63) = -1.24, p = 0.219$
- The simple effect of beverage group on startle potentiation for the average of 3 later probes is **significant**, $t(63) = -2.51, p = 0.015$.
 - This indicates that alcohol's effect on SP during Variable blocks was **sustained** to later time points



- This indicates that participants with higher baseline startle tended to experience greater stress dampening effects of alcohol, particularly during variable blocks

SUMMARY AND CONCLUSIONS

• This work provides a conceptual replication of both Moberg & Curtin (2009)'s and Hefner & Curtin (2011)'s findings that **alcohol selectively reduces startle potentiation during uncertain threat**.

- We have **extended** those findings by demonstrating alcohol's selective effect on anxiety utilizing a different dimension of uncertainty; that is, **threat imminence (proximal vs. distal)**.
 - The novel study design also enabled us to demonstrate that this effect **was sustained over a longer period of time**.

• In addition, the finding that **those who have greater** startle response magnitude even under neutral conditions (**baseline startle**) **experience greater levels of alcohol stress dampening** suggests that baseline startle may be an important biomarker to identify individuals who are most likely to experience these effects, and consequently, may be potentially more susceptible to developing problems with alcohol use.

- Furthermore, other studies in our laboratory **have identified baseline startle as a predictor of anxiety response** (Bradford et al. poster) **as well as drug deprivation effects** (Gloria & Curtin, 2009).

• Alcohol's effects on the neurobiological substrates of anxiety (e.g., BNST) may be one target for neuroplastic changes supporting alcohol (and other drug) dependence.

• These selective effects may help to account for high rates of co-morbidity between alcohol use disorders and anxiety disorders.