

UCLA

UCLA Previously Published Works

Title

Intravenous Alcohol Administration Selectively Decreases Rate of Change in Elasticity of Demand in Individuals With Alcohol Use Disorder

Permalink

<https://escholarship.org/uc/item/1258w2wq>

Journal

Alcohol Clinical and Experimental Research, 44(11)

ISSN

0145-6008

Authors

Nieto, Steven J
Green, Rejoyce
MacKillop, James
[et al.](#)

Publication Date

2020-11-01

DOI

10.1111/acer.14460

Peer reviewed



Published in final edited form as:

Alcohol Clin Exp Res. 2020 November ; 44(11): 2336–2342. doi:10.1111/acer.14460.

Intravenous Alcohol Administration Selectively Decreases Rate of Change in Elasticity of Demand in Individuals with Alcohol Use Disorder

Steven J. Nieto, PhD¹, ReJoyce Green, MA¹, James MacKillop, PhD², Lara A. Ray, PhD^{1,3,4}

¹University of California Los Angeles, Department of Psychology, Los Angeles, CA, USA

²McMaster University, Department of Psychiatry and Behavioural Neurosciences, Hamilton, ON, Canada

³University of California, Los Angeles, Department of Psychiatry and Biobehavioral Sciences, Los Angeles, CA, USA

⁴University of California Los Angeles, Brain Research Institute, Los Angeles, CA, USA

Abstract

Background: Alcohol demand is a key behavioral economic concept that provides an index of alcohol's relative reinforcing value. Initial studies have reported that alcohol demand increases during alcohol administration and in response to alcohol cues. However, the extent to which these effects are observed explicitly in samples composed of individuals with alcohol use disorder and are operative in conjunction with each other has not been studied.

Methods: To address this gap in the literature, we assessed alcohol demand during an alcohol challenge and subsequent alcohol cue-exposure paradigm in non-treatment seeking, alcohol dependent (i.e., DSM-IV criteria) participants (N = 27). Specifically, participants completed two counterbalanced intravenous, placebo-controlled, alcohol administration sessions followed by a controlled cue-exposure paradigm. At baseline and at breath alcohol concentration (BrAC) of 0.06 g/dl, participants completed the Alcohol Purchase Task (APT), assessing estimated alcohol consumption at escalating prices. Participants were also assessed for alcohol demand following each cue exposure.

Results: During alcohol administration there was a significant decrease in the rate of change in elasticity compared to placebo, and, during the cue-reactivity paradigm, there was a significant main effect such that alcohol cues decreased rate of change in elasticity relative to water cues. There were no statistically significant differences on other demand indices.

Conclusions: These findings provide further evidence that alcohol administration increases price insensitivity and extends the literature on alcohol's effects on demand by using a clinical sample with alcohol use disorder and by adding a placebo-alcohol condition.

Keywords

alcohol demand; alcohol use disorder; alcohol administration; cue-reactivity; behavioral economics

Introduction

Alcohol intoxication contributes to impairments in several domains including impaired judgement and decision making. Indeed, as blood alcohol concentrations rise, increasing intoxication often gives way to increases in the perceived beneficial effects of alcohol. Such impairments may reflect a loss of control in drinking in an episode, which is one of eleven DSM-5 diagnostic criteria for an alcohol use disorder (AUD) (APA, 2013). Despite the negative health consequences related to alcohol intoxication, the factors that continue to drive excessive alcohol consumption over the course of a drinking episode remain unclear. While behavioral effects of alcohol on inhibition may contribute to continued alcohol consumption as blood alcohol levels rise (Fillmore, 2003), motivational factors may also play a role (Field et al., 2010). Using a behavioral economic lens, one may argue that excessive drinking that occurs in AUD after alcohol administration and the subjective experience of intoxication reflects dynamic changes in the reinforcing value of alcohol, with each drink increasing motivation for the next.

Behavioral economic demand, which refers to the relationship between consumption of a commodity and its price, represents one approach to assessing motivation for alcohol (Hursh et al., 2005). Behavioral economic theory posits that AUD is a ‘reinforcer pathology,’ wherein an individual overvalues alcohol relative to other reinforcers, which manifests as increased demand for alcohol (Bickel et al., 2014). Alcohol demand is often indexed using hypothetical alcohol purchase tasks (APT), which estimate alcohol consumption across a range of prices (MacKillop, 2016). The relationship between alcohol consumption and its price is operationalized using demand curve analysis. Several interrelated, but separate, demand indices are provided from these demand curves: intensity (consumption when drinks are free), breakpoint (price at which consumption is zero), O_{\max} (maximum expenditure on alcohol), P_{\max} (price associated with O_{\max}), and rate of change (alpha or α) in elasticity of demand (elasticity represents the responsiveness of changes in consumption to changes in price) (Gilroy et al., 2020). Alcohol demand as a trait (reflecting general preferences) relates to real world alcohol consumption (Amlung et al., 2012, Murphy and MacKillop, 2006), alcohol-related problems (Kaplan et al., 2018, Murphy and MacKillop, 2006), and AUD symptomology (Kiselica et al., 2016, Bertholet et al., 2015). However, behavioral economic indicators of alcohol demand are also understood to be dynamic, fluctuating as a function of subjective state or changes in the environment (Heinz et al., 2012). From a reinforcer pathology theoretical standpoint, both generally stable trait-like factors and dynamic state factors determine an individual’s overall motivation for alcohol. However, the extent to which alcohol demand changes in participants under the influence of alcohol has been rarely studied.

A controlled alcohol administration in the laboratory, commonly referred to as an “alcohol challenge,” provides an ideal design for testing the effects of alcohol on demand indices across rising levels of breath alcohol concentrations (BrACs), but only two studies have examined alcohol demand in the context of a laboratory alcohol challenge. In the first, following an intravenous alcohol infusion, heavy drinking Asian-American participants reported greater breakpoint and P_{\max} on an APT when assessed at peak BrAC = 0.06 mg/dl (~75 min post-infusion), but intensity and O_{\max} were unaffected by alcohol administration (Bujarski et al., 2012). An intravenous alcohol administration has the advantage of dissociating the psychoactive effects of ethanol from the conditioned appetitive properties of beverage alcohol. In the second, following oral alcohol consumption (peak BrAC = ~0.10 mg/dl at ~60 min post-consumption), heavy drinkers self-reported greater intensity and breakpoint compared to placebo and compared to control groups (Amlung et al., 2015). Notably, the former study used a 16-item traditional APT whereas the latter study utilized single-item indicators of intensity, O_{\max} , and breakpoint. Although routes of alcohol administration, sample characteristics, and demand measures differed between the aforementioned studies (Amlung et al., 2015, Bujarski et al., 2012), both showed that alcohol increased the first price at which consumption was suppressed to zero (breakpoint). Additionally, while both studies demonstrate increased demand in human laboratory studies in heavy drinkers, many of whom may have met AUD criteria, further studies examining the effects of alcohol on demand indices in samples explicitly composed of individuals with AUD are warranted.

Similar to dynamic factors in alcohol challenge studies, the alcohol cue reactivity paradigm provides a platform for understanding dynamic changes in motivation that result from the presence of environmental drinking stimuli. In the case of demand, alcohol (beer) relative to neutral cues increases intensity, O_{\max} , breakpoint, and normalized P_{\max} (normalized values allow for examination of proportionate changes in consumption as price escalates independent of other demand indices) as assessed on a 19-item APT in heavy drinkers (MacKillop et al., 2010). In another sample of heavy drinkers, however, alcohol cues did not alter demand indices measured by a fully-consequated APT (wherein participants received real alcohol and money) (Amlung et al., 2012). A subsequent study of both stress and cues that also included actual alcohol revealed a significant effect of alcohol on breakpoint (Amlung and MacKillop, 2014). Finally, single-item measures of intensity, O_{\max} , and breakpoint increased after exposure to alcohol cues in heavy drinkers (Owens et al., 2015). Dynamic effects of environmental cues on drug demand have also been observed for other psychoactive drugs and a recent meta-analysis revealed these effects to be of medium effect size (Acuff et al., 2020), but with considerable heterogeneity. These divergent findings may be due to differences in APT assessments (hypothetical vs real) and methodological considerations (e.g., ceiling effects), but clarification of cue effects in this domain is clearly warranted. Furthermore, to our knowledge, no studies have examined the role of alcohol intoxication, vis-à-vis BrACs, on the effects of alcohol cues on behavioral economic measures of demand. In other words, are the effects of alcohol cues on demand indices different when cues are presented post placebo, versus post alcohol administration?

In light of the gaps in the literature highlighted above, the purpose of this study is to assess alcohol demand using the APT in a human laboratory protocol consisting of an alcohol

challenge (Target BrAC = 0.06g/dl) followed by an alcohol cue exposure paradigm. The current study uses a within-subjects design in a sample of non-treatment seeking individuals with a current diagnosis of DSM-IV alcohol dependence. All participants completed two counterbalanced intravenous placebo-controlled alcohol administration sessions (placebo vs. alcohol) followed by a controlled cue-exposure paradigm (neutral cues vs. alcohol cues). At baseline and BrAC = 0.06 g/dl, and following each cue exposure, participants completed the APT. We hypothesized that alcohol administration would enhance alcohol demand when BrAC=0.06 g/dl and after exposure to alcohol cues, but not during placebo and control/water cues.

Materials and Methods

Participants

Non-treatment seeking individuals with current DSM-IV alcohol dependence were recruited from the Los Angeles community via print and online advertisements. Inclusion criteria were as follows: 1) between the age of 21 and 65, 2) met current DSM-IV diagnosis of alcohol dependence, 3) and reported consuming a minimum of 48 standard drinks in the past month. Participants were excluded if they: 1) were in treatment for alcohol problems or seeking treatment; 2) had not drunk in 21 or more days; 3) had a history of bipolar disorder or any psychotic disorder; 4) met current DSM-IV diagnosis of dependence on any psychoactive substances other than alcohol and nicotine; 5) reported current use of psychoactive drugs, other than marijuana, as determined by a positive urine screen for narcotics, amphetamines, or sedative hypnotics; 6) had clinically significant physical abnormalities as indicated by physical examination and laboratory screens; 7) pregnancy, nursing, or refusal to use reliable method of contraception, if female; and 8) scored 10 or greater on the Clinical Institute Withdrawal Assessment for Alcohol-Revised (CIWA-AR; (Sullivan et al., 1989), indicating clinically significant alcohol withdrawal symptoms.

Screening and Experimental Procedures

Interested participants were first screened via a telephone interview and eligible participants were invited to the laboratory for an in-person screening session. Participants attended a physical examination prior to infusion sessions to ensure there were no medical contraindications to the intravenous protocol. A total of 52 participants were enrolled based on inclusion criteria and completed the physical exam. Of those, 43 were randomized. One participant did not return to the laboratory for the second infusion visit and was excluded from all analyses. Demographic data on participants who completed the study were previously reported (Ray et al., 2013). Briefly, the average age of participants was 29.02 ($SD = 9.36$; Range = 21 to 51), with 75.6% males and a median income of between \$15,000 and \$30,000 annually.

Participants completed 2 randomized infusion sessions: 1 alcohol infusion and 1 saline control infusion. Alcohol administration was conducted using a single-blinded, randomized, counterbalanced, crossover design. Participants were seated in a recliner chair and an IV was placed in their non-dominant arm. Three target BrAC's in the parent study were .02, .04, and .06 g/dl (Ray et al., 2013). Upon reaching each of the target BrAC levels, infusion rates

were reduced to half the target rate in order to maintain stable BrAC levels while participants completed assessments. During the placebo session, assessments were administered at 18, 43, and 75 minutes post-infusion to parallel the duration of dose titration and assessment completion during alcohol sessions. After the infusion procedure was finished, participants were given a meal and asked to remain in the lab until BrAC fell below 0.02 g/dl (or to 0.00 g/dl if driving). Infusion sessions were separated by 1 to 2 weeks, with the observed average time between infusion being 10.6 days. The cue exposure paradigm immediately followed alcohol/placebo administration.

Cue Exposure Paradigm

Participants were maintained at a steady BAC of 0.06 g/dl for approximately 10–15 minutes while cue exposure procedures were conducted. During the placebo session, cue exposure procedures occurred after assessments were completed at the 75 min time point. Alcohol cue exposure in the laboratory followed well-established procedures (Monti et al., 1987, Monti et al., 2001). Each session began with a 3 min. relaxation period. Next, participant held and smelled a glass of water for 3 minutes to control for the effects of simple exposure to any potable liquid. After this, participants held and smelled a glass of their preferred alcoholic beverage and were asked to recall sensory and psychological memories associated with their alcohol use. Order of presentation was not counterbalanced, due to carryover effects that are known to occur. Participants who self-identified as cigarette smokers were allowed a smoke break 15 minutes prior and immediately after the cue reactivity assessment.

Behavioral economic indicators of alcohol demand

The APT was used to assess alcohol demand at baseline (BrAC = 0.00) and when BrAC = 0.06 or 75 minutes (placebo) into the infusion session. During the cue-reactivity paradigm, alcohol demand was measured after the presentation of water and alcohol cues during the cue-reactivity procedure. The APT is a hypothetical alcohol purchase task (Murphy and MacKillop, 2006) wherein participants report how many standard drinks they would consume in a typical drinking situation at 16 price points: free, 1¢, 5¢, 13¢, 25¢, 50¢, \$1, \$3, \$6, \$11, \$35, \$70, \$140, \$280, \$560, and \$1120. A hypothetical APT was used given evidence that derived alcohol demand indices correlate with both self-reported drinking measures (Murphy and MacKillop, 2006) and alcohol consumption during actual purchase tasks (Amlung et al., 2012). Alcohol demand curves generated from the APT were used to calculate economic demand indices.

Data analytic plan

Prior to the primary analyses, invariant responding and excessive preference reversals (i.e. consuming more at higher prices) across the APT tasks were identified and removed from the analysis. Participants with missing data for intensity (consumption when free) were excluded from analyses. During initial data screening, one participant was removed for excessive reversals, six participants were removed for invariant responding (all six participants did not meet the Trend criteria of the proposed three-criterion algorithm (Stein et al., 2015); $Q_s < 0.017$, and eight participants were removed for consistently having missing intensity values and/or numerous other missing values across sessions. A total of 27 participants had valid and complete APT data. Importantly, participants removed for missing

data and the sample used for the present study did not differ on demographic or clinical variables.

Demand curve analysis was conducted using the exponentiated version (Koffarnus et al., 2015) of the Hursh and Silberberg (2008) exponential model:

$$Q = Q_0 \times 10^k (e^{-\alpha Q_0 C} - 1)$$

where Q = consumption at a given price; Q_0 = maximum consumption (consumption at zero or minimal price); k = a constant across conditions that denotes the range of consumption values in log powers of ten; C = the cost of the commodity (price), and α = the derived demand parameter reflecting the rate of decline of consumption associated with increasing price, also referred to as essential value (Hursh and Silberberg, 2008). The overall mean curves at all timepoints were examined to find the best-fitting k value. k ranged between 3 and 4, thus, 3.5 was selected as the k value resulting in $R^2 > .984$ at each timepoint.

Several indices were extrapolated from the demand curve, including intensity, O_{\max} , P_{\max} , and breakpoint. Intensity was defined as consumption when cost was free; O_{\max} was defined as the amount of money spent on alcohol at any price, P_{\max} was defined as the price point at which O_{\max} occurs (i.e., the price at which demand transitions from being inelastic to elastic), breakpoint was defined as the first price where consumption drops to zero. Rate of change in elasticity (α) reflects the rate of decline in consumption as price for alcohol is increased. Demand indices were log10 transformed to meet parametric assumptions.

A series of repeated measures analysis of variance (ANOVAs) tests were used to determine alcohol demand during alcohol administration and cue-reactivity. Alcohol (alcohol and placebo) was a 2-level within-subjects factor and Time (baseline and 75 minutes [or BrAC = 0.06]) was a 2-level within-subjects factor. During the cue-reactivity paradigm, Cue Type (water and alcohol) was a 2-level within-subjects factor. Cue-reactivity analyses included the respective alcohol demand indices measured during placebo and alcohol administration as a covariate. In addition, self-reported income and mu-opioid receptor genotype were included as covariates in initial analyses given that this study oversampled for genotype status based on a separate research question reported elsewhere (Ray et al., 2013). Tukey *post hoc* tests were used to conduct pairwise comparisons on significant interactions. Hypothesis testing was conducted using PROC GLM in SAS Statistical Software version 9.4. Effect sizes are reported as partial eta squared (η_p^2) and Cohen's d . To confirm the robustness of our findings, a sensitivity analysis using PROC MIXED was conducted using data from participant who provided systematic data on at least one time point (Krueger and Tian, 2004). Statistical significance was set a $p < 0.05$.

Results

Preliminary Analyses

Mu-opioid receptor genotype (rs1799971) and self-reported income were not significant covariates of any behavioral economic indices presented herein ($p > 0.30$) and were therefore excluded from final models.

Alcohol demand during alcohol administration and cue reactivity procedures

Demand curves during alcohol administration and cue-reactivity are shown in Figure S1. Rate of change in elasticity is shown in Figure 1. There was no significant main effect of Alcohol ($p = 0.711$; $\eta_p^2 = 0.11$), but there was a significant main effect of Time ($F_{1,26} = 9.78$, $p = 0.004$; $\eta_p^2 = 0.07$) and a significant Time by Alcohol interaction ($F_{1,26} = 4.91$, $p = 0.036$; $\eta_p^2 = 0.13$) during the alcohol challenge. Specifically, Tukey *post hoc* tests revealed that alcohol administration decreased rate of change in elasticity from baseline to 75 min (Cohen's $d = 0.301$) compared to placebo ($p < 0.05$; Cohen's $d = 0.097$). During the cue-reactivity paradigm, there was a significant main effect of Cue Type ($F_{1,26} = 7.55$, $p = 0.011$; $\eta_p^2 = 0.04$) such that alcohol cues decreased rate of change in elasticity relative to water cues. Importantly, a sensitivity analysis, which included participants who provided systematic data on at least one time point ($n=41$) confirmed the robustness of this finding (see results and Figure S2 in Supplemental information). There were no significant effects of Alcohol ($p = 0.808$; $\eta_p^2 = 0.002$) or a significant Alcohol by Cue Type interaction ($p = 0.478$; $\eta_p^2 = 0.01$).

For intensity of alcohol demand (Table S1), there was a significant main effect of Time ($F_{1,26} = 8.98$, $p = .006$; $\eta_p^2 = 0.22$), such that intensity increased 75 min across both alcohol and placebo administration. There were no effects of Alcohol ($p = 0.157$; $\eta_p^2 = 0.08$) or a significant Alcohol by Time interaction ($p = 0.298$; $\eta_p^2 = 0.05$) during the alcohol challenge. During the cue-reactivity paradigm, there were no significant main effects of Alcohol ($p = 0.062$; $\eta_p^2 = 0.02$), Cue Type ($p = 0.802$; $\eta_p^2 = 0.001$), or a significant Alcohol by Cue Type interaction ($p = 0.570$; $\eta_p^2 = 0.04$).

For maximum expenditure (O_{\max} ; Table S1) there were no significant effects of Alcohol ($p = 0.331$; $\eta_p^2 = 0.02$), Time ($p = 0.077$; $\eta_p^2 = 0.06$), or an Alcohol by Time interaction ($p = 0.501$; $\eta_p^2 = 0.04$) during the alcohol challenge. During the cue-reactivity paradigm, there were no significant effects of Alcohol ($p = 0.704$; $\eta_p^2 = 0.01$), Cue Type ($p = 0.186$; $\eta_p^2 = 0.03$), or a significant Alcohol by Cue Type interaction ($p = 0.145$; $\eta_p^2 = 0.09$).

For price at maximum expenditure (P_{\max} ; Table S1) there were no significant effects of Alcohol ($p = 0.688$; $\eta_p^2 = 0.03$), Time ($p = 0.859$; $\eta_p^2 = 0.001$), or their interaction ($p = 0.687$; $\eta_p^2 = 0.05$) during the alcohol challenge. During the cue-reactivity paradigm, there were no

significant main effects of Alcohol ($p = 0.063$; $\eta_p^2 = 0.16$), Cue Type ($p = 0.321$; $\eta_p^2 = 0.09$), or a significant Alcohol by Cue Type interaction ($p = 0.627$; $\eta_p^2 = 0.12$).

For breakpoints (Table S1), there were no effects of Alcohol ($p = 0.522$; $\eta_p^2 = 0.02$), Time ($p = 0.139$; $\eta_p^2 = 0.01$), or their interaction ($p = 0.835$; $\eta_p^2 = 0.07$) during the alcohol challenge. During the cue-reactivity paradigm, there were no effects of Alcohol ($p = 0.603$; $\eta_p^2 = 0.02$), Cue Type ($p = 0.257$; $\eta_p^2 = 0.02$), or their interaction ($p = 0.876$; $\eta_p^2 = 0.05$).

Discussion

The current study examined behavioral economic indicators of alcohol demand during alcohol administration compounded with a cue-reactivity paradigm in a sample with AUD. Alcohol administration decreased the rate of change in elasticity (small to medium effect size), reflecting increased alcohol demand relative to placebo. This finding suggests that motivation for alcohol, as measured by the rate of change in demand elasticity using hypothetical APTs, may increase in a phasic manner as BrACs rise. However, we did not observe differences on other demand indices. Previous work has shown that alcohol administration increases the amplitude and width of the demand curve (Amlung et al., 2015, Bujarski et al., 2012), and we add to this literature by demonstrating greater price insensitivity after alcohol versus placebo administration. Thus, in our sample composed of individuals with AUD, it is likely that the acute effects of alcohol may enhance motivation to continue drinking past the point of intoxication via increases in alcohol demand as indexed by an overall reduced sensitivity to increasing price.

Overall, results indicate that alcohol selectively blunted the rate of change in elasticity, but not other indices of alcohol demand at peak BrAC and during cue-reactivity procedures. Acute alcohol administration enhances demand at peak BrACs; however, alcohol demand may begin to decline after a certain point even when BrACs are maintained at pharmacologically relevant levels as seen in the current study. Thus, it is possible that alcohol administration increases alcohol demand in a phasic manner. That is, motivation for alcohol, as reflected by alcohol demand derived from hypothetical APTs, may be initially increased by the acute effects of alcohol but dissipates at a faster rate if BrACs are not ascending, even in the presence of alcohol cues. Partial support for this hypothesis is demonstrated in Amlung et al. (2015), wherein intensity values assessed during the descending limb (BrAC \approx 0.06) are lower relative to placebo. However, further work is needed to examine this hypothesis directly.

The influence of state effects of alcohol on behavioral economic indicators of alcohol demand is an understudied area. The few studies that have attempted to examine this domain have differed in sample characteristics (heavy vs moderate drinkers), route of alcohol administration (oral vs. i.v.), and APTs (16-items vs single open-ended questions). Despite the differences in study design, both studies demonstrated that alcohol administration increased the price at which consumption drops to zero (Amlung et al., 2015, Bujarski et al., 2012). Amlung et al. (2015) found that oral alcohol increased intensity, while Bujarski et al. (2012) found that i.v. alcohol increased P_{\max} during the ascending limb. It is important to

note that AUD criteria were not assessed in these studies; however, it is likely that a nontrivial portion of the study samples met AUD criteria based on their reported drinking patterns. Although there is a lack of congruence between our study (i.e., only one statistically significant demand index) and the previous work in this area, our results are generally in agreement with findings from these previous studies by demonstrating that i.v. alcohol administration decreased price sensitivity (rate of change in elasticity) in a sample explicitly composed of heavy drinkers with AUD.

It is important to note that intensity, O_{max} , P_{max} , and breakpoint did not differ when measured at peak BrAC relative to placebo. This is somewhat surprising considering previous studies, but it suggests that the rate of change in elasticity indicator is uniquely sensitive to intoxication in individuals with AUD. This is consistent with the notion of elasticity as being a critical facet of the demand curve, one that captures the “essential value” of the reinforcer (Hursh & Silberbreg, 2006). Although intensity and O_{max} tend to have larger effect sizes relative to other demand indices in alcohol studies (Kiselica et al., 2016), it is possible that the magnitude of these effect sizes are dynamic and can be shifted by environmental manipulations, such as being under the influence of alcohol. In support of this hypothesis, Merrill and Aston (2020) showed a substantial degree of within-person variability in alcohol demand when a 3-item APT is administered daily for 28 days. Environmental factors, such as negative consequences from drinking the day before, led to lower intensity the next day. These factors, in combination with alcohol expectancy effects during the alcohol/placebo administration session, may have contributed to the unexpected increases in intensity during the session. Further work examining the in-state effects of alcohol on the dynamic features of alcohol demand are warranted.

Contrary to our hypothesis, alcohol administration did not enhance alcohol demand during the cue-reactivity paradigm. Similar to alcohol administration studies, few studies have examined the relationship between alcohol demand and cues. To our knowledge, no studies to date have explored the effects of cues on alcohol demand during alcohol administration. Exposure to alcohol cues increases alcohol demand as measured by APTs for hypothetical outcomes (MacKillop et al., 2010, Owens et al., 2015), but not APTs for actual outcomes (Amlung et al., 2012), potentially due to ceiling effects. Our results showed no alcohol-induced changes on alcohol demand indices during the cue-reactivity paradigm. It may be that case that as individuals with AUD become intoxicated, cues exert less influence on demand because the goal of consuming alcohol and/or reaching a desired subjective state has already been achieved (i.e., a satiety effect). Taken together, alcohol may result in phasic decreases in rate of change in elasticity during the administration session, but when BrACs were maintained at the target dose of 0.06 during the cue reactivity paradigm (10–15 min), the influence of alcohol on rate of change in elasticity likely diminished. Congruent with this perspective, certain alcohol demand indices have greater intra-individual variability when assessed daily and are more sensitive to drinking-related consequences (Merrill and Aston, 2020).

The present study should be interpreted in light of the study’s strengths and limitations. Strengths include highly controlled intravenous alcohol administration and saline control administration, the integration of two well-established laboratory paradigms with the cue-

reactivity paradigm following alcohol administration, and the study sample meeting DSM-IV criteria for alcohol dependence. Study limitations include relatively small sample size and the lack of a comparison group of individuals without an AUD to examine how demand in this context differs from those with less hazardous drinking. While participants were not explicitly told whether they are receiving alcohol or placebo during the infusion sessions, subjective and physiological effects of alcohol may have compromised the blind and may have influenced participants perception of their intoxication. Given that we did not apply Type 1 error correction at the omnibus level, our results should be interpreted cautiously considering the lack of statistical significance on the other demand indices.

Taken together, our results indicate that alcohol administration, relative to placebo, increases price insensitivity, via decreases in the rate of change in demand elasticity, but does not affect reactivity to alcohol cues in heavy drinkers with AUD. Notably, alcohol's effects were specific to rate of change in demand elasticity in our sample because no differences were seen in other demand indices. This is the first study to examine the influence of state alcohol effects compounded with a cue-reactivity paradigm. Our results on rate of change in elasticity partially support findings from other groups showing that behavioral economic indicators of alcohol demand can fluctuate moment-to-moment and are influenced by environmental factors, such as BrACs.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

This work was supported by grants from the National Institute on Alcohol Abuse and Alcoholism to Lara Ray (K24AA025704). James MacKillop is a Senior Scientist in BEAM Diagnostics, Inc.; No other authors have conflicts of interest to disclose.

Funding: This work was supported by grants from the National Institute on Alcohol Abuse and Alcoholism (K24AA025704 to LAR) and the National Institute on Drug Abuse (T32DA024635 to SJN). RG was supported by funds from the Tobacco-Related Disease Research Program of the University of California (T30DT0950). JM is a Senior Scientist in BEAM Diagnostics, Inc.; No other authors have conflicts of interest to disclose.

References

- ACUFF SF, AMLUNG M, DENNHARDT AA, MACKILLOP J. & MURPHY JG 2020 Experimental manipulations of behavioral economic demand for addictive commodities: a meta-analysis. *Addiction*, 115, 817–831. [PubMed: 31656048]
- AMLUNG M. & MACKILLOP J. 2014 Understanding the effects of stress and alcohol cues on motivation for alcohol via behavioral economics. *Alcohol Clin Exp Res*, 38, 1780–9. [PubMed: 24890323]
- AMLUNG M, MCCARTY KN, MORRIS DH, TSAI C-L & MCCARTHY DM 2015 Increased behavioral economic demand and craving for alcohol following a laboratory alcohol challenge. *Addiction*, 110, 1421–1428. [PubMed: 25732875]
- AMLUNG MT, ACKER J, STOJEK MK, MURPHY JG & MACKILLOP J. 2012 Is Talk “Cheap”? An Initial Investigation of the Equivalence of Alcohol Purchase Task Performance for Hypothetical and Actual Rewards. *Alcoholism: Clinical and Experimental Research*, 36, 716–724.
- APA 2013 Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Arlington, VA, American Psychiatric Publishing.

- BERTHOLET N, MURPHY JG, DAEPPEN J-B, GMEL G. & GAUME J. 2015 The alcohol purchase task in young men from the general population. *Drug and alcohol dependence*, 146, 39–44. [PubMed: 25468819]
- BICKEL WK, JOHNSON MW, KOFFARNUS MN, MACKILLOP J. & MURPHY JG 2014 The behavioral economics of substance use disorders: reinforcement pathologies and their repair. *Annu Rev Clin Psychol*, 10, 641–77. [PubMed: 24679180]
- BUJARSKI S, MACKILLOP J. & RAY LA 2012 Understanding naltrexone mechanism of action and pharmacogenetics in Asian Americans via behavioral economics: a preliminary study. *Experimental and clinical psychopharmacology*, 20, 181–190. [PubMed: 22429255]
- FIELD M, WIERS RW, CHRISTIANSEN P, FILLMORE MT & VERSTER JC 2010 Acute alcohol effects on inhibitory control and implicit cognition: implications for loss of control over drinking. *Alcoholism, clinical and experimental research*, 34, 1346–1352.
- FILLMORE MT 2003 Drug abuse as a problem of impaired control: current approaches and findings. *Behavioral and cognitive neuroscience reviews*, 2, 179–197. [PubMed: 15006292]
- GILROY SP, KAPLAN BA & REED DD 2020 Interpretation(s) of elasticity in operant demand. *Journal of the Experimental Analysis of Behavior*, 114, 106–115. [PubMed: 32542726]
- HEINZ AJ, LILJE TC, KASSEL JD & DE WIT H. 2012 Quantifying reinforcement value and demand for psychoactive substances in humans. *Curr Drug Abuse Rev*, 5, 257–72. [PubMed: 23062106]
- HURSH SR, GALUSKA CM, WINGER G. & WOODS JH 2005 The economics of drug abuse: a quantitative assessment of drug demand. *Mol Interv*, 5, 20–8. [PubMed: 15731502]
- HURSH SR & SILBERBERG A. 2008 Economic demand and essential value. *Psychol Rev*, 115, 186–98. [PubMed: 18211190]
- KAPLAN BA, FOSTER RNS, REED DD, AMLUNG M, MURPHY JG & MACKILLOP J. 2018 Understanding alcohol motivation using the alcohol purchase task: A methodological systematic review. *Drug and alcohol dependence*, 191, 117–140. [PubMed: 30099174]
- KISELICA AM, WEBBER TA & BORNOVALOVA MA 2016 Validity of the alcohol purchase task: a meta-analysis. *Addiction (Abingdon, England)*, 111, 806–816.
- KOFFARNUS MN, FRANCK CT, STEIN JS & BICKEL WK 2015 A modified exponential behavioral economic demand model to better describe consumption data. *Exp Clin Psychopharmacol*, 23, 504–12. [PubMed: 26280591]
- KRUEGER C. & TIAN L. 2004 A Comparison of the General Linear Mixed Model and Repeated Measures ANOVA Using a Dataset with Multiple Missing Data Points. *Biological Research For Nursing*, 6, 151–157. [PubMed: 15388912]
- MACKILLOP J. 2016 The Behavioral Economics and Neuroeconomics of Alcohol Use Disorders. *Alcoholism: Clinical and Experimental Research*, 40, 672–685.
- MACKILLOP J, O'HAGEN S, LISMAN SA, MURPHY JG, RAY LA, TIDEY JW, MCGEARY JE & MONTI PM 2010 Behavioral economic analysis of cue-elicited craving for alcohol. *Addiction*, 105, 1599–607. [PubMed: 20626376]
- MERRILL JE & ASTON ER 2020 Alcohol demand assessed daily: Validity, variability, and the influence of drinking-related consequences. *Drug Alcohol Depend*, 208, 107838.
- MONTI PM, BINKOFF JA, ABRAMS DB, ZWICK WR, NIRENBERG TD & LIEPMAN MR 1987 Reactivity of alcoholics and nonalcoholics to drinking cues. *Journal of abnormal psychology*, 96, 122–126. [PubMed: 3584660]
- MONTI PM, ROHSENOW DJ, SWIFT RM, GULLIVER SB, COLBY SM, MUELLER TI, BROWN RA, GORDON A, ABRAMS DB, NIAURA RS & ASHER MK 2001 Naltrexone and Cue Exposure With Coping and Communication Skills Training for Alcoholics: Treatment Process and 1-Year Outcomes. *Alcoholism: Clinical and Experimental Research*, 25, 1634–1647.
- MURPHY JG & MACKILLOP J. 2006 Relative reinforcing efficacy of alcohol among college student drinkers. *Exp Clin Psychopharmacol*, 14, 219–27. [PubMed: 16756426]
- OWENS MM, MURPHY CM & MACKILLOP J. 2015 Initial Development of a Brief Behavioral Economic Assessment of Alcohol Demand. *Psychology of consciousness (Washington, D.C.)*, 2, 144–152.
- RAY LA, BUJARSKI S, MACKILLOP J, COURTNEY KE, MONTI PM & MIOTTO K. 2013 Subjective response to alcohol among alcohol-dependent individuals: effects of the μ -opioid

receptor (OPRM1) gene and alcoholism severity. *Alcoholism, clinical and experimental research*, 37 Suppl 1, E116–E124.

STEIN JS, KOFFARNUS MN, SNIDER SE, QUISENBERRY AJ & BICKEL WK 2015 Identification and management of nonsystematic purchase task data: Toward best practice. *Exp Clin Psychopharmacol*, 23, 377–86. [PubMed: 26147181]

SULLIVAN JT, SYKORA K, SCHNEIDERMAN J, NARANJO CA & SELLERS EM 1989 Assessment of alcohol withdrawal: the revised clinical institute withdrawal assessment for alcohol scale (CIWA-Ar). *Br J Addict*, 84, 1353–7. [PubMed: 2597811]

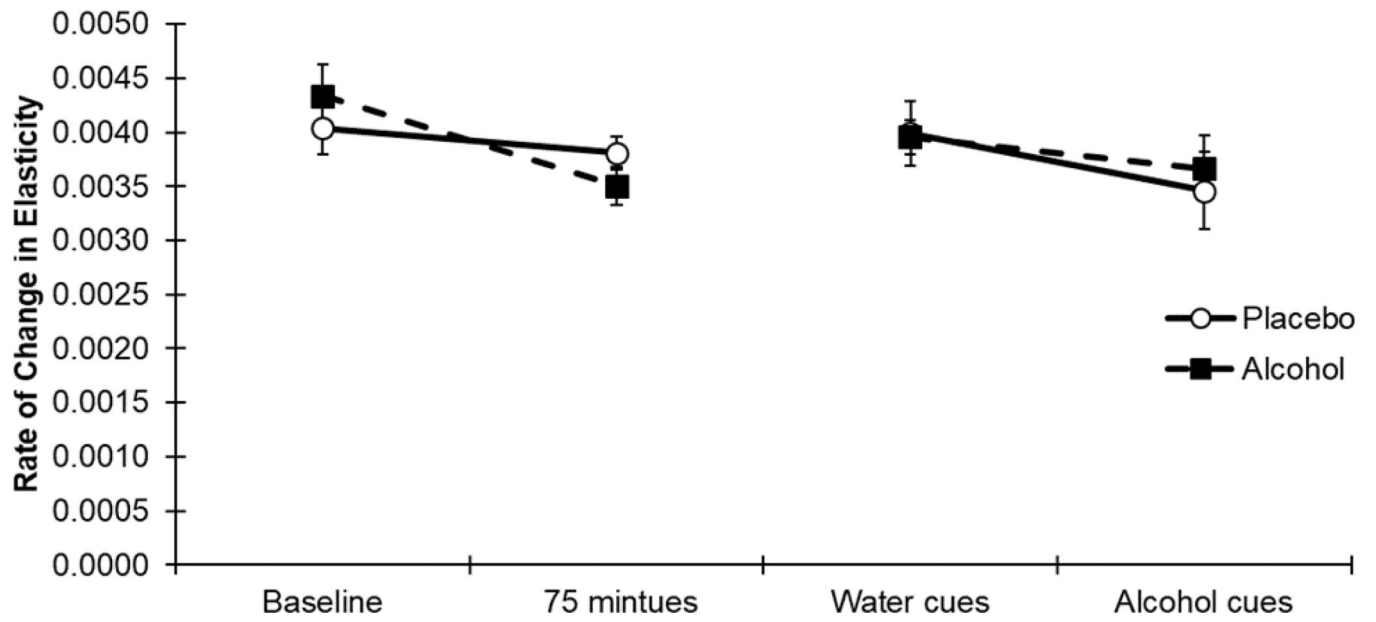


Fig 1.
Mean (\pm SEM) rate of change in elasticity of alcohol as a function of alcohol condition and cue exposure.