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BACKGROUND

To better treat problematic drinking, we must develop a clearer understanding of how and under which circumstances alcohol affects emotions and cognitions.

Recent research on alcohol's effects suggests that alcohol reduces subjective anxiety, innate defensive responding, and emotionally motivated attention more during unpredictable versus predictable stressors¹. Stressor predictability may be an important moderator of alcohol's stress-reducing effects yet other related but distinct aspects of stressors remain untested with current experimental methods.

We manipulated stressor predictability and controllability in a 2 x 2 design to experimentally assess alcohol's interactions with both stressor types in the same study.

ALCOHOL MANIPULATION

Participants were randomly assigned to one of three groups: Alcohol (N = 64), Placebo (N = 32), True No-Alcohol (N = 32).

Alcohol and Placebo groups were told they would receive a dose of alcohol designed to produce a peak blood alcohol concentration (BAC) of .08 percent. Actual achieved BAC was .074 before the start of the main task and .073 after.

For the Placebo manipulation, water was poured into placebo drinks from a vodka bottle in front of the participant. Out of participant view, 2 milliliters of 200 proof vodka was floated on the drink. A 200 proof alcoholic mist was also applied.

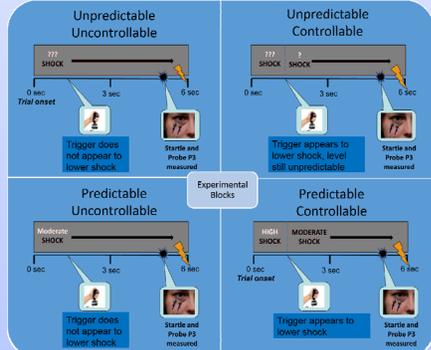
We observed no placebo effects in final analysis so we combined True No- Alcohol and Placebo in initial analysis to create equal No-Alcohol (N = 64) and Alcohol (N = 64) groups.

STRESSOR PREDICTABILITY AND CONTROLLABILITY TASK

Threat-of-shock cues (squares) were serially presented in blocks. There were 4 shock block types and a no shock block type.

Participants were told to pull a trigger on a joystick when each cue appeared on the screen.

At end of shock cues, participants received electric shocks to their fingers (intensity set based on participant's shock tolerance).



Predictable shock blocks: participants told the level of shock.

Unpredictable shock blocks: participants only told a possible range of shock levels.

Uncontrollable blocks: participants told they had no control over the level of shock.

Controllable shock blocks: participants told they had the ability to lower the level of shock by pulling the trigger.

Controllable shock blocks: participants flipped a rocker switch which triggered a light box reading "Shock Control ON".

Controllable blocks: participants told their trigger pulls lowered the shock by two levels. In reality all shock levels were predetermined and matched across all shock blocks.

MEASURES

We measured participants' subjective emotional response, defensive reactivity, and emotionally motivated attention using **self-reported anxiety**, **startle potentiation**, and **probe P3 suppression**.

Self-reported Anxiety

Startle Potentiation

Probe P3 Suppression

Participants retrospectively reported fear/anxiety during each cue on a 5 point scale (1 = Not Anxious/Fearful, 5 = Very Anxious/Fearful)².

We measured the EMG eye-blink startle response to acoustic startle probes using standardized procedures³.

We measured the ERP P3 wave to the acoustic startle probes using standardized procedures⁵.



Ratings from reports made half way through the task and at the end of the task were averaged for analysis.

Different stressor types elicit distinct, innate, defensive behaviors involving activation of overlapping sub-nuclei within the central extended amygdala. Through these pathways, the startle response is potentiated during presentation of cues signaling threat of shock⁴.

P3 is elicited by infrequent stimuli and reflects attentional processing. When attentional resources are engaged by emotionally relevant stimuli, P3 to background stimuli is suppressed. Given limited attentional resources, more engaging stimuli cause greater suppression of P3 to background stimuli⁶.

Self-reported anxiety is calculated as increased anxiety during shock cues — no-shock cues.

Startle potentiation is calculated as increased startle during shock cues — no-shock cues.

Probe P3 Suppression is calculated as increased P3 during shock cues — no-shock cues

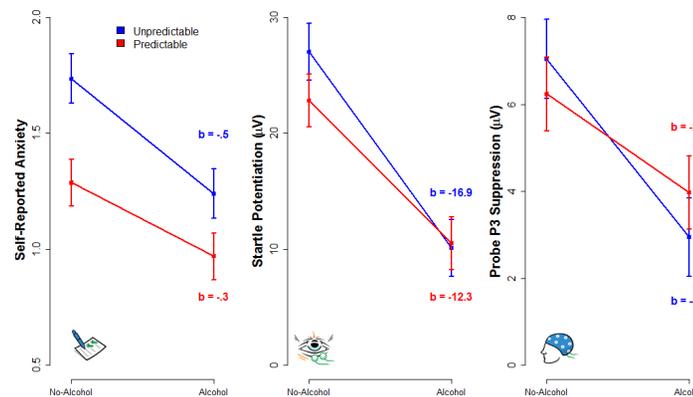
RESULTS

Table of effects

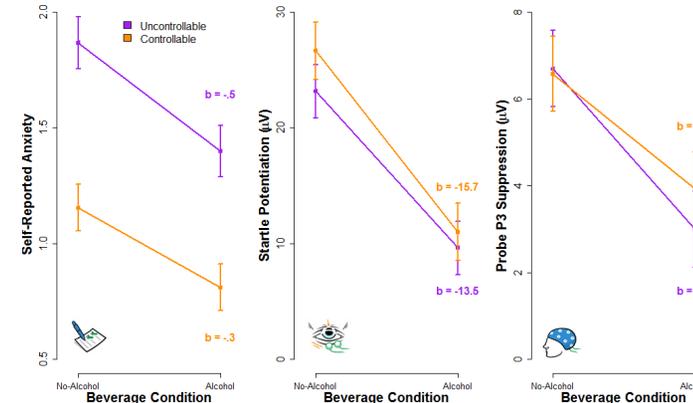
| Beverage Condition | Stressor Manipulation | Self-Reported Anxiety | Startle Potentiation | Probe P3 Suppression |
|--------------------|-----------------------|--|--|--|
| No-Alcohol | Predictability | Significantly greater during unpredictable vs. predictable stressors $t(118) = 4.72, p < .001^*$ | Significantly greater during unpredictable vs. predictable stressors $t(117) = 2.12, p = .036^*$ | Similar during unpredictable and predictable stressors $t(123) = 1.23, p < .222$ |
| | Controllability | Significantly greater during uncontrollable vs. controllable stressors $t(118) = 7.41, p < .001^*$ | Similar during uncontrollable and controllable stressors $t(117) = .87, p = .384$ | Similar during uncontrollable and controllable stressors $t(123) = .20, p = .840$ |
| Alcohol | Predictability | Alcohol effect significantly greater during unpredictable vs. predictable stressors $t(118) = 2.31, p = .023^*$ | Alcohol effect significantly greater during unpredictable vs. predictable stressors $t(117) = 2.12, p = .036^*$ | Alcohol effect significantly greater during unpredictable vs. predictable stressors $t(123) = 1.98, p = .049^*$ |
| | Controllability | Alcohol effect similar during controllable and uncontrollable stressors $t(118) = 1.26, p = .212$ | Alcohol effect similar during controllable and uncontrollable stressors $t(117) = .87, p = .384$ | Alcohol effect similar during controllable and uncontrollable stressors $t(123) = 1.23, p = .223$ |

RESULTS

Alcohol has significantly greater effects during unpredictable vs predictable stressors



The effects of alcohol are similar across uncontrollable and controllable stressors



SUMMARY AND FUTURE DIRECTIONS

Cues for all stressors elicited robust negative affective response and increased emotionally motivated attention among sober participants. However, unpredictable stressors increased defensive reactivity and subjective anxiety more potently than predictable stressors. These observations join recent experimental⁵ and other evidence indicating unpredictable stressors are more affectively aversive and/or aversive than predictable stressors.

In a novel finding, uncontrollable stressors elicited greater subjective anxiety than controllable stressors. However, this difference was not significant for defensive reactivity and emotionally motivated attention.

Cues for all stressors recruited comparable attention resources. Thus, all stressors appear to increase attentional processing that may be critical to support adequate appraisal and subsequent adaptive behavioral response, at least among sober individuals.

Consistent with recent research, alcohol caused a significantly greater reduction of self reported anxiety, defensive reactivity, and attention during unpredictable compared to predictable stressors. This implicates CRF and NE sensitive pathways in the central extended amygdala that selectively mediate startle potentiation during unpredictable stressors.

Across measures, alcohol had similar effects during uncontrollable and controllable threat. This may add additional clarification/specificity to the neuromechanisms involved with alcohol's effects and begins to rule out serotonergic and vmPFC relevant mechanisms responsible for response to uncontrollable stressors⁷.

Recently emerging theory and empirical evidence implicates the role of strong negative affective reinforcement in the form of reduced response to unpredictable stressors among alcoholics with a history of chronic, heavy alcohol use⁸.

These findings could inform pharmacological and psychological interventions for alcohol use disorders with emphasis on behavioral therapies or novel drugs that target the behavioral and/or brain mechanisms responsible for alcohol's effects on response to unpredictable stressors.

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