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Understanding the Effects of Stress and Alcohol Cues on Motivation for Alcohol via Behavioral Economics

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Abstract

Background—Psychological stress and alcohol cues are common antecedents of both ongoing drinking and relapse. One candidate mechanism of risk from these factors is acute increases in craving, but experimental support for this hypothesis is mixed. Furthermore, the combination of stress and cues has been largely unstudied. The current study employed a behavioral economic approach to investigate the combined roles of psychosocial stress and alcohol cues on motivation for alcohol.

Methods—In a sample of 84 adult heavy drinkers, we examined the effects of an acute laboratory stress induction and an alcohol cue exposure on subjective craving and stress, arousal, and behavioral economic decision-making. Primary dependent measures included an intertemporal cross-commodity multiple choice procedure (ICCMCP), incorporating both price and delay elements; an alcohol purchase task (APT), measuring alcohol demand; and a monetary delay discounting task (DDT), measuring intertemporal choice.

Results—The stress induction significantly increased stress, craving, and the incentive value of alcohol on the ICCMCP and APT. Stress-related increases in value on the ICCMCP were mediated by increased alcohol demand. Exposure to alcohol cues only significantly affected craving, APT breakpoint, and arousal. Delay discounting was not affected by either stress or cues.

Conclusions—These results reveal unique behavioral economic dimensions of motivation for alcohol following acute stress and an alcohol cue exposure. More broadly, as the first application of this approach to understanding the role of stress in drug motivation, these findings support its utility and potential in future applications.

Keywords

Alcohol; behavioral economics; craving; stress; incentive value

Introduction

Alcohol use disorders (AUDs) are a substantial public health problem, accounting for high rates of morbidity and mortality (Mokdad et al., 2004). Understanding the processes that maintain alcohol misuse and contribute to relapse following treatment remains a high priority. Two factors that have been reliably implicated in clinical research are stress and the presence of alcohol cues. For example, a recent study of non-mutually exclusive antecedents of post-treatment relapse found that 67% were associated with negative affective states (e.g., anxiety, frustration) and 55% were associated with giving in to temptations in presence of alcohol cues (Ramo and Brown, 2008).

Experimental research has helped characterize the roles of stress and alcohol cues in drinking and the underlying mechanisms of those influences. Several procedures exist for eliciting acute stress in the laboratory, including the Trier Social Stress Test (TSST) (Kirschbaum et al., 1993). These protocols produce robust increases in self-reported stress, arousal, and endocrine response (Dickerson and Kemeny, 2004). One proposed functional mechanism of stress effects on drinking is increased alcohol craving. This has been supported by some studies (Field and Powell, 2007, Fox et al., 2007), but not others (Pratt and Davidson, 2009, Thomas et al., 2011). Experimentally, cue reactivity paradigms are typically used to investigate the role of drug-related stimuli (Monti et al., 1987). These cues activate greater “wanting” that is thought to drive drug-seeking and drug-taking behaviors (Robinson and Berridge, 2001). Thus, again, the putative mechanism of cue effects is subjective craving, and there is considerable support that drug cues elicit significant increases in craving (Carter and Tiffany, 1999).

The majority of previous research has investigated the effects of stress and cues separately even though they presumably often occur concurrently. For instance, individuals may experience a distressing event, such as a conflict with a friend or spouse, and then encounter salient alcohol cues, such as driving past a bar or seeing alcohol for sale in a grocery store. A limited number of studies have examined whether acute stress potentiates cue-elicited craving and the results are mixed. Some studies suggest that stress and cues have additive effects (Coffey et al., 2002, Cooney et al., 1997, Liu and Weiss, 2002), but other studies have found no enhancement (McRae-Clark et al., 2011, Ray, 2011, Thomas et al., 2011).

One approach to potentially resolve these ambiguities is behavioral economics, which integrates concepts from psychology and microeconomics to understand how individuals make transactions with the world (Vuchinich and Heather, 2003). Behavioral economics has been increasingly applied to examine decision-making in addiction, particularly in the case of acute motivation for alcohol and other drugs (for a review, see MacKillop et al., 2011a). In particular, two domains of behavioral economic preferences are theorized to be important. These are drug demand, referring to the relationship between drug consumption and its cost, and delay discounting, referring to preferences for smaller-immediate rewards over larger-later rewards. In addition, cross-commodity measures (e.g., drug today versus money in the future) are increasingly being used to integrate these domains (Bickel et al., 2011, Benson et al., 2009).

Empirical studies to date have shown that cost-based behavioral economic measures of demand complement subjective craving measures and can enhance the understanding of acute alcohol motivation. Studies using alcohol purchase tasks (APTs) that assess alcohol consumption across a range of prices have found that higher demand is associated with drinking quantity/frequency, severity of dependence, and treatment response (MacKillop et al., 2010a, Murphy and MacKillop, 2006, MacKillop and Murphy, 2007). State-based increases in demand have been reported in response to drug-related cues (Amlung et al., 2012, MacKillop et al., 2010b, MacKillop et al., 2012), and acute nicotine withdrawal (MacKillop et al., 2012). In addition, purchase task assessments have been used to understand pharmacotherapy mechanisms in both drinkers (Bujarski et al., 2012) and smokers (McClure et al., 2013). The effects of stress on alcohol demand remain largely unexamined, though negative mood inductions were shown to increase the relative value of alcohol in social drinkers (Rousseau et al., 2011).

Delay discounting is typically assessed using intertemporal choice tasks that assess choices between immediate and delayed rewards (Bickel and Marsch, 2001). Although monetary rewards are most common, discounting of other outcomes, including hypothetical health outcomes (Odum et al., 2002) and drugs of abuse (Petry, 2001), has also been investigated. Individuals who abuse alcohol exhibit steeper discounting (e.g., greater preferences for smaller-immediate rewards) compared to controls (see MacKillop et al., 2011b). Acute stress has been shown to increase bias toward immediate rewards in some studies (Tice et al., 2001) but not others (White et al., 2008). Finally, delay discounting is increased by gambling-related cues (Dixon et al., 2006) but not smoking-related cues (Field et al., 2007). To date, no studies have examined the effects of alcohol cues on delay discounting.

These findings suggest that behavioral economic indices have considerable promise in clarifying the proximal antecedents of drinking. However, several empirical questions remain to be answered. For example, does stress acutely affect behavioral economic motivational indices and, if so, which of these indices are the most sensitive? Second, can behavioral economics be used to clarify how stress and alcohol cues jointly influence motivation for alcohol? As noted above, very few studies have examined these two risk domains concurrently and findings are inconsistent.

The current study addressed these questions by investigating the combined effects of acute stress and alcohol cues on craving, arousal, and behavioral economic measures in heavy drinkers. Specifically, we examined the effects of acute stress using the TSST, and then examined differences based on subsequent exposure to either alcohol or neutral cues. We used three different behavioral economic measures to have maximal resolution in clarifying the mechanisms of stress and cue effects: (1) a modified intertemporal cross-commodity multiple choice procedure (ICCMCP), which assessed preferences for immediately-available alcohol versus delayed money; (2) an APT; and (3) a monetary delay discounting task. Since the ICCMCP measure combined elements of demand and delay sensitivity into a single assessment, the APT and discounting measures were included to unpack whether stress and cue effects on the ICCMCP were attributable to increases in demand, discounting, or both (see Figure 1). We hypothesized that the TSST would significantly increase subjective stress, alcohol craving, arousal, and the value of alcohol on behavioral economic measures.

Second, we predicted that exposure to alcohol cues would further increase craving along with the behavioral economic variables. Where significant effects of stress or cues were present for the ICCMCP, we investigated whether the demand and delay discounting indices mediated the effects. Finally, we examined associations between the measures of acute motivation and predicted that the behavioral economic indices would be generally distinct from subjective stress and craving.

Materials and Methods

Experimental Design

This study employed a two-group, repeated measures design with successive within-subjects and between-subjects manipulations. All participants underwent the TSST (within-subjects), and participants were then randomly assigned to receive either alcohol cues or neutral cues (between-subjects). Block randomization was used to assign equal numbers of participants by sex to the two cue conditions. We used this sequential design to prioritize maximum power to examine stress effects on behavioral economic indices, which have not been examined previously. This design also sought to parallel the naturalistic interaction of these factors alluded to above.

Participants

Regular drinkers ($N = 90$) were recruited from the Athens, GA community. Inclusion criteria were: 1) Age 21–45; 2) Current heavy drinking (i.e., 14+ drinks per week for males; 7+ drinks for females (NIAAA, 2010); 3) Computer fluency (using a computer > 4 days per week) to ensure competency with computerized assessments. Exclusion criteria were: 1) Actively seeking or receiving treatment for alcohol problems in the past 90 days; 2) Taking any psychotropic medication or other medication that may affect response to alcohol; 3) Current DSM-IV Axis I psychiatric conditions (by self-report); 4) Attending sessions with a breath alcohol level (BrAC) > 0.00g%; and 5) Pregnancy or nursing (females). No participants reported seeking any form of alcohol-related treatment in the past 12 months. One participant was excluded for non-compliance with stress induction procedures; one was excluded due to an obligation after the session that prevented any possibility of consuming alcohol; and four were excluded due to ceiling or floor effects on the ICCMCP measure (i.e., either all alcohol choices or all money choices), resulting in a final n of 84. Sample characteristics are provided in Table 1.

Assessments

Demographics—Participants completed a demographics assessment that included sex, race, ethnicity, income, and other variables.

Alcohol measures—Alcohol consumption was assessed using the 28-day Timeline Follow-Back (TLFB) (Sobell and Sobell, 1992). The Alcohol Use Disorders Identification Test (AUDIT) (Saunders et al., 1993) served as an index of alcohol misuse. BrAC was measured using a breathalyzer device (Intoximeters, Inc; St Louis, MO).

Alcohol craving, subjective mood, and arousal—Subjective craving for alcohol was assessed using a multi-item measure that conceptualized craving as part of a continuum of urges and desires. This included four 10-point visual analog scales: “How much do you want a drink?”, “How much do you crave a drink?”, “How much do you desire a drink?”, and “How high is your urge for a drink?” These items were subsequently averaged into a single composite craving score at each time point (Cronbach’s $\alpha = .95-.97$). Subjective mood was assessed using 10-point scales that included the following items: stress, nervousness, relaxation, calmness, happiness, and sadness. These items were averaged into a single composite stress score at each time point (positive affect items were reverse-scored; $\alpha = .77-.87$). Measures of physiological arousal included heart rate and mean arterial pressure (MAP) measured using an electronic blood pressure cuff (Welch Allyn, Inc.; Skaneateles Falls, NY).

Alcohol multiple choice procedure—The primary behavioral economic measure was ICCMCP that was adapted from the measure used in Benson et al. (2009). The ICCMCP consisted of choices between immediate alcohol (a single standard-sized drink of the participant’s preferred alcoholic beverage, available today) and 18 delayed monetary reward amounts (\$0.01, \$0.10, \$0.50, and \$1 to \$15 in one-dollar increments, available after one week). Individual items were randomized. The ICCMCP also determined the actual alcohol or money outcome received during the self-administration period (see Procedure).

Alcohol purchase task—Participants completed a hypothetical APT that was based on previous state-based purchase task assessments (MacKillop et al., 2010b, Amlung et al., 2012). Participants were asked how many alcoholic beverages they would consume at 18 different prices ranging from \$0.01 to \$15 per drink, presented in a randomized order. Price intervals were identical to the monetary amounts on the ICCMCP.

Monetary delay discounting—A hypothetical delay discounting task (DDT) consisted of choices between hypothetical smaller-immediate and larger-delayed monetary rewards. The larger-delayed reward was \$15 available after 1 week; the smaller-immediate rewards were identical to the ICCMCP monetary amounts (with the exception of \$15) and were available today. A total of 17 discounting trials were presented in a randomized sequence. A brief discounting assessment was employed because acute experimental manipulations have relatively transient effects (Zwaan et al., 2000).

Procedure

Participants who met enrollment criteria after a telephone screening were invited to the laboratory for a single session lasting 4.5 hours (Figure 2). Sessions began in the late afternoon for correspondence with typical drinking hours. Participants provided informed consent, sobriety was confirmed via breathalyzer, and female participants took a pregnancy test. Participants were given an orientation to the study procedures, including instructions regarding which tasks were for real versus hypothetical rewards. Participants completed a demonstration version of the ICCMCP to illustrate the outcome selection procedure, described below. Next, a battery of individual differences measures was administered. Participants then completed a 10-minute baseline period, during which they sat in a neutral

room while listening to soothing music. This was followed by the first of three primary assessments (Baseline) that consisted of the ICCMCP, DDT, APT, craving, subjective mood, and heart rate/MAP, in that order.

Participants then underwent the TSST according to procedures described in Kirschbaum et al. (1993). Participants were told that they would complete a mock job interview and they were given 5 minutes to prepare a brief speech on their qualifications for their “dream job”. Next, participants were escorted to a separate laboratory room where three confederates were seated (see Figure S1A in Supplementary Materials). Participants were required to speak for a total of 5 minutes. Participants then completed a serial subtraction task consisting of counting aloud from 1,022 to 0 in units of 13. After each incorrect response, participants were required to start over until 5 minutes elapsed. Participants then completed the Post-Stress assessment consisting of the ICCMCP, DDT, APT, craving, subjective mood, and heart rate/MAP, in that order.

Participants next underwent either an alcohol or neutral cue exposure based on established procedures (MacKillop et al., 2010b, Monti et al., 1987). Alcohol cues included a simulated bar laboratory and the participants’ preferred alcoholic beverage (Figure S1B in Supplementary Materials). Neutral cues included a standard laboratory testing room with neutral décor and a bottle of spring water (Figure S1C in Supplementary Materials). In both conditions, a standardized audio recording instructed the participants to periodically view, handle, smell, and sip the beverage. The duration of the exposure was 15 minutes. Participants then completed the Post-Cues assessment consisting of the ICCMCP, DDT, APT, craving, subjective mood, and heart rate/MAP, in that order.

Participants received one randomly-selected choice from the three administrations of the ICCMCP (Kirby et al., 1999). Participants selected a poker chip from a bowl containing chips pertaining to all of their ICCMCP choices. If the participant’s choice on that item was for alcohol, they received one standard drink at that moment. If their choice was for the delayed money, they received the money in cash after one week. All participants remained in their respective exposure rooms for a 15-minute consumption period. Participants who received alcohol were permitted to consume their beverage during this time. This was followed by a 60-minute recovery period in a laboratory lounge. Finally, participants were debriefed and, if their BrAC was $<0.04\%$, they were dismissed (NIAAA, 2005). Participants were asked to not drive themselves home following the session. Participants received \$40 for participation and up to \$15 in additional compensation from the ICCMCP. All procedures were approved by the University of Georgia Institutional Review Board.

Data Analysis

All variables were initially screened for missing data, outliers, and distribution abnormalities (Tabachnick and Fidell, 2001). The dependent variable from the ICCMCP was the crossover point, defined as the mean of the last price that alcohol was chosen and the first price that the money was chosen. For the APT, three indices of alcohol demand were generated using an observed values approach (Murphy and MacKillop, 2006): Intensity (i.e., consumption at the minimum cost of \$0.01); O_{\max} (i.e., the maximum alcohol expenditure); and Breakpoint (i.e., the first price that suppressed consumption to zero). Elasticity of demand was derived

using the following nonlinear exponential demand curve equation (Hursh and Silberberg, 2008): $\ln Q = \ln Q_0 + k(e^{-\alpha P} - 1)$, where Q = quantity consumed, Q_0 = derived intensity, k = the range of the dependent variable (alcohol consumption) in logarithmic units (3.0 in the present study), P = price, and α = elasticity of demand. Delay discounting was quantified using an impulsive choice ratio (ICR) reflecting the proportion of choices for the small-immediate reward (Mitchell et al., 2005).

Repeated measures ANOVAs were used to examine the effects of the stress induction and cue exposure on subjective mood and arousal. Next, the effects of acute stress on alcohol craving and each behavioral economic index were examined using a series of repeated measures ANOVAs with time as a two-level within-subjects factor (Baseline to Post-Stress). The effects of cue exposure were examined using a series of mixed ANOVAs for each variable with time as a two-level within-subjects factor (Post-Stress to Post-Cues) and condition as a two-level between-subjects factor (Alcohol vs. Neutral). Mediation analyses were used to determine whether the effects of stress or cues on the ICCMCP were mediated by changes in discounting or demand for alcohol. Change in ICCMCP crossover points across time was regressed onto both the sum (mean-centered) and the difference score between the two time points for those APT and DDT indices that showed a significant effect across time (Judd et al., 2001).

Results

Preliminary Analyses

No missing data were present for any variables. A small number of outliers ($z_s > 3.29$) were present for the behavioral economic indices (0.3% of all data points). These values were recoded as one unit higher than the next non-outlying value (Tabachnick and Fidell, 2001). Intensity, O_{\max} , and Breakpoint were square root transformed, and elasticity was logarithmically transformed. These transformations resulted in non-significant levels of skewness and kurtosis. Alcohol and neutral cues groups did not significantly differ on any demographic or alcohol variables ($p_s > .39$). At all three time points, the ICCMCP was significantly correlated with the APT demand indices and ICR ($r_s = -.47-.48$, $p_s < .05$, see Table S1 in Supplementary Materials). This supports the internal validity of the ICCMCP as a cross-commodity measure that incorporates aspects of demand and delay discounting. Fifty-five percent of participants received money from the ICCMCP (M reward = \$9.14); 45% received alcohol. The majority of participants who received alcohol consumed the entire beverage (M percentage consumed = 83%). For those participants with a positive BrAC at departure, the mean BrAC was .016 g% ($SD = .008$).

Effects of Acute Stress

The effects of the stress induction are presented in Table 2 and Figure 3. Demand curves for the baseline and post-stress are provided in Supplementary Materials (Figure S2). Following the TSST, participants reported significantly greater stress and alcohol craving (Figure 3A–B). The objective stress measures (MAP and heart rate) also increased significantly (Figure 3C–D). Cross-commodity preference for alcohol on the ICCMCP increased following the stress induction (Figure 3E). Significantly higher alcohol demand for alcohol after stress was

evident for Intensity, Breakpoint, and O_{\max} , but not Elasticity (Figure 3F–H). The largest effect was for O_{\max} , which increased by approximately one dollar after stress. The TSST did not significantly affect ICR on the DDT. Correlations between subjective craving and the demand indices were significant, moderate, and in the expected directions ($r_s = -.38-.39$, $p_s < .01$; Table S1).

Effects of Alcohol Cues

The effects of alcohol cues are presented in Table 3 and Figure 4. Demand curves for the post-stress and post-cues assessments are provided in Supplementary Materials (Figure S3). A significant Time \times Condition interaction was found for subjective craving, indicating that exposure to alcohol cues but not neutral cues increased craving for alcohol (Figure 4A). A similar interaction was evident for heart rate, attributable to decreased heart rate following neutral cue exposure (Figure 4B). Stress and MAP significantly decreased following cues, regardless of the cue type. The only behavioral economic index to show a significant Time \times Condition interaction was Breakpoint, which decreased following neutral cues but remained at its post-stress level after alcohol cues (Figure 4C). In both conditions, ICCMCP crossover point, Intensity, and O_{\max} also decreased following the cue exposure. ICR was not significantly affected by cues. Subjective craving was significantly correlated with O_{\max} ($r = .23$, $p < .05$) but not with the other demand indices (Table S1).

Mediators of Stress and Cue Effects

Three potential mediators exhibited statistically-significant effects across time that were in the same direction as the ICCMCP effect: O_{\max} , Breakpoint, and Intensity. The results of the mediational regression analyses for these indices are presented in Table 4. Changes in ICCMCP crossover points were mediated by increases in O_{\max} , $\beta = .23$, $t(81) = 2.11$, $p = .04$. Furthermore, the intercept in this model (i.e., the non-mediated portion of the ICCMCP effect) was not statistically significant ($p = .10$). A trend-level effect was also observed for Breakpoint, $\beta = .21$, $t(81) = 1.90$, $p = .06$. However, Breakpoint and O_{\max} were highly correlated across assessments ($r_s = .84-.90$, $p_s < .001$), suggesting that these indices were capturing overlapping aspects of incentive value. Change in Intensity was not a significant mediator ($p = .46$). Since ICCMCP crossover points did not differ as a function of cue condition, mediation analyses were not performed for the cue exposure portion of this study.

Discussion

The primary goal of this study was to apply a behavioral economic framework to investigate the impact of acute psychosocial stress and alcohol-related cues on motivation for alcohol. As hypothesized, the TSST significantly increased subjective stress and craving for alcohol. For the ICCMCP, stress increased how much delayed money participants were willing to forgo for immediate alcohol and for the APT, the stress induction increased estimated consumption at minimal cost (Intensity), maximum expenditure on alcohol (O_{\max}), and maximum acceptable cost of alcohol (Breakpoint), but not elasticity of demand. In other words, stress produced an upward shift across the majority of prices on the demand curve, but the overall shape or slope of the curve was not affected. Furthermore, stress-related increases in ICCMCP crossover points were largely attributable to increases in demand for

alcohol. Subsequent exposure to alcohol cues sustained the increase in alcohol craving and heart rate, as predicted, but did not affect the behavioral economic indices. Delay discounting was not affected by either stress or alcohol cues.

The results from this study extend the literature in several ways. Most broadly, the findings further support using behavioral economics to enhance the assessment of acute motivation for alcohol and other drugs. Previous studies have reported increased demand following exposure to alcohol and smoking cues (Amlung et al., 2012, MacKillop et al., 2010b, MacKillop et al., 2012) as well as nicotine withdrawal (MacKillop et al., 2012). Here, we show that acute stress also dynamically increases behavioral economic indices of value. Importantly, the effect sizes for ICCMCP crossover point and O_{\max} were larger than for subjective craving. This is notable since previous studies have typically found that acute changes on behavioral economic measures are of smaller magnitude relative to craving ratings (Amlung et al., 2012, MacKillop et al., 2010b). This is also interesting in the context of prior research that failed to find increased craving after stress (Pratt and Davidson, 2009, Thomas et al., 2011). This suggests that behavioral economic measures of value may have been more sensitive to stress than traditional indices of subjective craving in those studies.

For the first time in this line of research, this study incorporated dimensions of both cost-based and time-based decision-making in order to examine the specific mechanisms of stress effects. Since the ICCMCP task combined aspects of demand and discounting, changes in one or both of these related processes could be responsible for the increase in ICCMCP crossover points following stress. Results of the mediation analysis supported the causal role of increased demand (O_{\max}), but not increased discounting of delayed rewards. Higher crossover points, therefore, appear to be attributed to dynamic increases in the value of alcohol rewards and not simply that they were the immediately-available option.

Counter to our hypotheses, acute stress did not affect the DDT. While this is inconsistent with prior studies showing that negative affect increases immediate reward preferences (e.g., Tice et al., 2001), previous studies of delay discounting have been equivocal (White et al., 2008, Lempert et al., 2012). One difference between the present study and past ones is that the current participants were heavy drinkers. Thus, it is possible that for drinkers, acute stress may increase the salience of alcohol specifically and monetary rewards may not be similarly affected. Since this is the first study to investigate acute stress effects on delay discounting in drinkers, further research is needed to test these hypotheses. Future studies should examine acute changes in delay discounting for a variety of reward types, including alcohol rewards (Petry, 2001)

The second component of this study sought to determine whether changes in craving and incentive value were further augmented by alcohol-related stimuli. Stress and alcohol cues had an additive effect on alcohol craving, which is consistent with some prior studies (Coffey et al., 2002, Liu and Weiss, 2002). However, not all studies have found these manipulations to be additive (Thomas et al., 2011, Ray, 2011). Differences in clinical severity and stress induction type across studies may account for these mixed findings. All participants in Thomas et al. (2011) had an AUD whereas the present participants were selected based on drinking quantity and not clinical diagnosis. Second, Ray (2011) used a

personalized stress induction rather than the TSST used here. Future studies are needed to examine changes in craving in clinical vs. non-clinical samples and to compare different stress manipulations.

Rather surprisingly, the behavioral economic indices did not show additive effects of stress and alcohol cues. With the exception of Breakpoint, the value of alcohol conformed to an inverted U-shape, with moderate levels at baseline, a significant increase following stress, and then returning to near baseline levels after the cue exposure for both conditions. This is inconsistent with previous studies indicating that alcohol cues increase demand (Amlung et al., 2012, MacKillop et al., 2010b). However, one unique aspect of the present study was that participants were given an acute stressor prior to interacting with the beverage cues. It is possible that the TSST elevated incentive value to individual's maximum level, thus preventing any further influence by the cues. These results also align with the finding that acute stress attenuates responses to alcohol cues (Ray, 2011). However, the absence of a non-stress control group in the present study prevented us from fully characterizing whether our findings were explained by suppressive effects of stress.

These findings should be viewed in the context of the study's limitations. Although the participants were all heavy drinkers, they were predominately young, relatively well-educated, and Caucasian. Participants were also selected based on level of alcohol consumption, not the presence of an AUD. As such, caution is needed when generalizing these findings to the larger population of drinkers or to clinical samples. We also did not collect biochemical markers of stress response (e.g., cortisol) to further validate the TSST. The DDT only assessed choices for one delay length, and, as such, we were unable to estimate hyperbolic temporal discounting functions (k_s) or area under the curve. However, assessing multiple delay lengths would have lengthened the time required to complete the task which was considered to be suboptimal given that the effects of stress and cues may be short-lived (e.g., Zwaan et al., 2000). Of note, abbreviated delay discounting measures have recently been developed that may be useful targets for future studies (Gray et al., 2014, Koffarnus and Bickel, in press). The order of the three behavioral economic measures was also not counterbalanced across participants. As such, we were unable to account for potential order effects on these measures. Finally, the study design was specifically oriented to examining within-subjects effects of the stress manipulation. As a result, it did not include a non-stress control group, which precluded examining independent effects of stress and cues. This design may have also constrained power to detect cue effects. Future studies using a full factorial 2x2 design and larger samples would allow for more direct comparisons to previous studies (e.g., Ray, 2011).

In summary, the present study found that both subjective craving and incentive value of alcohol were dynamically influenced by the experience of acute stress. The combined effects of stress and alcohol cues on incentive value were generally not additive, despite additive effects on craving. These results support the notion that subjective craving and behavioral economic indices of incentive value are complementary multi-dimensional channels of drug motivation that are more or less sensitive in different contexts. More broadly, this study suggests that adding the behavioral economic construct of incentive value to existing

laboratory stress models may aid in future development of psychological and pharmacological interventions for alcoholism and other addictive disorders.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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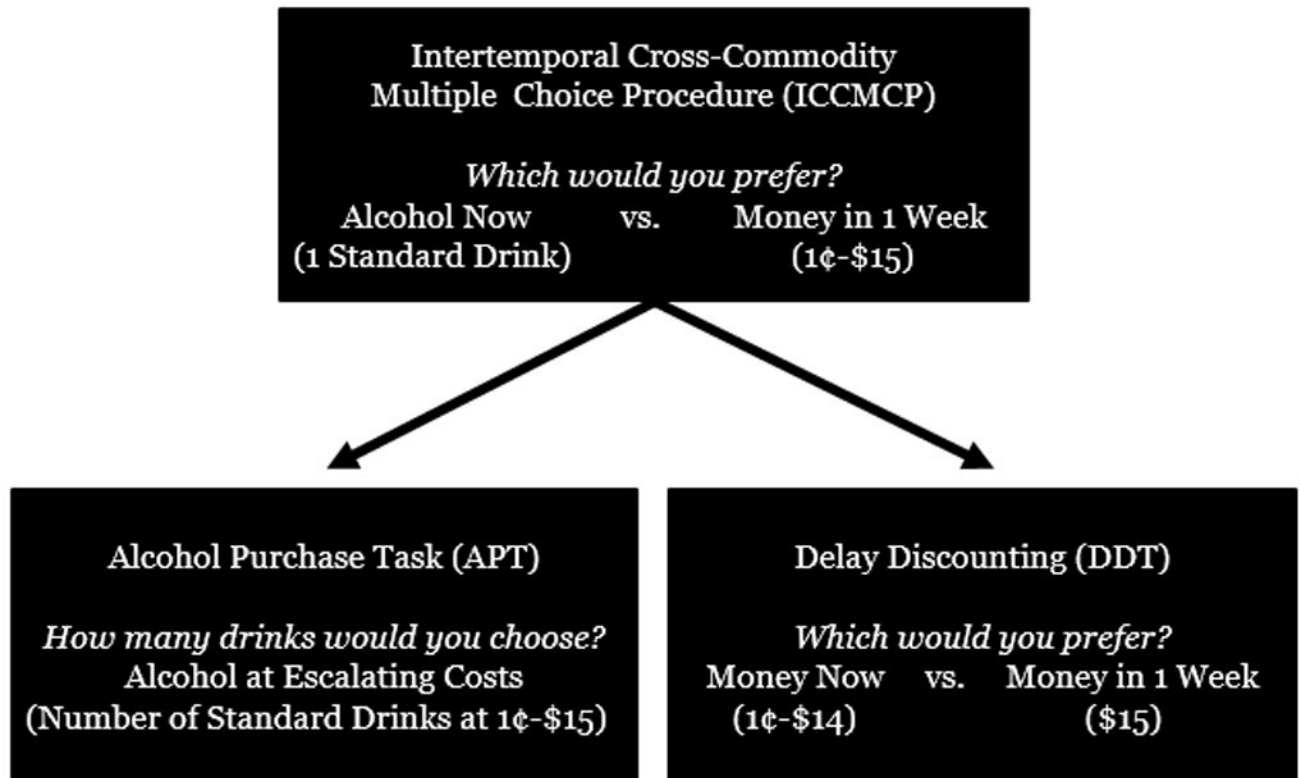


Figure 1. Relationship between behavioral economic measures

The primary behavioral economic measure—the intertemporal cross-commodity multiple choice procedure (ICCMCP)—combined elements of cost and delay into a single assessment. Effects on the ICCMP were further disentangled using the two secondary measures. The alcohol purchase task (APT) and delay discounting task (DDT) examined the influence of alcohol demand and intertemporal choice, respectively. Sample items from each measure are provided.

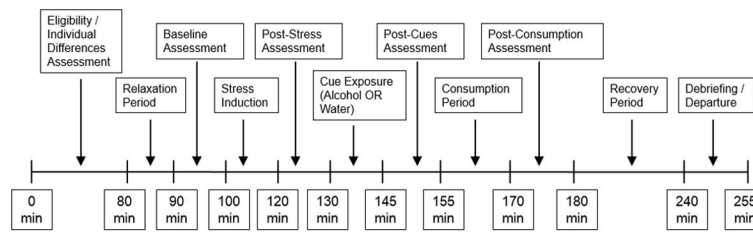


Figure 2. Schematic diagram of laboratory session components

Assessments are listed in top row, exposures and other key events are listed in middle row, and corresponding time points relative to the start of the session are provided in the bottom row. Random selection and provision of ICCMCP outcome (alcohol or money) occurred following Post-Cues assessment.

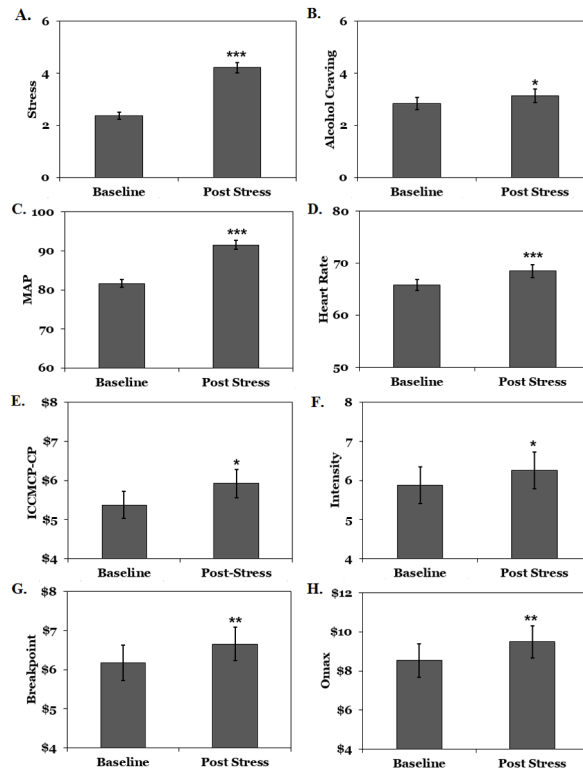


Figure 3. Significant effects of acute stress on affect, arousal, craving, and behavioral economic indices

Panel A depicts composite stress ratings; Panel B depicts subjective craving for alcohol; Panels C–D depict physiological arousal (MAP: Mean Arterial Pressure); Panel E depicts crossover point on the intertemporal cross-commodity multiple choice procedure (ICCMCP); Panels F–H depict Intensity, Breakpoint and O_{\max} from the alcohol purchase task. Bars reflect mean (\pm standard error). * $p < .05$; ** $p < .01$.

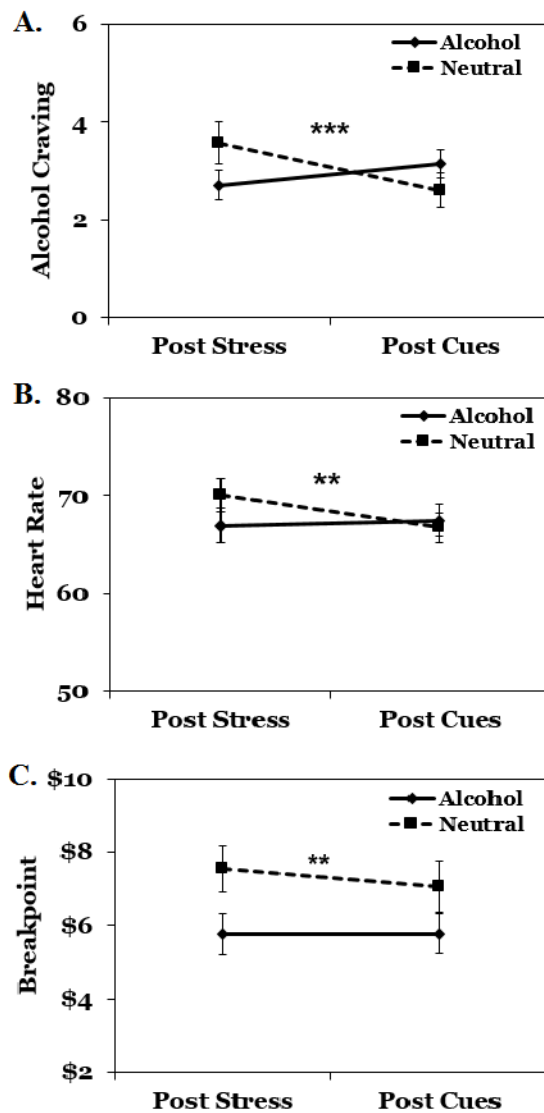


Figure 4. Effects of alcohol cues on arousal, craving, and alcohol demand

Panel A depicts change in alcohol craving; Panel B depicts change in heart rate; Panel C depicts change in Breakpoint on the alcohol purchase task. Note, in Panel C, the two groups were significantly different at the Post-Stress time point ($p = .04$). In each panel, solid lines reflect the alcohol cues group; dashed lines reflect the neutral cues group. Data points reflect mean (\pm standard error). ** $p < .01$; *** $p < .001$.

Table 1

Sample Characteristics.

Characteristic	Alcohol Cues	Neutral Cues	Overall
N	42	42	84
Sex	50% Female	50% Female	50% Female
Race			
Caucasian	64%	64%	64%
African American	19%	22%	20%
Asian	10%	12%	11%
American Indian/Alaskan Native	2%	0%	1%
Mixed Race	5%	3%	4%
Ethnicity	7% Hispanic	7% Hispanic	7% Hispanic
Age, <i>M</i> (<i>SD</i>)	22.10 (2.42)	22.38 (2.06)	22.24 (2.24)
Income, Median [IQR]	\$60k [\$20k–\$80k]	\$65k [\$40k–\$80k]	\$65k [\$40k–\$80k]
Drinks / Week, <i>M</i> (<i>SD</i>)	16.80 (8.75)	15.38 (9.19)	16.08 (8.95)
AUDIT, <i>M</i> (<i>SD</i>)	10.62 (4.54)	10.29 (4.76)	10.45 (4.65)

Note: AUDIT = Alcohol Use Disorders Identification Test; *M* = mean; *SD* = standard deviation; IQR = inter-quartile range. No significant differences were present between the alcohol and neutral cue groups.

Table 2

Effects of Acute Stress Induction

Variable	$F_{(1,83)}$	η_p^2
<i>Subjective Mood and Alcohol Craving</i>		
Stress Composite	132.12***	.61
Alcohol Craving	4.15*	.05
<i>Arousal</i>		
MAP	82.16***	.50
Heart Rate	13.64***	.14
<i>Behavioral Economic Indices</i>		
ICCMCP-CP	5.92*	.07
Intensity	4.61*	.05
Breakpoint	8.20**	.09
Omax	9.23**	.10
Elasticity	1.84	.02
ICR	3.15	.04

Note:

* $p < .05$;

* $p < .01$;

*** $p < .001$.

ICCMCP-CP = crossover point on alcohol multiple choice procedure; ICR = impulsive choice ratio on delay discounting task; MAP = mean arterial pressure; M = mean; SE = standard error of the mean.

Table 3

Effects of Alcohol Cue Exposure

Variable	ME Time		ME Condition		T × C	
	F _(1,82)	η ²	F _(1,82)	η ²	F _(1,82)	η ²
<i>Subjective Mood and Alcohol Craving</i>						
Stress Composite	66.80***	.45	0.75	.01	1.34	.02
Alcohol Craving	2.46	.03	0.12	.00	17.97***	.18
<i>Arousal</i>						
MAP	16.76***	.17	1.86	.02	0.01	.00
Heart Rate	4.39*	.05	0.28	.00	8.11**	.09
<i>Behavioral Economic Indices</i>						
ICCMCP-CP	10.68**	.12	1.37	.02	1.04	.01
Intensity	9.33**	.10	0.12	.00	0.44	.01
Breakpoint	2.98	.04	2.69	.03	4.42*	.05
O _{max}	9.78**	.11	1.93	.02	3.21	.04
Elasticity	1.82	.02	2.74	.03	0.06	.00
ICR	0.04	.00	1.79	.02	0.16	.00

Note:

* $p < .05$;

** $p < .01$;

*** $p < .001$.

ICCMCP-CP = crossover point on alcohol multiple choice procedure; ICR = impulsive choice ratio on delay discounting task; MAP = mean arterial pressure; ME = main effect; T × C = time × condition interaction.

Table 4

Mediational Analyses of Stress Effects on ICCMCP Crossover Point

Mediator	B	SE	β	<i>p</i>
<i>O</i> _{max}				
<i>Difference</i>	0.75	0.35	0.23	.04
<i>Sum</i>	0.05	0.10	0.06	.58
<i>Intercept</i>	0.39	0.24	—	.10
Breakpoint				
<i>Difference</i>	0.99	0.52	0.21	.06
<i>Sum</i>	0.20	0.15	0.15	.19
<i>Intercept</i>	0.41	0.23	—	.08
Intensity				
<i>Difference</i>	0.39	0.53	0.08	.46
<i>Sum</i>	0.02	0.15	0.02	.88
<i>Intercept</i>	0.51	0.24	—	.03

Note: SE = standard error; Difference = value of mediator at Post-Stress minus value of mediator at Baseline; Sum = value of mediator at Post-Stress plus value of mediator at Baseline (mean-centered); Intercept = residual effect on criterion variable above and beyond mediation.