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BEHAVIORAL ECONOMIC ANALYSIS OF STRESS EFFECTS ON ACUTE MOTIVATION FOR ALCOHOL

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Due to issues of definition and measurement, the heavy emphasis on subjective craving in the measurement of acute motivation for alcohol and other drugs remains controversial. Behavioral economic approaches have increasingly been applied to better understand acute drug motivation, particularly using demand curve modeling via purchase tasks to characterize the perceived reinforcing value of the drug. This approach has focused on using putatively more objective indices of motivation, such as units of consumption, monetary expenditure, and price sensitivity. To extend this line of research, the current study used an alcohol purchase task to determine if, compared to a neutral induction, a personalized stress induction would increase alcohol demand in a sample of heavy drinkers. The stress induction significantly increased multiple measures of the reinforcing value of alcohol to the individual, including consumption at zero price (intensity), the maximum total amount of money spent on alcohol (O_{max}), the first price where consumption was reduced to zero (breakpoint), and the general responsiveness of consumption to increases in price (elasticity). These measures correlated only modestly with craving and mood. Self-reported income was largely unrelated to demand but moderated the influence of stress on O_{max}. Moderation based on *CRH-BP* genotype (rs10055255) was present for O_{max}, with T allele homozygotes exhibiting more pronounced increases in response to stress. These results provide further support for a behavioral economic approach to measuring acute drug motivation. The findings also highlight the potential relevance of income and genetic factors in understanding state effects on the perceived reinforcing value of alcohol.

Key words: behavioral economics, stress, demand, alcohol, state effects, *CRH-BP*

The role of craving in addiction has been studied scientifically for more than 50 years (Tiffany & Wray, 2012; World Health Organization, 1954). However, the significance of craving in maintaining addictive behavior and leading to posttreatment relapse remains controversial, in part because of conflicting empirical findings (e.g., Niaura et al., 1999; Perkins, 2009; Tiffany & Carter, 1998; Wray, Gass, & Tiffany, 2013). One major reason for this may be the inherent difficulties in the measurement of craving (Sayette et al., 2000). For example, many studies rely on single-item self-report measures, which provide only a narrow definition of the phenomenon, and participants may vary considerably in their interpretation of the term "craving." Furthermore, craving reports are often made retrospectively and experiential states may not be as robustly encoded in memory compared to episodic events (Sayette et al., 2000). One further issue is that craving is inherently subjective in nature, meaning that it is subject to the general challenges to introspection (Wilson & Dunn, 2004).

A possible strategy to address these issues is the use of behavioral economics to quantify aspects of an individual's motivation to use a drug. Behavioral economics is a hybrid field that applies principles of psychology and economics to study values, preferences, and decision making. From a behavioral economic perspective, craving is only one facet of acute drug motivation (i.e., an individual's state-level drive for the drug that is multidimensional in nature); another critical facet is the reinforcing value of the drug to an organism (MacKillop et al., 2012), defined as the amount of work an

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organism will engage in to obtain a given reinforcer. More specifically, this approach proposes that dynamic increases in motivation reflect acute increases in the reinforcing value of the drug to the organism (Loewenstein, 1999; MacKillop et al., 2010). Reinforcing value for a drug is often measured using purchase tasks in which participants are offered the opportunity to purchase their drug of choice at various prices. The results of this task are translated into a demand curve and several resulting indices of demand are generated. Demand indicates the reinforcing value of a drug to an individual, using monetary terms as the operant response cost. Demand curve analysis is considered to be the most comprehensive means currently available of studying reinforcing value (Hursh, Galuska, Winger, & Woods, 2005).

Although this is a recent line of research, the empirical studies to date are generally supportive. For example, the perceived reinforcing value of alcohol has been shown to increase in the presence of alcohol cues (MacKillop et al., 2010). Similar patterns have also been observed in studies on dynamic changes in motivation for tobacco (Acker & MacKillop, 2013; Hitsman et al., 2008; MacKillop et al., 2012). Furthermore, laboratory studies that include both measures of craving and indices of demand have revealed significant correlations between the two (e.g., MacKillop, Menges, McGeary, & Lisman, 2007; MacKillop et al., 2010; McKee, O'Malley, Shi, Mase, & Krishnan-Sarin, 2008; O'Malley, Krishnan-Sarin, Farren, Sinha, & Kreek, 2002). However, craving is still only modestly-to-moderately associated with demand (Acker & Mackillop, 2013; MacKillop et al., 2010, 2012). Thus, demand appears to provide unique information about an individual's acute drug motivation. From a theoretical perspective, reinforcing value is putatively critical in an individual's deciding whether or not to drink and is more proximal to consumption than craving, although this this has not been tested empirically.

Current neurobiological theories of addiction emphasize disruption of the stress pathways in the brain as an essential component of addiction (Koob & Kreek, 2007; Sinha, 2012). Stress has frequently been linked to severity of drug addiction and posttreatment relapse (Sinha, 2001). Furthermore, numerous studies have been conducted linking stress and relapse in alcoholics (e.g., Brown, Vik, Patterson, Grant, & Schuckit, 1995; Levy, 2008; Vuchinich & Tucker, 1996). However, most of these studies are correlational or qualitative in nature. It has been significantly more difficult to demonstrate a causal relationship of stress on alcohol relapse (Thomas, Bacon, Randall, Brady, & See, 2011; Thomas, Randall, Brady, See, & Drobes, 2011). This is partially due to ethical concerns, which preclude experimentally testing this hypothesis in clinical populations directly. As a result, most research in this area has focused on laboratory studies of analogue populations, such as social drinkers or non-treatment-seeking heavy drinkers. There are multiple methods that have been used to induce stress, including the Trier Social Stress Task and guided imagery inductions. Each of these methods has its own strengths and weaknesses (Thomas, Bacon, Sinha, Uhart, & Adinoff, 2012) and the results of well-controlled studies examining stress-induced alcohol craving have been mixed, with some finding stress increases craving (e.g., Coffey, Stasiewicz, Hughes, & Brimo, 2006; Cooney, Litt, Morse, Bauer, & Gaupp, 1997; Fox, Bergquist, Hong, & Sinha, 2007; George et al., 2008; Sinha, 2009; Thomas, Bacon, et al., 2011) but others not finding that to be the case (e.g., Brady et al., 2006; Jansma, Breteler, Schippers, De Jong, & Van Der Staak, 2000; Pratt & Davidson, 2009; Rubonis et al., 1994; Thomas, Randall et al., 2011). Given these mixed findings, behavioral economic measures of demand may clarify the ambiguity that exists regarding the role of stress on motivation to use alcohol. The primary aim of the current study was to use a behavioral economic approach to examine the effects of an imaginal stress-imagery mood induction on alcohol demand. The study is a secondary analysis from a parent study on the role of stress in subjective craving for alcohol (Ray, 2011). Within the parent study, a well-validated procedure comprising a stressful and neutral imaginal induction (Sinha, 2007, 2008) was used to elicit an acute increase in stress and a state-oriented alcohol purchase task (APT) was completed as an exploratory assessment following each induction, permitting alcohol demand curve analysis at each time point. Demand curves and indices of demand were compared between induction conditions to test the prediction that the stress induction would significantly increase alcohol demand. Analyses were also completed to evaluate the relationship between demand, craving, and self-reported mood. It was hypothesized that the alcohol demand indices would be only moderately correlated with craving and self-reported mood, suggesting they are not simply redundant with traditional measures. The study also explored two potential moderating variables. First, the relationship between income and stress effects on alcohol demand was investigated, as it is possible that a person's demand preferences could be affected by proximal financial resources. Second, we investigated the effects of a genetic moderator, a single nucleotide polymorphism (SNP) in the corticotropin releasing factor-binding protein gene (*CRH-BP;* rs10055255). Substantial genetic influences on addiction are well-established (Goldman, Oroszi, & Ducci, 2005) and there is considerable interest in using laboratory studies to probe the mechanisms of genetic influences on alcohol-related motivation (Ray & Hutchison, 2004), including behavioral economic variables in particular (MacKillop & Acker, 2013). In this case, the *CRH-BP* gene has been shown to modulate the effects of stress-induced relapse in preclinical models (Wang et al., 2005; Wang, You, Rice, & Wise, 2007) and rs10055255 was found to moderate the effects of stress on craving in the parent study (Ray, 2011). Therefore, we investigated whether this locus would have a similar moderating effect on behavioral economic indices.

Method

Participants

Participants were non-treatment-seeking heavy drinkers. All participants were between 18 and 65 and had scores of 8 or higher on the Alcohol Use Disorder Identification Test (AUDIT; Allen, Litten, Fertig, & Babor, 1997). Participants who were currently seeking or had recently (last 30 days) sought treatment for alcohol problems were excluded. Exclusion criteria also included lifetime diagnosis with any psychotic or bipolar disorder and current weekly (or greater) use of any psychoactive drug, other than marijuana.

A total of 64 participants enrolled, though 2 were subsequently excluded for data quality reasons (see Data Analysis). Of the valid participants, 23 were female (36%). The average age was 20.76 (SD = 2.55). Forty-six participants were Caucasian, eleven were Asian, four were Latino, and one was African-American. Self-reported, household income was recorded in the following categories: Under $9,999/year ($n = 35$), $10,000-$19,999/year ($n = 9$), $20,000–29,999/year ($n = 1$), $30,000–39,999/year ($n = 1$), $40,000–49,999/year ($n = 4$), $50,000–59,999/year ($n = 3$), $60,000 and over/year ($n = 9$). Participants' average AUDIT score was 15.88 (SD = 6.08).

Measures

Alcohol purchase task. Alcohol demand was assessed using a state-oriented alcohol purchase task (APT) that has been demonstrated to be effective at measuring alcohol demand in previous studies (MacKillop et al., 2010; Murphy & MacKillop, 2006). The alcohol purchase task was administered in pencil and paper format and the instructions read: "Please respond to these questions honestly. Imagine that you could drink RIGHT NOW. The following questions ask how many drinks you would consume if they cost various amounts of money. The available drinks are standard size domestic beer (12 oz.), wine (5 oz.), shots of hard liquor (1.5 oz.), or mixed drinks containing one shot of liquor. Assume that you would consume every drink you request; that is, you cannot stockpile drinks for a later date or bring drinks home with you." Participants then reported their estimated consumption at the following 16 price intervals: free, 1¢, 5¢, 13¢, 25¢, 50¢, $1, $3, $6, $11, $35, $70, $140, $280, $560 and $1120. These prices were based on the doubling response requirement of a progressive-ratio operant schedule and were originally developed to investigate tobacco and opiate demand (Jacobs & Bickel, 1999).

Alcohol Urge Questionnaire. The Alcohol Urge Questionnaire (AUQ) is an eight-question scale for assessing state-based craving for alcohol. The AUQ has been shown to be sensitive to state-based changes in craving and effective for repeated administrations over a short duration (Bohn, Krahn, & Staehler, 1995; Drummond & Phillips, 2002; MacKillop, 2006).

Profile of Mood States. The Profile of Mood States (POMS; McNair, Lorr, & Droppleman, 1971) is an assessment of current mood state commonly used in human laboratory studies of addiction (e.g., Ray, MacKillop, Leventhal, & Hutchison, 2009). Participants completed only 40 items from the original POMS and only the Tension and Negative Mood subscales were analyzed to characterize the effects of the stress induction on subjective mood. Each subscale contains 10 items rated 0 to 5 on a Likert scale.

Procedures

Participants were recruited from the Los Angeles, California area using local media. Participants were initially screened by telephone for eligibility and if eligible were scheduled for two in-person laboratory sessions. After arriving to the first session, participants were given further details of the study and provided written informed consent. All procedures were approved by the Human Research Committee at the University of California, Los Angeles. Subsequently, participants completed demographic and other individual difference assessments and completed training for the imaginal exposures that would be used in the second laboratory session, scheduled for a later date. Participants also provided information about recent stressful and neutral life events that would be used to generate scripts for use in the imaginal exposures. Stressful events were assessed on a Likert scale of 0 to 10, with 10 being the most stressful, and only events greater than 8 were used.

Between the first and second sessions, personalized scripts were written and tape recorded that recounted the participant's reported stressful and neutral events. At the second visit, participants completed two imaginal exposures (stress and neutral), each of which was followed by an exposure to an alcohol cue. Each imaginal exposure consisted of participants listening to a 5-min audio recording recounting the event described at the previous session. Recordings included details of both the events themselves and the feelings associated with them, as described by the participants. The order of the stress exposures was counterbalanced and each set of exposures was separated by a 1-hr break to avoid carryover effects. Mood, alcohol craving, and alcohol purchase tasks were completed following stress and neutral exposures. For more details, see Ray (2011).

Data Analysis

The data were initially examined for missing data, outliers, performance validity, and distributions. Among all participants, nine data points were missing on the APT. Missing values occurred entirely within the first three prices ($0.00, $0.01, $0.05) and were imputed as the number of drinks purchased at the next highest price (when the missing response was to the first price) or at the average of the prices before and after the missing response (when the missing response was to the second or third price). Defining outliers as $Z > 4.00$, one participant's responses to the alcohol purchase task were entirely outliers and this individual was excluded from further analysis. In addition, another participant exhibited invariant low responding, reporting no preferences for alcohol at any price (including $.00) and preventing calculation of several demand indices. This participant was also excluded from further analysis. No other outliers were identified for price responses to the alcohol purchase task, but three outliers were detected for O_{max}, four outliers were detected for breakpoint, and three outliers were detected for elasticity. These outliers were recoded as the next highest non-outlying value to retain the data and reflect the position of the response, but also minimize excessive leverage (Tabachnick & Fidell, 2006). Examination of histograms suggested that the demand variable distributions were adequate.

The behavioral economic indices were primarily generated using an observed-values approach (Murphy & MacKillop, 2006). Specifically, intensity was defined as consumption at the price of $.00; O_{max} was defined as the maximum amount of money expended on alcohol at any price; breakpoint was defined as the first price where consumption was reduced to 0. In addition, using nonlinear regression, elasticity was generated as the α parameter in the exponential demand equation, $\log_{10}Q = \log_{10} Q_0 + k(e^{-\alpha Q_0 C} - 1)$, derived by Hursh & Silberberg (2008). In this equation, Q = consumption at a given price; Q_0 = maximum consumption (consumption at $.00); k = a constant that denotes the range of consumption values in $\log_{10}$ across individuals, in this case 3; C = price; and α = the derived elasticity parameter. The primary analyses focused on the demand indices, which were compared across each condition (neutral induction/stress induction) using one-way repeated measures analyses of variance (ANOVAs). For descriptive purposes, estimated alcohol consumption at each price was examined using the same approach. Of note, no participants reported drinking above the twelfth price ($70) and no analysis was conducted on these prices. To examine the overlap between demand and subjective craving and mood, Pearson's product-moment correlations (r) were conducted on performance after each induction. Moderating analyses for income were conducted where correlations

Table 1

Differences in BE indices following neutral and stress inductions

	Neutral Induction *M*	Neutral Induction *SE*	Stress Induction *M*	Stress Induction *SE*	*F*	*p*	η^2_p
Intensity	8.089	0.632	10.000	0.698	11.090	.001	.154
O_{max}	13.645	1.241	19.177	1.679	18.037	<.001	.228
BP	22.807	1.925	29.274	1.891	15.472	<.001	.202
Elasticity (α)	.021	.004	.009	.001	9.830	.003	.143

were observed between income and demand indices. Moderating analyses by genotype comprised 3 (*CRH-BP* genotype) x 2 (neutral induction/stress induction) mixed ANOVAs.

Results

Stress Effects on Behavioral Economic Indices of Alcohol Motivation

One-way repeated measures ANOVAs revealed that intensity, O_{max}, and breakpoint were significantly higher following stress induction compared to neutral induction, reflecting higher motivation for alcohol in each case. Similarly, elasticity of demand for alcohol was significantly lower following stress induction than following neutral induction, reflecting diminished price sensitivity. These effects are presented in Table 1. Price-level ANOVAs revealed significantly higher demand at the first 10 prices, \$0/drink to \$11/drink, and are depicted in Figure 1. Illustrative individual-level data are presented in Figure 2. Additionally, one-way repeated measures ANOVAs found that craving [$F(1,61) = 28.864$; $p < .001$; $\eta^2_p = .321$], stress [$F(1,61) = 4.181$; $p = .045$; $\eta^2_p = .045$], and negative mood [$F(1,61) = 56.671$; $p < .001$; $\eta^2_p = .482$] were all significantly higher following stress induction.

Relationship between Indices of Alcohol Demand, Subjective Craving, and Mood

Pearson product-moment correlations were conducted between indices of demand and self-reported craving (Table 2). Correlations between demand indices and craving were generally small in magnitude, with only intensity and craving following neutral induction reaching significance (~5% of variance shared). Additionally, correlations were conducted between the demand indices and self-reported stress and negative mood. Here, the only significant relationships observed were between stress and depression (~31% of variance shared) and between depression and craving (~22% of variance shared), both selectively following the stress induction. No significant associations were present between the demand indices and subjective mood.

Moderators of Stress Effects on Alcohol Demand: Income and CRH-BP Genotype

Pearson product-moment correlations were completed examining the relationship between alcohol consumption/demand and income (Table 2). This indicated a significant relationship between income and O_{max} (~9% of variance accounted for) following the stress induction. Because of the bimodal distribution of this sample (87.5% of participants reporting income in the two highest or two lowest brackets), we dichotomized participants into lower or higher income groups. We then performed a 2 (lower income/higher income) x 2 (neutral induction/stress induction) mixed ANOVA for O_{max} which revealed a significant interaction [$F(1,60) = 4.602$; $p = .03$,

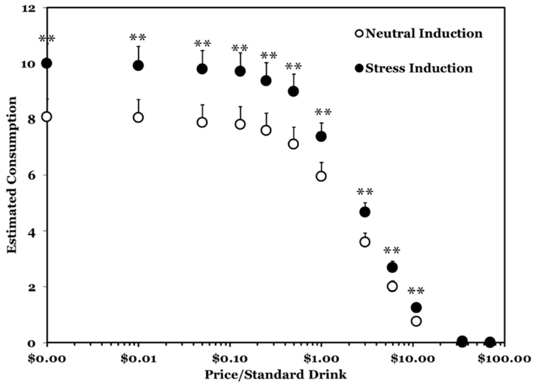

Fig. 1. Demand curves for alcohol following neutral induction and stress induction.
Notes: $^{**}p < .01$; since zero price cannot be depicted in logarithmic terms, in this figure .001 is used as a placeholder on the x-axis.

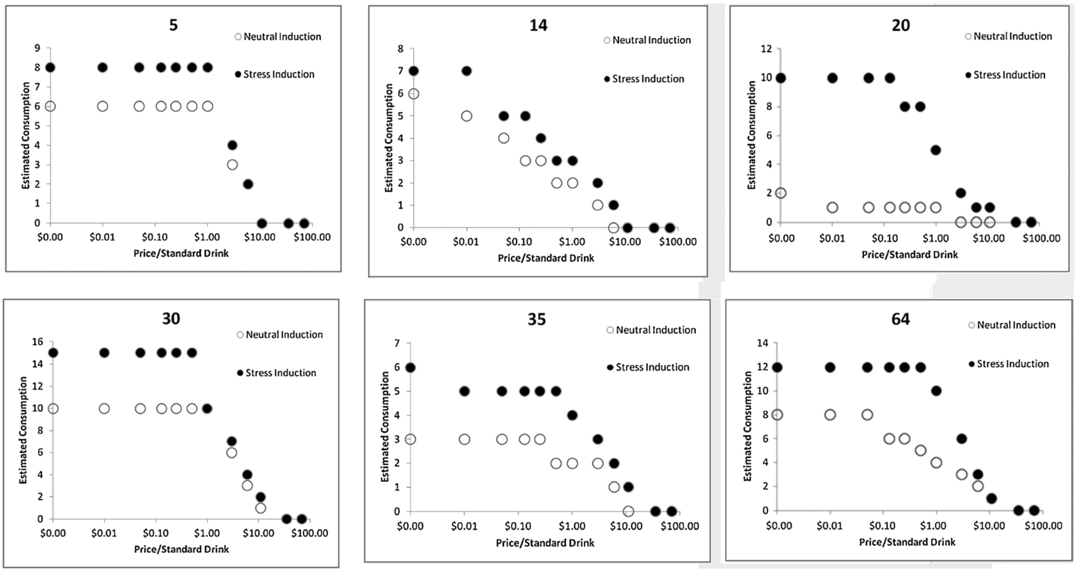

Fig. 2. Illustrative effects of the stress induction on alcohol demand preferences in six participants.

$\eta^2_p = .071$]. Individuals in the higher income group exhibited differentially greater O_{max} following the stress induction, illustrated in Figure 3.

For *CRH-BP* genotype (rs10055255), allele frequencies were as follows: AA ($n = 16$), AT ($n = 31$), TT ($n = 15$). This single nucleotide polymorphism (SNP) was in conformity with Hardy-Weinberg Equilibrium [$\chi^2(1) = 0$, $p = 1.0$]. The SNP was not associated with sex [χ^2 (2) = .127, $p = .939$] or income [χ^2 (2) = 3.016, $p = .221$]. Moderator analyses using 3 (genotype) x 2 (neutral induction/stress induction) mixed ANOVAs revealed a significant interaction effect between *CRH-BP* rs10055255 genotype and induction type on O_{max} [$F(2,59) = 4.073$, $p = .022$, $\eta^2_p = .121$]. As illustrated in

Table 2

Correlations between BE indices, craving, and mood following neutral and stress induction

Correlations Neutral	1	2	3	4	5	6	7	8
Intensity	1							
O_{max}	.490**	1						
BP	.452**	.742**	1					
Elasticity	−.539**	−.600**	−.634**	1				
State Craving	.253*	.176	.185	−.174	1			
State Stress	−.037	.061	.030	−.180	.190	1		
State Depression	.148	.085	.035	−.042	.193	.125	1	
Income	.016	.125	.049	−.154	.116	.129	.068	1
Correlations Stress	9	10	11	12	13	14	15	16
Intensity	1							
O_{max}	.443**	1						
BP	.384**	.719**	1					
Elasticity	−.415**	−.565**	−.698**	1				
State Craving	.154	.211	.151	−.142	1			
State Stress	−.055	−.083	.012	−.069	.240	1		
State Depression	.083	.213	.176	−.164	.470**	.557**	1	
Income	.094	.297*	.196	−.198	.105	−.233	.064	1

$^{**}p < .01$.

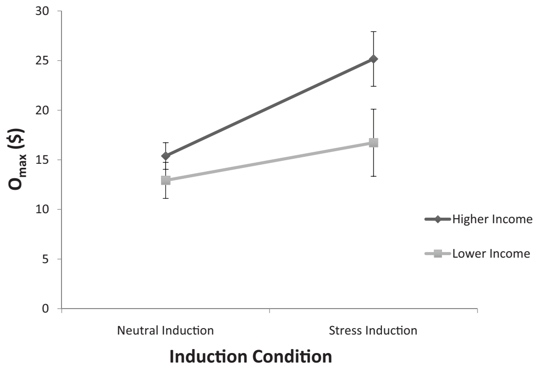

Fig. 3. Changes in O_{max} for participants of higher and lower income levels.

Figure 4, the pattern of findings suggested that TT homozygotes were particularly sensitive to the stress induction. No other interactions were observed: intensity [$F(2,59) = 2.820$, $p = .068$, $\eta^2_p = .087$], elasticity [$F(2,59) = 1.009$, $p = .371$, $\eta^2_p = .034$], and breakpoint [$F(2,59) = 2.362$, $p = .103$, $\eta^2_p = .074$].

Discussion

This study sought to use behavioral economics to improve the understanding of the effects of stress on acute motivation to use alcohol. Consistent with our predictions, demand for alcohol was significantly greater following stressful induction compared to a neutral induction. Specifically, this study suggests that stress increases the reinforcing value of alcohol on key facets of the demand curve, including its initial intercept (intensity), maximum expenditure (O_{max}), maximum acceptable price (breakpoint), and overall price sensitivity (elasticity). In other words, after the stress induction, participants wanted to drink more alcohol at no cost, they were willing to spend more total money on alcohol, they were willing to drink to higher prices, and they were generally less affected by the price of alcohol. The results provide further evidence that perceived reinforcing value is state-dependent and that it can be affected by stressful events occurring in the life of an individual. Phasic shifts in reinforcing value of drugs to the individual are thought to underlie the preference reversals that are common in alcohol use disorders, such as decisions to keep drinking beyond a self-imposed limit or to return to drinking following treatment. These results demonstrate the change in reinforcing value that putatively underlies such dynamic inconsistency.

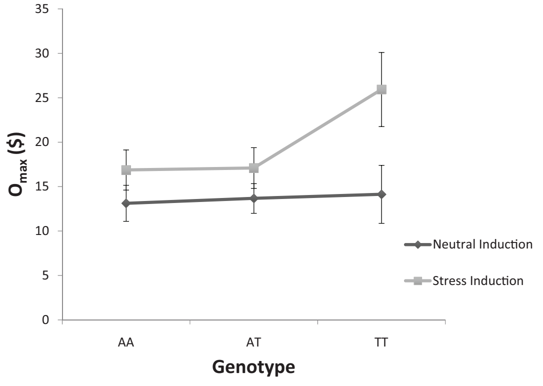

Fig. 4. Interaction between induction condition and *CRH-BP* rs10055255 genotype for O_{max}.

Notably, the traditional motivational measure of subjective craving was only modestly correlated with demand, which corresponds with the existing literature showing that behavioral economic indices do not appear to be redundant with craving (Acker & MacKillop, 2013; MacKillop et al., 2010, 2012). Similarly, the indices of demand were not significantly correlated with self-reported emotional state following either induction. In general, the current findings suggest that the perceived reinforcing value of alcohol is generally distinct from experiential states. If additional research supports the current findings, adding behavioral economic indices may help to clarify the ambiguity that exists regarding the causal effects of stress on motivation for alcohol (e.g., Cooney et al., 1997; Fox et al., 2007; Jansma et al., 2000; Pratt & Davidson, 2009; Rubonis et al., 1994; Sinha, 2009; Thomas, Bacon, et al., 2011; Thomas, Randall, et al., 2011). Specifically, it is possible that stress effects on behavioral economic indices of motivation may be more reliably observed compared to subjective craving. Additionally, it is possible that behavioral economic indices may have clinical applications. For example, indices of demand may complement subjective craving in predicting posttreatment relapse (Higley et al., 2011) or contribute to understanding the mechanisms of candidate pharmacotherapies that influence dysregulation of stress systems (e.g. Higley, Koob, & Mason, 2012). These are necessarily open empirical questions.

We explored two potential moderators in the current study, participant income and *CRH-BP* genotype. With regard to income, this study provides evidence that income may influence the effects of stress on aspects of demand, in this case O_{max}. Higher-income individuals appeared to be more sensitive to stress effects, as O_{max} differentially increased in those individuals. O_{max} is the index reflecting total allocation of money to spend on alcohol, so it is certainly plausible that it might be affected by an individual's current financial situation. To our knowledge, this is a novel finding and it makes the point that consideration of personal resources is important when using behavioral economic variables that are necessarily contextualized within an individual's personal resources. With regard to genotype, our hypothesis that demand indices would be moderated by the *CRH-BP* rs10055255 genotype was partially confirmed, as this gene showed significant moderation effects on O_{max}. The finding that the *CRH-BP* rs10055255 gene moderates the effects of stress on some, but not all, aspects of demand further demonstrates how the indices of demand reported each reveal different aspects of motivation. As the effect was significant for O_{max} and nonsignificant for intensity, breakpoint, and elasticity, it seems that this gene may be a moderator for maximum financial expenditure rather than the consumption intercept or measures of price sensitivity. Because this is the first study investigating the effects of this genetic locus on the reinforcing value of alcohol, further research is needed to verify that this is a consistent effect. Nonetheless, existing research suggests that this gene modulates the effectiveness of stress at inducing drug use (Wang et al., 2005, 2007), making it highly plausible as a modulator of the impact of stress on motivation. This study thus provides a starting point for clarifying ways that this genotype, and almost certainly others, influence stress effects on alcohol-related decision making.

There are several limitations of the current study that are worth noting. The sample was modest in size and a larger sample may have brought some of the findings into sharper relief. In particular, a larger sample may reveal significant moderating effects of *CRH-BP* genotype on intensity and elasticity, which were directionally consistent with the effect on O_{max}. Replicating these findings in a larger sample will be important to confirm they are robust and would appear to be generally feasible in light of the small-to-medium magnitude effects detected ($\eta^2_p = .143$ to .228 for main effects and .071 to .121 for interactions). Another consideration is that the APT used estimated preferences for alcohol consumption, rather than consequated preferences that would directly result in an alcohol or monetary outcome. However, there is evidence that behavioral economic decision making is generally consistent between hypothetical- and actual-outcome versions of measures (e.g., Irwin, McClelland, & Schulze, 1992; Johnson & Bickel, 2002; Lagorio & Madden, 2005; Madden, Begotka, Raiff, & Kastern, 2003; Madden et al., 2004), which mitigates this concern somewhat. Finally, although a strength of the study was employing an extensively validated stress manipulation (Sinha, 2001, 2009, 2013), it did not employ biological or psychophysiological methods to assess stress, such as cortisol, heart rate, or skin conductance. It would be of considerable interest in future work to contextualize stress effects on behavioral economic indices with biological indices of stress reactivity and, further, to explore mediating or moderating roles between biomarker indices and behavioral economic indices. Another potential extension of this line of research would be to further investigate the neural correlates of the effects of stress on craving and reinforcing value using neuroimaging methods. This would allow further clarification of potential differences in the effects of stress on subjective desire and the reinforcing value of alcohol.

Acknowledging these limitations, the current study nonetheless demonstrates several novel findings, including evidence that an imaginal stress induction acutely increases the perceived reinforcing value of alcohol according to multiple demand indices; that this effect is generally distinct from effects on subjective craving; and that income and *CRH-BP* genotype play important moderating roles. Taken together, these findings provide further support for the utility of behavioral economics in measuring acute motivation for alcohol and other drugs and suggest several new avenues for future research.

References

Acker, J., & MacKillop, J. (2013). Behavioral economic analysis of cue-elicited craving for tobacco: a virtual reality study. *Nicotine & Tobacco Research: Official Journal of the Society for Research on Nicotine and Tobacco, 15*(8), 1409–1416. doi: 10.1093/ntr/nts341

Allen, J. P., Litten, R. Z., Fertig, J. B., & Babor, T. (1997). A review of research on the Alcohol Use Disorders

Identification Test (AUDIT). *Alcoholism, Clinical and Experimental Research, 21*, 613–619. doi: 10.1111/j.1530-0277.1997.tb03811.x

Bohn, M. J., Krahn, D. D., & Staehler, B. A. (1995). Development and initial validation of a measure of drinking urges in abstinent alcoholics. *Alcoholism. Clinical and Experimental Research, 19*, 600–606. doi: 10.1111/j.1530-0277.1995.tb01554.x

Brady, K. T., Back, S. E., Waldrop, A. E., McRae, A. L., Anton, R. F., Upadhyaya, H. P., … Randall, P. K. (2006). Cold pressor task reactivity: predictors of alcohol use among alcohol-dependent individuals with and without comorbid posttraumatic stress disorder. *Alcoholism, Clinical and Experimental Research, 30*, 938–946. doi: 10.1111/j.1530-0277.2006.00097.x

Brown, S. A., Vik, P. W., Patterson, T. L., Grant, I., & Schuckit, M. A. (1995). Stress, vulnerability and adult alcohol relapse. *Journal of Studies on Alcohol, 56*(5), 538–545.

Coffey, S. F., Stasiewicz, P. R., Hughes, P. M., & Brimo, M. L. (2006). Trauma-focused imaginal exposure for individuals with comorbid posttraumatic stress disorder and alcohol dependence: revealing mechanisms of alcohol craving in a cue reactivity paradigm. *Psychology of Addictive Behaviors: Journal of the Society of Psychologists in Addictive Behaviors, 20*, 425–435. doi: 10.1037/0893-164X.20.4.425

Cooney, N. L., Litt, M. D., Morse, P. A., Bauer, L. O., & Gaupp, L. (1997). Alcohol cue reactivity, negative-mood reactivity, and relapse in treated alcoholic men. *Journal of Abnormal Psychology, 106*(2), 243–250.

Drummond, D. C., & Phillips, T. S. (2002). Alcohol urges in alcohol-dependent drinkers: further validation of the Alcohol Urge Questionnaire in an untreated community clinical population. *Addiction, 97*(11), 1465–1472.

Fox, H. C., Bergquist, K. L., Hong, K.-I., & Sinha, R. (2007). Stress-induced and alcohol cue-induced craving in recently abstinent alcohol-dependent individuals. *Alcoholism, Clinical and Experimental Research, 31*(3), 395–403. doi: 10.1111/j.1530-0277.2006.00320.x

George, D. T., Gilman, J., Hersh, J., Thorsell, A., Herion, D., Geyer, C., … Heilig, M. (2008). Neurokinin 1 receptor antagonism as a possible therapy for alcoholism. *Science (New York, N.Y.), 319*, 1536–1539. doi: 10.1126/science.1153813

Goldman, D., Oroszi, G., & Ducci, F. (2005). The genetics of addictions: uncovering the genes. *Nature Reviews. Genetics, 6*, 521–532. doi: 10.1038/nrg1635

Higley, A. E., Crane, N. A., Spadoni, A. D., Quello, S. B., Goodell, V., & Mason, B. J. (2011). Craving in response to stress induction in a human laboratory paradigm predicts treatment outcome in alcohol-dependent individuals. *Psychopharmacology, 218*(1), 121–129. doi: 10.1007/s00213-011-2355-8

Higley, A. E., Koob, G. F., & Mason, B. J. (2012). Treatment of alcohol dependence with drug antagonists of the stress response. *Alcohol Research: Current Reviews, 34*, 516–521.

Hitsman, B., MacKillop, J., Lingford-Hughes, A., Williams, T. M., Ahmad, F., Adams, S., … Munafò, M. R. (2008). Effects of acute tyrosine/phenylalanine depletion on the selective processing of smoking-related cues and the relative value of cigarettes in smokers. *Psychopharmacology, 196*, 611–621. doi: 10.1007/s00213-007-0995-5

Hursh, S. R., Galuska, C. M., Winger, G., & Woods, J. H. (2005). The economics of drug abuse: a quantitative assessment of drug demand. *Molecular Interventions, 5*, 20–28. doi: 10.1124/mi.5.1.6

Hursh, S. R., & Silberberg, A. (2008). Economic demand and essential value. *Psychological Review, 115*(1), 186–198. doi: 10.1037/0033-295X.115.1.186

Irwin, J. R., McClelland, G. H., & Schulze, W. D. (1992). Hypothetical and real consequences in experimental auctions for insurance against low-probability risks. *Journal of Behavioral Decision Making, 5*, 107–116. doi: 10.1002/bdm.3960050203

Jacobs, E. A., & Bickel, W. K. (1999). Modeling drug consumption in the clinic using simulation procedures: demand for heroin and cigarettes in opioid-dependent outpatients. *Experimental and Clinical Psychopharmacology, 7*(4), 412–426.

Jansma, A., Breteler, M. H. M., Schippers, G. M., De Jong, C. A. J., & Van Der Staak, C. P. F. (2000). No effect of negative mood on the alcohol cue reactivity of inpatient alcoholics. *Addictive Behaviors, 25*, 619–624. doi: 10.1016/S0306-4603(99)00037-4

Johnson, M. W., & Bickel, W. K. (2002). Within-subject comparison of real and hypothetical money rewards in delay discounting. *Journal of the Experimental Analysis of Behavior, 77*, 129–146. doi: 10.1901/jeab.2002.77-129

Koob, G., & Kreek, M. J. (2007). Stress, dysregulation of drug reward pathways, and the transition to drug dependence. *American Journal of Psychiatry, 164*(4), 1149–1159.

Lagorio, C. H., & Madden, G. J. (2005). Delay discounting of real and hypothetical rewards III: Steady-state assessments, forced-choice trials, and all real rewards. *Behavioural Processes, 69*, 173–187). doi: 10.1016/j.beproc.2005.02.003

Levy, M. S. (2008). Listening to our clients: the prevention of relapse. *Journal of Psychoactive Drugs, 40*, 167–172. doi: 10.1080/02791072.2008.10400627

Loewenstein, G. (1999). A visceral account of addiction. In J. Elster & O.-J. Skog (Eds.), *Getting hooked: Rationality and addiction*. Cambridge, UK: Cambridge University Press.

MacKillop, J. (2006). Factor structure of the alcohol urge questionnaire under neutral conditions and during a cue-elicited urge state. *Alcoholism, Clinical and Experimental Research, 30*(8), 1315–1321. doi: ACER159 [pii] 10.1111/j.1530-0277.2006.00159.x

MacKillop, J., & Acker, J. (2013). Enhancing addiction genetics via behavioral economic phenotypes. In J. MacKillop & M. R. Munafò (Eds.), *Genetic Influences on Addiction: An Intermediate Phenotrype Approach*. Cambridge, MA: MIT Press.

MacKillop, J., Brown, C. L., Stojek, M. K., Murphy, C. M., Sweet, L., & Niaura, R. S. (2012). Behavioral economic analysis of withdrawal- and cue-elicited craving for tobacco: an initial investigation. *Nicotine & Tobacco Research: Official Journal of the Society for Research on Nicotine and Tobacco, 14*(12), 1426–1434. doi: 10.1093/ntr/nts006

MacKillop, J., Menges, D. P., McGeary, J. E., & Lisman, S. A. (2007). Influences of craving and DRD4 VNTR genotype on the relative value of alcohol. *Behavioral and Brain Functions, 3*. doi: 10.1186/1744-9081-3-11

MacKillop, J., O'Hagen, S., Lisman, S. A., Murphy, J. G., Ray, L. A., Tidey, J. W., … Monti, P. M. (2010). Behavioral economic analysis of cue-elicited craving for alcohol. *Addiction, 105*(9), 1599–1607. doi: 10.1111/j.1360-0443.2010.03004.x

Madden, G. J., Begotka, A. M., Raiff, B. R., & Kastern, L. L. (2003). Delay discounting of real and hypothetical rewards. *Experimental and Clinical Psychopharmacology, 11*, 139–145. doi: 10.1037/1064-1297.11.2.139

Madden, G. J., Raiff, B. R., Lagorio, C. H., Begotka, A. M., Mueller, A. M., Hehli, D. J., & Wegener, A. A. (2004). Delay discounting of potentially real and hypothetical rewards: II. Between- and within-subject comparisons. *Experimental and Clinical Psychopharmacology, 12*, 251–261. doi: 10.1037/1064-1297.12.4.251

McKee, S. A., O'Malley, S. S., Shi, J., Mase, T., & Krishnan-Sarin, S. (2008). Effect of transdermal nicotine replacement on alcohol responses and alcohol self-administration. *Psychopharmacology, 196*, 189–200. doi: 10.1007/s00213-007-0952-3

McNair, D. M., Lorr, M., & Droppleman, L. F. (1971). Manual for the profile of mood states (POMS). San Diego, CA: Educational and Industrial Testing Services.

Murphy, J. G., & MacKillop, J. (2006). Relative reinforcing efficacy of alcohol among college student drinkers. *Experimental and Clinical Psychopharmacology, 14*(2), 219–227.

Niaura, R., Abrams, D. B., Shadel, W. G., Rohsenow, D. J., Monti, P. M., & Sirota, A. D. (1999). Cue exposure treatment for smoking relapse prevention: a controlled clinical trial. *Addiction (Abingdon, England), 94*(5), 685–695.

O'Malley, S. S., Krishnan-Sarin, S., Farren, C., Sinha, R., & Kreek, M. J. (2002). Naltrexone decreases craving and alcohol self-administration in alcohol-dependent subjects and activates the hypothalamo-pituitary-adrenocortical axis. *Psychopharmacology, 160*, 19–29. doi: 10.1007/s002130100919

Perkins, K. A. (2009). Does smoking cue-induced craving tell us anything important about nicotine dependence? *Addiction, 104*, 1610–1616. doi: 10.1111/j.1360-0443.2009.02550.x

Pratt, W. M., & Davidson, D. (2009). Role of the HPA axis and the A118G polymorphism of the mu-opioid receptor in stress-induced drinking behavior. *Alcohol and Alcoholism, 44*(4), 358–365. doi: 10.1093/alcalc/agp007

Ray, L. A. (2011). Stress-induced and cue-induced craving for alcohol in heavy drinkers: Preliminary evidence of genetic moderation by the OPRM1 and CRH-BP genes. *Alcoholism, Clinical and Experimental Research, 35*(1), 166–174. doi: 10.1111/j.1530-0277.2010.01333.x

Ray, L. A., & Hutchison, K. E. (2004). A polymorphism of the mu-opioid receptor gene (OPRM1) and sensitivity to the effects of alcohol in humans. *Alcoholism, Clinical and Experimental Research, 28*, 1789–1795. doi: 10.1097/01.ALC.0000148114.34000.B9

Ray, L. A., MacKillop, J., Leventhal, A., & Hutchison, K. E. (2009). Catching the alcohol buzz: an examination of the latent factor structure of subjective intoxication. *Alcoholism, Clinical and Experimental Research, 33*(12), 2154–2161. doi: 10.1111/j.1530-0277.2009.01053.x

Rubonis, A. V., Colby, S. M., Monti, P. M., Rohsenow, D. J., Gulliver, S. B., & Sirota, A. D. (1994). Alcohol cue reactivity and mood induction in male and female alcoholics. *Journal of Studies on Alcohol, 55*, 487–494.

Sayette, M. A., Shiffman, S., Tiffany, S. T., Niaura, R. S., Martin, C. S., & Shadel, W. G. (2000). The measurement of drug craving. *Addiction (Abingdon, England), 95* Suppl 2 (November 1999), S189–210.

Sinha, R. (2001). How does stress increase risk of drug abuse and relapse? *Psychopharmacology, 158*(4), 343–359. doi: 10.1007/s002130100917

Sinha, R. (2007). The role of stress in addiction relapse. *Current Psychiatry Reports, 9*, 388–395. doi: 10.1007/s11920-007-0050-6

Sinha, R. (2008). Chronic stress, drug use, and vulnerability to addiction. *Annals of the New York Academy of Sciences, 1141*, 105–130. doi: 10.1196/annals.1441.030

Sinha, R. (2009). Modeling stress and drug craving in the laboratory: implications for addiction treatment development. *Addiction Biology, 14*(1), 84–98. doi: 10.1111/j.1369-1600.2008.00134.x

Sinha, R. (2012). How does stress lead to risk of alcohol relapse? *Alcohol Research: Current Reviews, 34*(4), 432–440. Retrieved from http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3788822&tool=pmcentrez&rendertype=abstract

Sinha, R. (2013). Modeling relapse situations in the human laboratory. *Current Topics in Behavioral Neuroscience, 13*, 379–402. doi: 10.1007/7854_2011_150

Tabachnick, B. G., & Fidell, L. S. (2006). *Using Multivariate Statistics* (5th ed.). Boston: Pearson.

Thomas, S. E., Bacon, A. K., Randall, P. K., Brady, K. T., & See, R. E. (2011). An acute psychosocial stressor increases drinking in non-treatment-seeking alcoholics. *Psychopharmacology, 218*(1), 19–28. doi: 10.1007/s00213-010-2163-6

Thomas, S., Bacon, A. K., Sinha, R., Uhart, M., & Adinoff, B. (2012). Clinical laboratory stressors used to study alcohol-stress relationships. *Alcohol Research & Health, 34*, 459–467.

Thomas, S. E., Randall, P. K., Brady, K., See, R. E., & Drobes, D. J. (2011). An acute psychosocial stressor does not potentiate alcohol cue reactivity in non-treatment-seeking alcoholics. *Alcoholism, Clinical and Experimental Research, 35*(3), 464–473. doi: 10.1111/j.1530-0277.2010.01363.x

Tiffany, S. T., & Carter, B. L. (1998). Is craving the source of compulsive drug use? *Journal of Psychopharmacology, 12* (1), 23–30.

Tiffany, S. T., & Wray, J. M. (2012). The clinical significance of drug craving. *Annals of the New York Academy of Sciences, 1248*, 1–17. doi: 10.1111/j.1749-6632.2011.06298.x

Vuchinich, R. E., & Tucker, J. A. (1996). Alcoholic relapse, life events, and behavioral theories of choice: A prospective analysis. *Experimental and Clinical Psychopharmacology, 4*(1), 19–28. doi: 10.1037/1064-1297.4.1.19

Wang, B., Shaham, Y., Zitzman, D., Azari, S., Wise, R. A., & You, Z.-B. (2005). Cocaine experience establishes control of midbrain glutamate and dopamine by corticotropin-releasing factor: a role in stress-induced relapse to drug seeking. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience, 25*, 5389–5396. doi: 10.1523/JNEUROSCI.0955-05.2005

Wang, B., You, Z.-B., Rice, K. C., & Wise, R. A. (2007). Stress-induced relapse to cocaine seeking: roles for the CRF(2) receptor and CRF-binding protein in the ventral tegmental area of the rat. *Psychopharmacology, 193*, 283–294. doi: 10.1007/s00213-007-0782-3

Wilson, T. D., & Dunn, E. W. (2004). Self-knowledge: its limits, value, a nd potential for improvement. *Annual Review of Psychology, 55*, 493–518. doi: 10.1146/annurev.psych.55.090902.141954

World Health Organization. (1954). WHO Expert Committee on Alcohol. *Medical Societies, 70*, 698. doi: 10.1016/S0140-6736(01)85992-4

Wray, J. M., Gass, J. C., & Tiffany, S. T. (2013). A systematic review of the relationships between craving and smoking cessation. *Nicotine & Tobacco Research: Official Journal of the Society for Research on Nicotine and Tobacco, 15*, 1167–1182. doi: 10.1093/ntr/nts268

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