How bad could it be? Alcohol dampens stress responses to uncertain
intensity threat

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Key Words: drug/substance abuse, stress reactions, emotions, startle
reflex

Preprint. This article may not exactly replicate the final version published in
the journal. It is not the copy of record.

Final published citation: Bradford DE, Shapiro BL, Curtin JJ (2013). How
Bad Could It Be? Alcohol Dampens Stress Responses to Threat of Uncertain
Intensity. *Psychological Science*, 24, 2541-2549. PMC3951286.

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Abstract

Stress response dampening (SRD) is an important motive for alcohol use. However, alcohol SRD is observed inconsistently in and out of the laboratory. This has raised questions about precise mechanisms and boundary conditions required for stress reduction from alcohol. Emerging evidence indicates that alcohol SRD may be observed selectively during uncertain but not certain threats. We measured stress response via potentiation of participants' defensive startle reflex to threat of shock in blocks of certain (low and high) intensity and uncertain intensity shock. We manipulated 92 participants' blood alcohol concentrations (BACs) across a broad range (0.00%-0.12%). Increasing BACs were associated with linearly decreasing startle potentiation and self-reported anxiety. This alcohol SRD effect was greater during uncertain than certain threat. Furthermore, we identified binge drinking as a moderator of alcohol SRD. More broadly, these results suggest that distinct mechanisms are involved in response to uncertain vs. certain intensity threats.

Imagine you have arrived early to a restaurant with the intention to break up with your significant other. You know this conversation will be stressful but you can't anticipate how strongly your partner will react. You could be met with any reaction ranging from uncomfortable silence to loud shouting and crying. You order a large glass of wine to steady your nerves in response to this uncertainty.

Will this glass of wine have the desired effect? Drinkers expect alcohol to reduce their negative affective response to stressors (Sher, 1987). Furthermore, both recreational and problem drinkers report that stress reduction is an important motive for their alcohol use (Cooper, 1994; Schroder & Perrine, 2007). However, three decades of research have yet to specify the precise mechanisms and boundary conditions for alcohol's stress response dampening (SRD) properties (Levenson, Sher, Grossman, Newman, & Newlin, 1980; Sher, 1987; see Curtin & Lang, 2007 for review). We need to clarify when, how, and for whom alcohol SRD occurs to understand fundamental questions about this popular drug's reinforcing effects and how to treat problems of excessive use. In addition, answers to these questions promise to advance our understanding of the psychological and neurobiological mechanisms involved in the affective response to stressors more generally.

Uncertain vs. Certain Threat

In the above scenario, we exemplify anticipation of an uncertain stressful encounter. Stressors vary on several dimensions of threat uncertainty. For example, threats or other stressors can be probabilistically and temporally uncertain. Affective scientists have developed tasks to examine the mechanisms that mediate the impact of uncertainty about threat probability (*if* the threat will occur) and threat onset (*when* the threat will occur) in humans and animal models (Davis, Walker, Miles, & Grillon, 2010; Mobbs et al., 2007). Multiple lines of evidence suggest that these uncertain threats can be distinguished from certain threats by the emotional, behavioral, and cognitive-attentional responses they elicit, the time course of these responses, and the neural mechanisms mediating these responses (Davis, 2006). For instance, uncertain vs.

certain threats produce distinct emotional responses characterized in humans as anxiety vs. fear, respectively (Grillon, 2008). Uncertain threats elicit freezing and hyper-vigilance while certain threats elicit active avoidance and/or defensive attack in animals (Blanchard & Blanchard, 1989). Imminent, certain threats focus attention on the threat itself, whereas distal, temporally uncertain threats encourage distributed attention to the overall environment (Cornwell, Echiverri, Covington, & Grillon, 2008; Fanselow & Lester, 1988; Mobbs et al., 2007). Response to temporally uncertain threats appears sustained whereas response to certain threats is phasic and time-locked to the threat (Davis et al., 2010). Finally, neuroscience research with rodents has detailed a corticotrophin-releasing factor (CRF) and norepinephrine (NE) sensitive pathway involving the lateral divisions of the central nucleus of the amygdala (CEA_L) and the bed nucleus of the stria terminalis (BNST_L) that appears to selectively mediate sustained response to temporally uncertain threats (Walker & Davis, 2008).

Grillon and colleagues have manipulated uncertainty about *if* and *when* threats will occur in humans in their “No-shock, Predictable shock, Unpredictable shock (NPU) task (Schmitz & Grillon, 2012). Predictable and unpredictable shock both potentiate the startle reflex, a cross species, physiological index of defensive reflexive responding. Patients with Post Traumatic Stress and Panic disorders exhibit selectively increased startle potentiation during unpredictable but not predictable shock in the NPU task (Grillon et al., 2008; Grillon et al., 2009). Medications prescribed to treat anxiety appear to have greater effect on startle potentiation during unpredictable shock in the NPU task (Grillon, Chavis, Covington, & Pine, 2009).

Most alcohol SRD research has not included attempts to vary threat uncertainty. However, Moberg & Curtin (2009) demonstrated that a moderate dose of alcohol (approximately 4 standard drinks over 1 hour in a 180 pound man) selectively reduced startle potentiation during threat of unpredictable but not predictable shock in the NPU task. In two follow-up experiments, Curtin and colleagues confirmed that greater alcohol SRD during uncertain versus certain threat was observed with more precise separate manipulations regarding *if* (probabilistic uncertainty; Hefner & Curtin, 2012) or *when*

(temporal uncertainty; Hefner, Moberg, Hachiya, & Curtin, in press) the threat would occur.

If, When, and How Bad?

Initial basic affective science and alcohol SRD research from our laboratory has focused on uncertainty regarding if and/or when threats will occur (Davis et al., 2010; Hefner & Curtin, 2012; Hefner et al., in press; Moberg & Curtin, 2009). It is now time to probe the boundary conditions of uncertainty to better define this construct. In the opening scenario, you are relatively certain about if and when your partner's reaction will occur. The uncertainty is constrained primarily to the severity dimension (*how bad will it be?*). In this experiment, we follow emerging interest in this understudied dimension of threat uncertainty (Shankman, Robison-Andrew, Nelson, Altman, & Campbell, 2011) to test the novel prediction that alcohol SRD will be more robust under conditions of uncertainty regarding threat severity.

Alcohol Dose Response and Uncertain Threat

In the opening scenario, you might expect the amount of wine to impact its effectiveness. In fact, Sher (1987) made the observation that alcohol SRD was consistently observed with intoxicating doses of alcohol. Thus, initial theoretical accounts predicted that alcohol dose would moderate the magnitude of alcohol SRD but did not specify the form of the dose response function (e.g., linear, threshold, asymptotic). However, only a small handful of alcohol SRD experiments have examined alcohol dose response (Donohue, Curtin, Patrick, & Lang, 2007; Moberg, Weber, & Curtin, 2011; Sher & Walitzer, 1986; Stewart, Finn, & Pihl, 1992). Furthermore, these experiments included no more than three active doses, which prevents clear specification of the dose response function (but see Moberg et al., 2011). None of these studies have tests for dose response effects on alcohol SRD during uncertain vs. certain threat.

The Current Study

We manipulated threat uncertainty and severity by exposing participants to blocks of certain low intensity, certain high intensity and uncertain intensity shock threat. We administered various doses of alcohol to manipulate participants' blood alcohol concentrations (BACs) quantitatively across a broad range of ecologically meaningful levels from sober to moderately high intoxication (approximately 6 standard drinks over 1 hour in a 180 pound man). We assessed participants' stress response by measuring the potentiation of their defensive startle reflex during the certain and uncertain intensity threats. We tested the following two predictions: 1. Alcohol SRD will be dose dependent with increasing SRD (i.e., decreasing startle potentiation) associated with increasing BACs; 2. Alcohol will produce selectively greater SRD during uncertain intensity versus certain intensity shock threat. We included two intensities of certain threat to evaluate a competing hypothesis that alcohol SRD magnitude varies by the intensity of the stress response rather than the uncertainty of the stressor. We conducted supplemental analyses to examine potential individual difference moderators of alcohol SRD on startle potentiation. Finally, we assessed a measure of self-reported anxiety to index participants' subjective emotional response to the certain and uncertain intensity threats.

Methods

Participants

We recruited 89¹ participants (45 female; mean age=21.7 years, sd=1.2 years) from the university community who were at least 21 years old, had experience within the last year with the highest study dose of alcohol, reported no history of alcohol-related problems (CAGE, Mayfield, Mcleod, & Hall, 1974), no current psychiatric medication use, no alcohol contraindicated medical condition, and were not pregnant (verified by urine sample). We instructed participants to abstain from alcohol and other drugs for 24h and all food and beverages except water for 4h prior to their experimental session. We verified that all participants were sober on arrival via breathalyzer (Alcosensor IV; Intoximeters Inc., St. Louis, MO). We paid participants \$10/h or class extra-credit points.

Baseline startle assessment

Participants' startle response was assessed during a pre-task baseline procedure. Participants viewed a series of 12 colored squares presented on a CRT monitor for 5 s each with a variable inter-trial interval (ITI, range=10–20 s). Baseline startle response was included in analyses as a covariate to control for individual differences in startle potentiation (Hefner & Curtin, 2012; Hogle, Kaye, & Curtin, 2010; Moberg et al., 2011). See supplemental material available online (S1) for details on measurement of the startle response in the baseline and main task.

BAC manipulation

An equal number of male and female participants were randomly administered varied alcohol doses (placebo and target BACs from 0.01% to 0.11%, by 0.01%). All participants were informed that they would receive a moderately impairing dose of alcohol which should produce a BAC of approximately 0.08%. The beverage consisted of 100 proof vodka (Smirnoff Blue Label) and a juice mixer in a 3:1 mixer/alcohol ratio. We calculated the alcohol dose to produce the target BAC approximately 30 min after beverage consumption (see Curtin & Fairchild, 2003 for details regarding the dosing formula). Participants assigned to the placebo group received beverages consisting of fruit juice mixed with water poured from a vodka bottle in their presence. The total volume of all beverages was matched to the 0.11% BAC group beverage with water replacing the equivalent volume of alcohol. Outside of participants' view, all drinks were misted with alcohol, and 2 ml of alcohol was floated on top of the beverages to provide sensory stimulation to support the placebo manipulation. The total beverage was divided into four drinks, each consumed in 10 min, for a total drinking period of 40 min. The experimental session began 15 min after the end of the drinking period. We measured BAC immediately before, at midpoint, and immediately after completion of the main task. We used mean achieved BAC (average BAC across the three assessment times) to evaluate alcohol's effects on startle potentiation.

Subjective shock tolerance assessment

We measured participants' subjective shock tolerance per standardized procedures from our laboratory (e.g., Curtin, Patrick, Lang, Cacioppo, & Birbaumer, 2001; Moberg & Curtin, 2009). Five minutes after the drinking period, participants reported their response to a series of increasing intensity, 200 ms duration, electric shocks. Shocks were administered across the distal phalanges of the index and ring fingers of their left hand. The procedure was stopped once participants reached the maximum level of shock they could tolerate.

Cued threat task

The cued threat task included eight blocks. In each block, participants viewed a series of five colored square cues presented on a CRT monitor for 5 s each separated by a variable ITI (10–20 s, mean=15 s). There were four block types: certain low intensity shock, certain high intensity shock, uncertain intensity shock, and no shock. We instructed participants that shocks at the indicated intensity level would be administered at 4.8 s post-cue onset during all shock blocks and that no shocks would be administered during any ITI or at any time in no-shock blocks. We set the intensity levels for the low shock and high shock blocks to 33% and 100% of each participant's maximum reported subjective shock tolerance, respectively. In uncertain blocks, we instructed participants that shock intensity would vary across cues but would never exceed the intensity of shocks delivered in the high intensity block. In fact, participants received either low or high intensity shocks (equi-probable) intermixed randomly across cues in uncertain shock blocks.

A pre-block message on the monitor informed participants of the next block type. Two character condition abbreviations were presented in the center of each cue to further reinforce condition information: Low(LO), High(HI), Uncertain(??), and No Shock(NS). We counterbalanced blocks across three between-subjects orders with no block repeated more than once in series. We scored mean startle potentiation (i.e., increase in startle response to probes during threat block relative to no-threat block) separately for the three threat types (uncertain vs. high vs. low). After the cued threat task and final BAC assessment, participants rated how anxious they were when they saw each threat cue on a 5 point rating scale (1=Not at all anxious; 5=Extremely

anxious). Participants then completed self-report individual difference measures, were debriefed, compensated, and dismissed once reaching a BAC < .03%.

Results

We analyzed data and prepared figures with R (R Development Core Team, 2013). Mean BAC's and standard deviations were: Pre-Task: 0.048(0.03), Mid-Task: 0.049(0.04), and Post-Task: 0.050(0.04). Mean BAC for each individual is included in Figure 1 (strip plot).

Startle Potentiation

We analyzed startle potentiation in a general linear model (GLM) with repeated measures for threat type (uncertain vs. high vs. low). Fully interactive between subject regressors for Mean BAC, Gender, Block Order, and Baseline Startle were included in the GLM². We report unweighted BAC effects across Baseline Startle, Gender, and Block Order covariates. We report the effects of these covariates as well as individual difference moderators related to personality and alcohol use in the supplement available online (S2, S3). We examined two planned orthogonal contrasts for threat type to test predictions regarding threat uncertainty and intensity: (1) uncertain intensity vs. the average of certain low and certain high intensity and (2) certain low vs. certain high intensity. We report raw GLM coefficients (*b*) and partial eta squared (η_p^2) to document effect sizes.

Mean startle potentiation was significant (non-zero) across threat types at BAC=0.00%, $b=36.2$, $t(65)=9.10$, $p<0.001$, $\eta_p^2=0.56$ (Figure 1). Startle potentiation was increased significantly during uncertain threat vs. the average of certain high and certain low threat, $b=17.1$, $t(65)=3.69$, $p<0.001$, $\eta_p^2=0.17$. Startle potentiation was significantly increased during certain high vs. certain low threat, $b=10.1$, $t(65)=2.04$, $p=0.046$, $\eta_p^2=0.06$. Despite differences across threat type, startle potentiation was significant (non-zero) for each threat type (p 's < 0.001).

As predicted, the overall effect of mean BAC across threat types was significant such that startle potentiation decreased 2.5 μ V for every 0.01% increase in BAC, $b=-2.5$, $t(65)=3.48$, $p=0.001$, $\eta_p^2=0.16$. As predicted, interaction contrasts indicated that this

mean BAC effect was significantly greater during uncertain ($b=-3.8$) than certain high/low ($b=-1.8$) threat, $b=-2.0$, $t(65)=2.44$, $p=0.018$, $\eta_p^2=0.08$. In contrast, the magnitude of the mean BAC effect was comparable across certain high ($b=-1.7$) and certain low ($b=-1.9$) threat, $b=0.2$, $t(65)=0.22$, $p=0.825$, $\eta_p^2=0.00$.

Figure 1: Startle potentiation by Mean BAC and Threat Type

Dark colored lines display the relationship between BAC and startle potentiation by threat type. Translucent colored bands indicate confidence envelopes ($\pm$ one standard error) for point estimates of mean startle potentiation from the general linear model. We included a green strip plot of observed BACs for all participants along the x-axis. We

report GLM coefficients for the simple effects of BAC for each threat type in the right margin (* $p < 0.050$; ** $p < 0.010$; *** $p < 0.001$).

Linearity of BAC effect on Startle Potentiation

We assessed the linearity of the BAC effect on startle potentiation in two ways. First, we confirmed that the patterns of residuals in Component Plus Residual plots for BAC were consistent with linear effects for BAC for both certain and uncertain threat via visual inspection (Fox, 2008; left and right panels in Figure 2). Second, we included regressors for higher order (i.e., quadratic & cubic) BAC effects in supplemental GLMs. The effects of these higher order regressors were not significant for either certain (quadratic $p = 0.479$, cubic $p = 0.408$) or uncertain (quadratic $p = 0.233$, cubic $p = 0.484$) threat contrasts.

Figure 2. Component Plus Residual Plots for BAC during Certain and Uncertain Threat

Component Plus Residual plots are used to assess linearity of effects in GLMs (Fox, 2008). Startle potentiation scores in these plots are adjusted to control for all regressors in the GLMs other than BAC. Visual inspection of these plots reveals residuals that are symmetrically distributed around the BAC regression line for all BACs. This is the expected pattern given a linear BAC effect.

Self-Reported Anxiety to Cues

We conducted analyses of self-reported anxiety during the cues in a GLM using the same model that we used to analyze startle potentiation. We report the effects of the covariates from this analysis in the supplement (S4).

At BAC=0.00%, self-reported anxiety was increased significantly during uncertain threat vs. the average of certain high and certain low threat, $b=0.84$, $t(65)=4.65$, $p<0.001$, $\eta_p^2=.25$ (Figure 3). Self-reported anxiety was increased during certain high vs. certain low threat, $b=1.47$, $t(65)=7.23$, $p<0.001$, $\eta_p^2=.45$.

The overall effect of mean BAC across threat types was significant such that self-reported anxiety decreased 0.09 units for every 0.01% increase in BAC, $b=-0.09$, $t(65)=3.06$, $p=0.003$, $\eta_p^2=0.13$. Interaction contrasts indicated that this mean BAC effect was significantly greater during uncertain ($b=-0.14$) than certain high/low ($b=-0.07$) threat, $b=-0.07$, $t(65)=2.09$, $p=0.041$, $\eta_p^2=0.06$. In contrast, the magnitude of the mean BAC effect was comparable across certain high ($b=-0.06$) and certain low ($b=-0.08$) threat, $b=0.02$, $t(65)=0.49$, $p=0.629$, $\eta_p^2=.00$. In sum, the pattern of results for self-reported anxiety match closely that for startle potentiation.

Figure 3. Self-reported Anxiety by Mean BAC and Threat Type.

Dark colored lines display the relationship between BAC and self-reported anxiety (1=Not at all anxious; 5=Extremely anxious) by threat type. Translucent colored bands indicate confidence envelopes ($\pm$ one standard error) for point estimates of self-reported anxiety from the general linear model. We included a green strip plot of observed BACs for all participants along the x-axis. We report GLM coefficients for the simple effects of BAC for each threat type in the right margin (* $p < 0.050$; ** $p < 0.010$; *** $p < 0.001$).

Discussion

This experiment provided clear evidence that the magnitude of alcohol SRD is greater in conditions that are characterized by uncertainty about the severity of the upcoming threat relative to well-defined threats. This finding emerged from a task that included careful matching across conditions for threat probability and timing (100% cue-shock pairings at 4.8 s post-cue onset), amount and density of aversive stimulation (10 shocks with 15 s mean ITI in each condition), and the perceptual demands for threat cue processing (all cues were simple colored squares). Shocks administered in the uncertain threat condition were matched in probability, frequency, duration and intensity to the shocks administered during low and high certain threat. The careful matching of these threat characteristics increases confidence that the differences in alcohol SRD across conditions results from differences in uncertainty about the intensity of the threat.

Uncertain threat intensity elicited more robust defensive response than comparably intense (i.e., high and low) certain threats. This appears to confirm the proverb “Better the devil that you know than the devil you don’t.” It also raises the possibility that the increased alcohol SRD observed during uncertain threat resulted from the increased defensive responding in that condition rather than uncertainty per se (e.g., Moberg et al., 2011). However, this appears unlikely given we observed comparable alcohol SRD during certain high and certain low intensity threat, even though certain high threat elicited significantly greater startle potentiation than certain low threat. This significant moderation of alcohol SRD by threat uncertainty (uncertain vs. high/low) but not threat intensity (high vs. low) strongly implicates threat uncertainty as the necessary characteristic for increased alcohol SRD. As such, intoxicated drinkers may be less anxious about “the devil you don’t know,” leading to increases in certain types of risk-taking when drinking (Corte & Sommers, 2005).

The current results join previous research that demonstrated greater alcohol SRD when participants were uncertain if/when shocks would occur (Hefner & Curtin, 2012; Hefner et al., in press; Moberg & Curtin, 2009). This provides an important conceptual replication of these prior findings at a time when psychological science has

been criticized for its inattention to replicable findings in research (e.g., special section in *Perspectives on Psychological Science* on replication, Pashler & Wagenmakers, 2012). More importantly, uncertainty about the nature of a threat, including its severity/intensity, appears qualitatively different from uncertainty about the occurrence of that threat. However, its impact on the magnitude of alcohol SRD was comparable. This suggests that threat uncertainty is emerging as a *broadly* relevant threat characteristic regardless of the source of the uncertainty. This begins to implicate higher level cognitive processes including appraisal and attention that may be involved in response to uncertain threats generally (Curtin et al., 2001; Sayette, 1993). Direct measurement of these cognitive processes with varied methods (e.g., event related potentials, startle pre-pulse inhibition; self-report of subjective risk and controllability) represents an important next step on the path to specify mechanism(s) of action.

Our confidence in the conclusion that magnitude of alcohol SRD is greater during uncertain threat is increased by the supplemental analyses of self-reported anxiety. This program of research on alcohol SRD during uncertain threat builds on basic affective neuroscience research in rodents (Davis et al., 2010) that relies on startle potentiation as the primary dependent measure of threat response (Hefner & Curtin, 2012; Hefner et al., in press; Moberg & Curtin, 2009). This report is the first to measure self-reported anxiety explicitly during uncertain and certain threat. Comparable BAC results across both physiological and self-report measures in the same experiment eliminate many alternative methodological/measurement explanations. It also generalizes the alcohol SRD effect to the domain of subjective emotional experience and suggests that participants are aware to some degree of the greater alcohol SRD reinforcement available during uncertain threat.

Early alcohol SRD theory and research identified alcohol dose as a potential important moderator of SRD effects, regardless of whether the threats were certain or uncertain. Alcohol dose also has important implications for understanding how alcohol SRD will influence real-world drinking. Unfortunately, the majority of SRD research has used only a single moderate dose of alcohol. We used a novel quantitative manipulation of BAC to probe the alcohol dose response function across a broader range of BACs.

We established that alcohol SRD is linear during both certain and uncertain threat up to a moderately high BAC (0.12%). This suggests that alcohol use is negatively reinforced even from the first drink (i.e., at very low BACs) within a drinking occasion, which suggests that preliminary, modest reinforcing effects are available to most drinkers. However, our results indicate that the magnitude of reinforcement from alcohol SRD may increase with increasing BACs. As such, higher BACs associated with heavier, binge drinking episodes may be more strongly reinforced despite the longer term negative consequences associated with heavy drinking.

Our supplement analyses of individual differences (S3) indicated that the magnitude of alcohol SRD during uncertain threat was reduced among individuals who self-reported typical binge use of alcohol in their own drinking outside the laboratory. Additional developmental and/or longitudinal research is necessary to determine if this individual difference moderator reflects a pre-morbid etiological risk factor for alcoholism (Schuckit & Smith, 2006; Schuckit et al., 2009) or the development of tolerance following frequent heavy use. Regardless, these drinkers may need to pursue particularly heavy, hazardous levels of use to obtain rewarding alcohol SRD effects.

Alcohol SRD during uncertain threat may contribute meaningfully to the putative reward that drinkers receive from alcohol. The moderating role of alcohol dose and binge use patterns suggest this presumed reinforcement mechanism may encourage heavy, high BAC, hazardous use. The alcohol SRD effects manifest both in drinkers' defensive physiology and subjective emotional response to uncertain threats. Programmatic next steps can contrast these effects of alcohol to other relevant drugs (e.g., anxiolytics, sedatives; (Grillon et al., 2006)), The current findings should be directly linked to alcohol use itself via simultaneous measurement of stress and ad lib drinking in the laboratory and/or real world.

In real world contexts (e.g., our opening scenario), both certain and uncertain threats are often appraised to some degree prior to drinking. Sayette (1993) has suggested that the timing of drinking relative to threat appraisal may have an important moderating effect on the magnitude of alcohol SRD. This thesis was outside the scope

of our current experiment. However, future research should examine the impact of these temporal factors regarding drinking on alcohol SRD to uncertain threats.

Compensatory neuroadaptation in the response to uncertain threats following chronic alcohol or other drug use and/or early chronic stress have been implicated in addiction (Koob & Volkow, 2010). In other recent research, we have provided preliminary evidence of neuroadaptation in response to uncertain threat among smokers (Hogle et al., 2010). Confirmation of a similar effect among alcoholics would implicate this mechanism in alcoholism etiology.

More broadly, these results join an emerging body of evidence from affective neuroscience about response to uncertain threat. Research with rodents suggests distinct neural mechanisms are involved in response to uncertain vs. certain threats (Davis et al., 2010). Clinical research implicates response to uncertain but not certain threats in humans with anxiety disorders (Grillon et al., 2008; Grillon et al., 2009). The use of alcohol in the current experiment can be viewed as a coarse pharmacological dissociation of uncertain from certain threat in humans that implicates a common mechanism across uncertainty from different sources (see Hefner et al., in press for additional discussion). Future neuropharmacological challenge with CRF and NE agonists/antagonists in humans can more precisely probe these neural mechanisms that have been implicated in basic affective neuroscience with uncertain threats (Davis et al., 2010).

Endnotes

¹ Four additional participants were regression outliers (i.e., studentized residual with Bonferroni corrected $p < 0.05$) in preliminary GLM analyses involving startle potentiation. We removed these from the sample.

² BAC was multiplied by 100 to increase interpretability of its GLM coefficients such that a one unit increase represented a 0.01% increase in BAC. Baseline startle was mean-centered. Unit weighted, centered orthogonal regressors were included for Sex (male=0.5, female=-0.5) and Block Order (Helmert coding).

Contributions

J.J.C and D.E.B. developed the study concept and design. Data collection was performed by D.E.B and B.L.S. D.E.B performed the data analysis and interpretation under J.J.C.'s supervision. D.E.B drafted the paper, and J.J.C provided critical revisions. All authors approved the final manuscript.

Acknowledgements

Funding was provided by grants to J.J.C from NIAAA (R01 AA15384) and NIDA (R01 DA033809) and D.E.B from NIMH (T32 MHD18931-21).

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