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Journal
Alcoholism Clinical and Experimental Research, 46(3)

ISSN
0145-6008

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Publication Date
2022-03-01

DOI
10.1111/acer.14783

Peer reviewed

HHS Public Access

Author manuscript

Alcohol Clin Exp Res. Author manuscript; available in PMC 2023 March 01.

Published in final edited form as:

Alcohol Clin Exp Res. 2022 March ; 46(3): 468–476. doi:10.1111/acer.14783.

Moderators of subjective response to alcohol in the human laboratory

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Abstract

Background: Subjective response (SR) to alcohol represents a biobehavioral risk factor for heavy drinking and for developing alcohol use disorder (AUD). Identifying moderators of SR has been hindered by small sample sizes that are often used in alcohol administration studies.

Methods: This study culled from multiple alcohol administration trials to test whether sex, family history of alcohol problems, and impulsivity (via delay discounting) predict SR to alcohol, comprised of four domains: stimulation, sedation, negative affect, and craving. Non-treatment-seeking heavy drinkers (N=250) completed a battery of self-report scales and behavioral measures of alcohol use and problems, mood, and impulsivity. All participants completed an intravenous alcohol administration session wherein SR domains were measured at baseline, 20, 40, and 60mg%.

Results: Analyses using multilevel modeling found that male sex independently predicted higher alcohol-induced stimulation and alcohol craving, after controlling for other moderators. Family history of alcohol problems independently predicted alcohol craving controlling for other moderators.

Conclusions: Through a large sample and advanced data analytic methods, this study extends the literature by suggesting important moderators of SR in heavy drinkers, namely male sex and family history of alcohol problems. These findings consolidate and extend a growing body of research on who is most likely to report the SR features that confer risk for AUD.

Keywords

alcohol; alcohol use disorder; impulsivity; sex differences; subjective response

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Conflict of Interest

There are no actual or potential conflicts of interest.

Introduction

Alcohol use disorder (AUD) is a chronic, relapsing condition with substantial individual and societal costs (Sacks et al., 2015). Due to this enormous burden, identifying risk factors that predict the development of AUD has great potential to mitigate the adverse consequences of heavy drinking (Schuckit et al., 2016, Conrod et al., 2013). Toward this goal, biobehavioral risk factors for the development of AUD have been researched for decades. One of the more widely studied set of biobehavioral risk factors are those capturing acute subjective response (SR) to alcohol in the human laboratory (Ray et al., 2016, Schuckit, 1984, King et al., 2021). The underlying premise is that the subjective experience of alcohol, whether rewarding or aversive, serves as a determinant to subsequent consumption and the development of problems (Bujarski and Ray, 2016, Schuckit, 1994, King et al., 2021).

Two separate lines of longitudinal research combining alcohol administration in the human laboratory with clinical assessments at follow-up have provided ample support for SR as a risk factor for AUD. While early studies framed SR as a unidimensional construct, the field has moved toward a multifaceted understanding of SR. Schuckit and colleagues (Schuckit, 1994, Schuckit, 1984, Schuckit and Smith, 1996), have found that a low level of response to alcohol (marked by low sensitivity to intoxicating and sedative effects) was associated with the prospective risk of developing AUD a decade later. King and colleagues (King et al., 2011, King et al., 2014), have found that the stimulant and rewarding effects of alcohol in the laboratory are predictive of long-term outcomes, such that individuals experiencing more stimulant and rewarding effects were more likely to develop AUD up to a decade later (King et al., 2021). In turn, the differentiator model by Newlin & Thompson (Newlin and Thomson, 1990) emphasized SR as a risk factor and contributed a nuanced understanding of alcohol effects across both ascending and descending limbs of intoxication. Tolerance to sedative effects of alcohol and sensitization to stimulant and rewarding effects of alcohol are key themes in neurobiological theories of the development and progression of addiction (Robinson and Berridge, 1993, Koob and Le Moal, 1997).

Our group has investigated SR in the context of genetic risk factors (Ray et al., 2014, Ray et al., 2013), functional neuroimaging (Courtney and Ray, 2014), neurobiological theories of addiction (Bujarski et al., 2017, Bujarski and Ray, 2014), and as early efficacy endpoints for testing pharmacotherapies for AUD (Ray et al., 2008). Our laboratory has used intravenous (IV) alcohol administration models whereas others have used both IV and oral administration with comparable results across a host of SR domains (Ray et al., 2007). IV alcohol administration methods allow precise control over breath alcohol concentration levels that is a large source of between-subject variability in oral alcohol challenge studies (Ramchandani et al., 2009). This approach also eliminates alcohol cues and reduces alcohol expectancy effects that could non-pharmacologically influence SR to alcohol. This is important to highlight because SR methodology and sample characteristics are relevant factors to consider when interpreting SR findings (Schuckit, 2018, Schuckit, 2014). Recently, we have demonstrated a four-level multivariate classification to the construct of SR, namely stimulation, sedation, negative mood, and alcohol craving (Bujarski et al., 2015, Ray et al., 2009). These domains are associated with a host of experimental and clinical endpoints. For example, in human laboratory self-administration studies, alcohol-

induced craving predicted greater alcohol self-administration, whereas alcohol-induced sedation predicted lower self-administration (Bujarski et al., 2018). The importance of alcohol craving is underscored by recent evidence that craving represents a more proximal determinant of alcohol self-administration compared to alcohol-induced stimulation (Green et al., 2019). Because SR to alcohol can be leveraged to answer central questions about AUD, we proposed that SR phenotypes represent a unique research domain criterion (Ray et al., 2016).

While behavioral pharmacology research on SR as a risk factor for AUD is robust and well developed, a host of opportunities for refinement exist. Notably, most behavioral pharmacology studies of SR are comprised of small sample sizes; albeit the San Diego Prospective Study is a notable exception (Schuckit et al., 2014). For example, a recent meta-regression study from our laboratory found that the average sample size in AUD medication behavioral pharmacology studies (published between 1993 and 2016) was 31 participants (Green et al., 2021). This is consistent with the time-intensive and often costly nature of the assessment of SR in the human laboratory, particularly using IV administration methods. And while small sample sizes may be appropriate for focal research questions, such as medication effects, they fall short of allowing for fine-grained analyses of moderators. Therefore, one of the gaps in the SR literature has been the analysis of moderators of SR in the laboratory in large sample sizes.

A number of putative moderators of SR encompassing genetic and environmental factors have been proposed (Morean et al., 2015). The contribution of sex as a moderator of SR is unclear with studies reporting no sex differences (McCance-Katz et al., 2005, Schuckit et al., 2000) and others reporting sex differences (Luczak et al., 2002, Miller et al., 2009), albeit the directionality of the findings are not consistent. Family history of AUD has been commonly studied as a contributing factor to higher-risk patterns of subjective response (Knopik et al., 2004, Morean and Corbin, 2010). Impulsivity has also been linked to SR (Berey et al., 2019, Leeman et al., 2014) and alcohol-related problems (Berey et al., 2017, Magid et al., 2007). Recently, a study by Gowin et al. (2017) collapsed across multiple alcohol administration datasets and found that male sex, family history of AUD, and higher impulsivity were associated with higher rates of binge drinking in the human laboratory. Low level of response was not significantly associated with rate of binge drinking; however, the influence of other SR domains (i.e., stimulation, negative affect, and craving) on alcohol self-administration were not examined.

The present study takes a similar approach to Gowin et al. (2017) by collapsing across six IV alcohol administration studies to allow for a robust analysis of moderators of SR in the human laboratory. Using established multilevel modeling approaches, we hypothesize that male sex, family history of AUD, and impulsivity (via delay discounting rate) would be associated with enhanced alcohol-induced stimulation and craving, thereby increasing AUD risk, in heavy drinkers. Conversely, we also posit that these moderators would blunt alcohol-induced sedation and alcohol-induced decreases in negative mood, which would also increase AUD risk.

Materials and Methods

Data source and sample

The current sample is culled from six separate clinical and experimental psychopharmacology studies with similar inclusion criteria and recruitment methods, all conducted in the Addictions Laboratory at the University of California, Los Angeles. Specifically, the sample analyzed herein were drawn from studies dissociating alcohol's pharmacology from alcohol cues, studies investigating the relationship between SR and operant alcohol self-administration, and studies examining the efficacy of pharmacotherapies for AUD (i.e., naltrexone, quetiapine, and ibudilast). Although some studies involved pharmacological manipulations, *participants were only included in the current analyses if they were randomized to the placebo condition.* All studies recruited community samples of non-treatment-seeking drinkers from the greater Los Angeles Area. Recruitment procedures were identical across all studies (i.e., advertisements), with more recent studies benefiting more from social media as a recruitment tool. All study procedures were approved by the University of California, Los Angeles Institutional Review Board. All participants provided written informed consent after receiving a full explanation of the study procedures, with the alcohol administration procedures discussed with a licensed physician. All study procedures were carried out in accordance with the Declaration of Helsinki.

Interested individuals called the laboratory and completed a telephone interview for preliminary eligibility. After providing written informed consent, participants were breathalyzed, provided urine for toxicology screening, and completed a battery of self-report questionnaire and interviews. Heavy drinking was verified through one of the following methods: (i) greater than 48 drinks per month; (ii) greater than 4 or 7 drinks per week for females and greater than 6 or 14 drinks per week for males; (iii) an Alcohol Use Disorder Identification Test (Saunders et al., 1993) (AUDIT) score of 8 of higher; (iv) a score of 2 or higher on the CAGE questionnaire(Ewing, 1984).

All studies had the following exclusion criteria: (i) current involvement in treatment programs for alcohol use or have received treatment in the prior 30 days to study participation; (ii) use of non-prescription psychoactive drugs or use of prescription medications for recreational purposes; (iii) self-reported history of psychiatric disorders (e.g., bipolar disorder or psychotic disorders); (iv) current use of antidepressants, mood stabilizers, sedatives, anti-anxiety medications, seizure medications, or prescription painkillers; (v) self-reported history of contraindicated medical conditions (e.g., chronic liver disease, cardiac disease); (vi) if female, pregnant (as verified by a urine sample), nursing, or planning to get pregnant in the next 6 months or refusal to use a reliable method of birth control; (vii) score ≥10 on the Clinical Institute Withdrawal Assessment for Alcohol-Revised (Sullivan et al., 1989) (CIWA-Ar) indicating clinically significant alcohol withdrawal requiring medical management; (viii) breath alcohol concentration (BrAC) of greater than 0.000 g/dl as measured by the Dräger Inc. Alcotest® 6510; (ix) positive urine toxicology screen for any drug (other than cannabis), as measured by Medimpex United Inc. 10 panel drug test, and (x) fear of, or adverse reactions to, needle puncture.

Alcohol administration procedures

Alcohol administration was conducted at the UCLA Clinical and Translational Research Center (CTRC). In this study, the same participants were assessed at all timepoints (i.e., baseline/BrAC = 0.00, BrAC = 0.02, BrAC = 0.04, and BrAC = 0.06 g/dl) during a single alcohol challenge. Detailed methodology can be found in our previous work (Ray et al., 2013). Briefly, at intake, vitals, height, and weight were measured and IV lines were placed by a registered nurse. Participants then completed baseline assessments. Study staff remained in the room to monitor the infusion, breathalyze the participant, take vital signs, administer questionnaires and answer questions but did not significantly engage with participants otherwise. To enable precise control over BrAC and to dissociate biobehavioral responses to alcohol from responses to cues, alcohol was administered IV (5% ethanol v/v in saline) using an established nomogram that considers participants' sex and weight. Infusion rates were: 0.166-ml/minute × weight, in kilograms, for males, and 0.126-ml/minute × weight, for females. During the alcohol challenge, participants were administered alcohol designed to reach target BrACs of 20, 40 and 60 mg%, each over 15–20 minutes. Infusion rates were reduced to half upon reaching each target BrAC, so that BrACs would remain stable while participants completed questionnaires (~5 minutes). Participants were required to have a BrAC ≤ 0.02 g/dl before leaving the laboratory (or a BrAC = 0.00 g/dl if driving).

Measures

Alcohol use and problems were measured using: (1) The Timeline Follow Back (Sobell and Sobell, 1992) to measure frequency of alcohol consumption in the previous 30 days, (2) the CIWA-Ar (Sullivan et al., 1989) to assess alcohol withdrawal severity, (3) the Alcohol Dependence Scale (Skinner et al., 1984) to measure severity of alcohol use problems, (4) the Penn Alcohol Craving Scale (Flannery et al., 1999) to measure tonic (unprovoked) alcohol craving, and (5) the Family Tree Questionnaire (Mann et al., 1985), which assesses family history of alcohol problems. A family history of AUD density score was calculated by dividing the number of biological relatives with reported alcohol problems by the total number of first- and second-degree relatives. The Structured Clinical Interview of DSM-IV (SCID) or DSM-5 (First et al., 2015, First et al., 1995) was administered by a master's level clinician to assess for current AUD symptoms. In order to streamline the merging of data across multiple human laboratory studies using both DSM-IV and DSM-5 criteria, participants who were diagnosed with alcohol dependence using DSM-IV terminology are considered to have an AUD.

Individual difference measures included: (1) the Monetary Choice Questionnaire(Kirby et al., 1999) to capture delay discounting rate for monetary reinforcers, (2) the Beck Depression Inventory-II (Beck et al., 1996) to measure depressive symptomology, and (3) the Beck Anxiety Inventory (Beck et al., 1988) to assess anxiety severity and level. Individual responses on the Monetary Choice Questionnaire were processed using a freely available, automated tool (Kaplan et al., 2016).

The delay discounting task has a unique scoring system as it is not consistent over time, but rather a hyperbola-like function so that the reward disproportionately gains value as the time to receipt approaches and disproportionately loses value when initially delayed. The

hyperbolic function is characterized by the equation $Vd = V/(1 + kd)$ in which Vd is the present discounted value of the reward, V is the objective value of the reward, k is a constant that reflects the rate of discounting and d is the temporal delay. Therefore, a higher k value indicates a more impulsive tendency to prefer smaller, immediate rewards over larger, future rewards. As k is not normally distributed, we use ln(k) as the interpretable delay discounting score.

Subjective responses were captured using the following measures given at baseline and at each target BrAC (i.e., .02, .04, and .06 g/dl): (1) The Biphasic Alcohol Effects Scale (BAES) that captures the stimulant and sedative subjective effects of alcohol (Martin et al., 1993, Erblich and Earleywine, 1995); (2) The Subjective High Assessment Scale (SHAS) to capture sedation (Schuckit, 1984); The Alcohol Urge Questionnaire (AUQ) to measure state levels of alcohol craving (Bohn et al., 1995); and (3) The Profile of Mood States (POMS (McNair, 1992)) that was used to record positive and negative mood states. Stimulation included the BAES stimulation subscale and the POMS positive mood and vigor subscales. Sedation included the BAES sedation subscale and the SHAS. Negative affect included the POMS negative mood and tension subscales. Craving was captured using the AUQ. As in our previous work, combined scores were computed within each SR domain by first Z-score transforming each measure across the entire challenge and then summing the scores (Bujarski et al., 2018, Grodin et al., 2019). These methods allow for the incorporation of multiple scales per SR domain.

Statistical Analyses

Due to the nested data structure, a series of multilevel models tested whether potential moderators predicted SR during the alcohol challenge across four domains: stimulation, sedation, negative affect, and craving. The nested structure of the data was as follows: repeated SR measurements across the alcohol challenge (Level 1) nested within individuals (Level 2), who were nested within studies (Level 3). These 3-level models were selected to account for any potential between study variability; thus, a categorical study variable was not included as a covariate in analyses because study-related variability is accounted for in the multilevel models. In each model, SR was predicted by BrAC time point (coded 0–3), potential moderators, and their interaction. Intercepts and BrAC slopes were random at Level 2. All analyses were conducted in SAS 9.4 with statistical significance set at $p < 0.05$. Cohen's f^2 was calculated as a measure of effect size using PROC MIXED according to published methods (Selya et al., 2012). Cohen's f^2 was selected because it is appropriate for hierarchical and repeated-measure data (Selya et al., 2012). According to Cohen's guidelines (Cohen, 1992), f^2 is considered small at a value of 0.02, medium at a value of 0.15, and large at a value of 0.35. Similar analyses were conducted using traditional approaches to construct SR domains and are reported in supplemental materials. Sub-group analyses were conducted to examine the effect of SR moderators by race and among individuals without AUD (see supplemental materials). It is important to note that the findings from sub-group analyses are preliminary and likely underpowered but may offer insights that can inform future research. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Results

Sample demographic and clinical characteristics

Participants were, on average, 28.13 (SD = 7.70) years old and were 67% male. Participants reported an average of 20.62 (SD = 16.10) drinks per week and an average Alcohol Dependence Scale score of 13.15 (SD = 6.22). Additional demographic and clinical variables are presented in Table 1.

Alcohol challenge manipulation check

Stimulation (B = .36, SE = .05, p < .001), sedation (B = .53, SE = .04, p < .001), and alcohol craving (B = .17, SE = .01, p < .001) increased over rising BrAC. Negative affect decreased over rising BrAC (B = −.27, SE = .03, p < .001). These BrAC effects provide a manipulation check such that, as expected, as BrAC increased so did alcohol craving, stimulation, and sedation, whereas negative affect decreased.

3.3. SR moderators across the alcohol challenge

Sex predicted overall stimulation (B = .820, SE = .32, p = .011, f^2 = .069; Table 2), such that males had higher stimulation levels relative to females controlling for other SR moderators in the model. Delay discounting and family history density did not predict overall stimulation as main effects (p's > .05). The effect of sex on stimulation varied as a function of BrAC (B = .375, SE = .12, p = .002; Figure 1A), such that mean differences between males and females were greater as BrAC increased. No other interaction terms between SR moderators and BrAC were statistically significant (p's > .05).

Sex, delay discounting, family history density, nor their respective interactions with BrAC predicted sedation or negative affect (all p's > .05; Table 2).

Sex predicted overall alcohol craving (B = .295, SE = .10, p = .005; f^2 = .075; Table 2), such that males had greater alcohol craving relative to females controlling for other variables in the model. Participants with greater family history density scores reported greater overall alcohol craving (B = .995, SE = .26, p = .0001; f^2 = 0.20). Delay discounting did not predict overall alcohol craving as a main effect (p > .05). The effect of sex on alcohol craving varied by BrAC (B = .04, SE = .02, p = .009; Figure 1B) such that mean differences between males and females were greater as BrAC increased. No other interaction terms between SR moderators and BrAC were statistically significant (p's > .05).

Secondary analyses evaluating moderators on each individual scale (as compared to the factors that capture core SR domains) resulted in similar findings (Supplemental Table 1).

Discussion

For decades the alcohol field has attempted to identify biobehavioral phenotypes that might explain heterogeneity in AUD. One of the more promising risk factors for AUD is acute SR to alcohol, which can be measured in controlled human laboratory paradigms. Identifying moderators of SR may inform prevention and intervention efforts for AUD, but have been difficult to detect because of the small sample sizes that are often used in alcohol

administration studies. Thus, the purpose of this study was to identify and evaluate SR moderators in a large sample of heavy drinkers who completed an IV alcohol administration in the laboratory.

One of the consistent findings in this study was that SR was sex-dependent for stimulation and craving such that males reported greater alcohol-induced stimulation and craving across the entire alcohol administration. This is notable as the BrACs were well-controlled for through sex and BMI adjustments to the alcohol administration protocol. Sex effect sizes for stimulation and craving fell in the small to medium range suggesting that sex has a greater impact on these SR domains than family history and delay discounting. It is possible that the risk of AUD through SR mechanisms may be more prominent for males. For instance, a seminal study found that male heavy drinkers experienced a sizeable release of dopamine in the ventral striatum during IV alcohol administration (Ramchandani et al., 2011), while the same has not been demonstrated in females. Conversely, a recent review has suggested that females may be more vulnerable to alcohol misuse and AUD through mechanisms associated with stress, trauma, negative affect, and mood and anxiety disorders (Guinle and Sinha, 2020). Thus, it is plausible that while the SR mechanisms represent a distinct pathway to AUD, they may be a more probable causal factor in males versus females. Clearly, longitudinal studies testing sex differences in the relationship between SR and drinking outcomes would be informative. Nevertheless, even if the relationship between SR domain and drinking outcomes remains consistent between men and women, if in absolute terms women are less likely to experience alcohol-induced stimulation and craving, they will be inherently less likely to escalate their use and to develop AUD through this distinct, SR-driven, risk pathway. This is a good example of the need for larger samples sizes in SR research since these effects may be obscured or undetected in small studies that are underpowered to test moderators. In fact, given the robust nature of the SR literature, a large-scale multi-site study may be warranted to fine tune methods, confirm critical findings, and apply these results toward clinically meaningful questions going forward.

Family history was associated with greater alcohol-induced craving. SR to alcohol is heritable (~60%)(Viken et al., 2003), however, the focus of this work has been on the low level of response domain with considerably less attention to other SR domains. Notably, Gowin and colleagues (2017) reported that family history of alcoholism was associated with higher binge drinking rates in the human laboratory. In a separate intravenous alcohol self-administration study, individuals with a positive family history of alcoholism had higher alcohol self-administration compared to individuals with negative family history of alcoholism (Zimmermann et al., 2009). While we expected family history of alcoholism to be associated with lower sensitivity to the sedative effects of alcohol, based on the influential work of Schuckit and colleagues (2013), we found no effects of family history on sedation, perhaps due to notable differences in the sociodemographic makeup of the respective study samples (i.e., older, diverse, community sample of drinkers compared to drinkers recruited from college settings). The effect size for family history was small suggesting that future studies examining the effects of family history on SR will need larger sample sizes than those typically used in behavioral pharmacology studies.

Impulsivity, hereby tested using the delay discounting paradigm, did not influence any subjective response domain. This finding was relatively surprising given that impulsive individuals experienced higher alcohol-induced stimulation and positive mood in one of the six studies included in these analyses (Westman et al., 2017). Impulsive behaviors, like poor inhibitory control, are associated with stimulatory effects of alcohol (Weafer et al., 2020) and other drugs (Weafer et al., 2017). Notably, in the current analyses, positive mood and stimulation are combined into a single factor; yet, we did get a modest delay discounting signal when the BAES stimulation subscale was examined. An association between trait impulsivity and subjective response was reported in an independent sample, whereby individuals with greater trait impulsivity showed a steeper increase in the stimulant effects of alcohol and dampened sedative response (Leeman et al., 2014). However, in the aforementioned study, the effects were dose dependent. And in a study using low-dose alcohol, the relationship between trait impulsivity and SR was not detected (Berey et al., 2019). In a separate study we found that impulsivity via delay discounting was associated with alcohol self-administration in both traditional and machine learning analyses (Grodin et al., 2020). Perhaps there is a lack of phenotypic overlap between AUD risk conferred through SR and AUD risk conferred through impulsive decision-making captured by delay discounting. Nevertheless, when phenotypes such as binge drinking or self-administration are employed, impulsivity may play a larger role.

There are several strengths and limitations to our study. Strengths include a large and racially diverse sample size to investigate SR moderators and the use of well-validated scales and measurements to construct SR domains. Notable limitations include the use of IV alcohol administration, which allows for precise control of BrAC at the expense of face validity, as well as the exclusion criteria used across studies may have limited the generalizability of our findings. The repeated and relatively rapid increases in BrAC may have magnified SR effects, particularly since the same participants were assessed at each timepoint. Given that the study sample was comprised of non-treatment-seeking heavy drinkers, future work should validate SR moderators across various alcohol drinking profiles. Additionally, the maximum BrAC during alcohol administration was capped at 60mg% while timepoints that capture the descending BrAC limb were not included in the current study. It is possible that the effects of some moderators may only be detectable when assessed at higher BrAC concentrations or during the descending limb, especially for very heavy drinkers. It is also likely that SR reported at each timepoint are confounded with alcohol dose. That is, the alcohol dose that was administered differed at each timepoint. Previous work has shown changes in SR across timepoints while the dose is clamped at a particular level (Kerfoot et al., 2013). The alcohol challenge procedure used in the current study precludes us from assessing SR changes over time at a consistent alcohol dose. The absence of a placebo condition limits the specificity of moderator effects on SR. Lastly, these results may not generalize to oral alcohol administration paradigms in which alcohol cues are inherently present.

In conclusion, this study culled data from multiple studies using common methods of recruitment of heavy drinkers and alcohol administration procedures using IV alcohol. Through a large sample and advanced data analytic methods, this study extends the literature by suggesting important moderators of SR in heavy drinkers, namely sex and family history.

Men were more likely than women to report alcohol-induced stimulation and craving, which in turn render them vulnerable to escalating their drinking and developing AUD. Individuals with a family history of alcoholism reported greater alcohol craving during alcohol administration. Together these findings consolidate and extend a growing body of research on who is most likely to report the SR features that confer risk for AUD. Identifying males and those with a family history of AUD as more likely to display "risky" subjective responses to alcohol in the laboratory positions our field to realize the application of decades of SR research more fully toward informing prevention and treatment development efforts for AUD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Funding:

This study was supported by funds from the National Institute on Drug Abuse (T32DA024635 to SJN) and the National Institute on Alcohol Abuse and Alcoholism (K24AA025704 to LAR; F32AA029288 to SJN).

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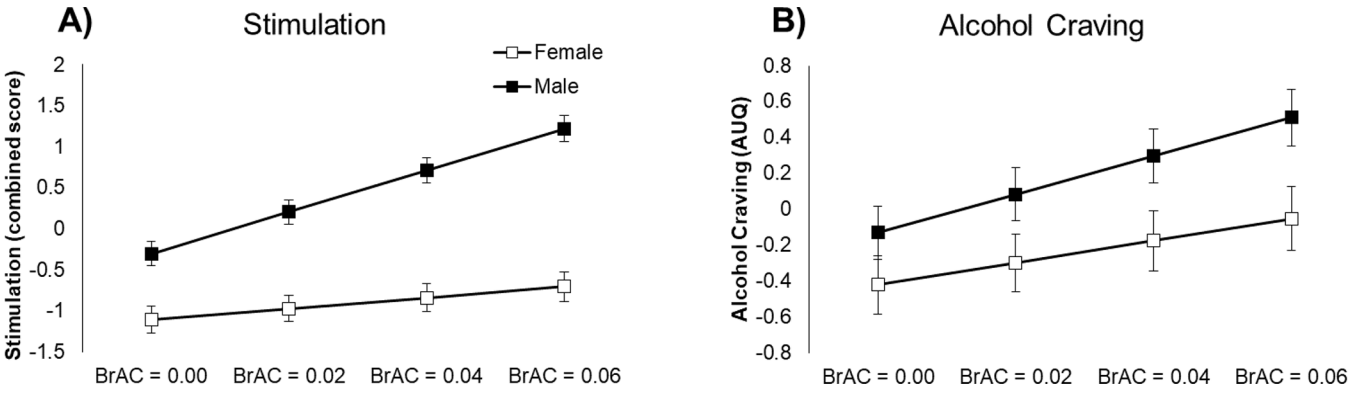

Figure 1.

Sex and subjective response across the alcohol administration session. Mean ± SEM stimulation (A) and craving (B) scores are presented for males (closed squares) and females (open squares) as a function of breath alcohol concentration.

Table 1.

Sample demographic and clinical characteristics (n = 250).

Variables	Means (SD) or N (%)
Age	28.13 (7.70)
Sex - Male	167 (66.80%)
Race/Ethnicity	
White, Non-Hispanic	78 (31.20%)
White, Hispanic	24 (9.60%)
Black	17 (6.80%)
Asian	114 (45.60)
Other	17 (6.80%)
Income	
Below $30,000	105 (42.00%)
$30,000 – $74,999	80 (32.00%)
Above $75,000	65 (26.00%)
Cigarette smoker	113 (45.20%)
CIWA-Ar[a]	1.26 (1.69)
Total Drinks past 30 days	88.37 (68.98)
Drinks per Week	20.62 (16.10)
Alcohol Dependence Scale[a]	13.15 (6.22)
Current AUD[a]	
Yes	69 (27.6%)
No	150 (60.00%)
Penn Alcohol Craving Scale[a]	10.44 (6.56)
Family History Density	0.14 (0.20)
Beck Depression Inventory-II	9.03 (8.35)
Beck Anxiety Inventory	6.10 (6.78)
Delay Discounting (ln(k))[a]	−4.35 (1.66)

Note. CIWA-Ar, Clinical Institute Withdrawal Assessment for Alcohol-Revised

[a]indicates missing data or measure not assessed for some participants: N = 31 for CIWA-Ar, N = 31 for Alcohol Dependence Scale, N = 31 for current AUD, N = 4 for Penn Alcohol Craving Scale, N = 9 for delay discounting.

Table 2.

Multilevel models of moderators on subjective response to alcohol

	Stimulation			Sedation			Negative Affect			Alcohol Craving		
	B	**SE**	***t***	**B**	**SE**	***t***	**B**	**SE**	***t***	**B**	**SE**	***t***
Age	.042	.021	1.96	.022	.013	1.74	.020	.015	1.39	.008	.007	1.26
Sex[a]	**.820**	**.321**	**2.55** *	.196	.193	1.02	−.010	.239	−0.04	**.295**	**.103**	**2.84** **
ln(*k*)	−.179	.096	−1.86	−.081	.057	−1.41	.024	.072	0.34	−.012	.031	−0.41
FH density	−.184	.791	−0.23	−.130	.475	−0.27	.519	.589	0.88	**.995**	**.256**	**3.89** ***
BrAC	.184	.195	0.95	**.691**	**.148**	**4.69** ***	−.184	.121	−1.51	**.160**	**.064**	**2.49** *
Sex X BrAC	**.375**	**.118**	**3.19** **	−.076	.089	−0.86	−.071	.073	−0.97	**.091**	**.038**	**2.35** *
FH density X BrAC	−.009	.285	−0.03	.082	.216	0.38	−.005	.177	−0.03	.093	.094	0.99
ln(*k*) X BrAC	.011	.034	0.34	.023	.025	0.90	.007	.021	0.35	.012	.011	1.03

Note. FH = Family history of alcoholism; BrAC = breath alcohol concentrations; ln(*k*) = natural log of *k* representing delay discounting rate.

[a]Female sex is the reference group.

* $p < .05$

** $p < .01$

*** $p < .001$.