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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 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; Davis, 1989; Grillon & Baas, 2004)
• Startle potentiation (SP) is defined as the increase in startle response to an acoustic "Startle probe" during threat vs. no-threat conditions
• SP is non-invasive, operates outside of consciousness, and can be assess across species

Fear vs. Anxiety
• Phasic (brief) 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 SP during stimuli of variable (unpredictable) duration

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= startle   **= shock**

Analytic Design
Block Type (within subjects): 4 types
Cue Type (within subjects): 2 types (Fixed vs. Variable)
Beverage Group (between subjects): 3 groups (No Alcohol, Placebo, and Alcohol), collapsed into 2 groups (No Alcohol & Placebo vs. Alcohol)

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 (6 cues per block)
2. Variable duration no shock (6 cues per block)
3. Fixed duration shock (5 cues per block)
4. Fixed duration no shock (5 cues per block)

Startle probes occurred at 4.5s during fixed duration blocks
Startle probes occurred at 4.5s, 19.5s, 49.5s, and 79.5s during variable duration
During shock cue presentations shocks occurred 0.25s before cue offset.
Participants did not know the length of each specific cue during the variable cue blocks, only that cues could be 5, 20, 50, or 80 seconds.

Measures
• EMG eyeblink 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.

• 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

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Startle Potentiation By Beverage Group and Cue Type

• The main effect of **Block type** was significant (p < .001). 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 **Beverage group X Cue type** interaction was significant (p = .019)

• Within variable cue blocks, the **Beverage effect** is significant (p = .025)

Startle Potentiation During Variable Shock Blocks

• The **Beverage group X Cue time** interaction was not significant (p = .081)

• The simple effect of beverage group on startle potentiation for the average of 4 later probes is **not significant** (p = .195)

INTERPRETATIONS

• Whereas alcohol does not reduce startle potentiation during fixed duration threat cues, it does reduce potentiation to cues whose timing is unknown and potentially more distal

• This study design also allowed us to demonstrate that participants' startle potentiation is maintained over a long duration cue, extending a current animal model to humans

• 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 co-morbidity of alcohol use disorders with anxiety disorders.

REFERENCES

Davis, M. (1989). *Annals of NY Academy of Sciences, 563,*165-183.
Grillon, C., et al. (2004). *Behavioral Neuroscience, 118* (5), 916-924.
Hefner, K. R. & Curtin, J.J. (in prep)
Moberg, C.A. & Curtin , J.J. (2009). *Journal of Abnormal Psychology, 118*(2), 335-347.