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Alcohol Craving in the Natural Environment: Moderating Roles of Cue Exposure, Drinking, and Alcohol Sensitivity

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Effects of cue exposure and alcohol consumption (e.g., priming doses) on craving for alcohol have been examined in largely separate literature, limiting what is known about their potential interaction. Individuals with low alcohol sensitivity, a known risk factor for alcohol use disorder (AUD), exhibit stronger cue-elicited craving than their higher-sensitivity (HS) peers in both laboratory and real-world contexts. Here, underage drinkers ($N = 155$) completed a 21-day ecological momentary assessment (EMA) protocol in which they recorded exposure to alcohol cues and levels of craving during both nondrinking and postdrinking moments. Multilevel modeling detected a significant interaction of cue exposure and postdrinking status on craving. Cue-induced craving was increased in postdrinking moments compared to nondrinking moments. Contrary to prediction, cue-elicited increase in craving during nondrinking moments was stronger in participants reporting higher sensitivity to alcohol. In the presence of cues, lower sensitivity was robustly related to craving intensity in the postdrinking state but unrelated to craving during nondrinking moments. Craving during drinking episodes in the natural environment is magnified by the presence of alcohol cues, potentially contributing to the maintenance or acceleration of drinking episodes. Moreover, lower-sensitivity drinkers may be particularly susceptible to the combined effects of cue exposure and postdrinking status on alcohol craving.

Public Health Significance

This study provides evidence that, in natural settings, craving for alcohol is especially high when drinkers are exposed to alcohol cues during a drinking episode. The study also suggests that individuals lower in sensitivity to alcohol's acute effects may be especially vulnerable to the craving-provoking effects of alcohol cues during drinking episodes. These findings are the first to demonstrate a combined effect of cue exposure and postdrinking status on craving for alcohol in the natural environment.

Keywords: alcohol, alcohol sensitivity, craving, ecological momentary assessment, incentive salience

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Craving is the conscious experience of wanting, an urge stemming from motivations to pursue and consume a substance (see Robinson & Berridge, 1993; Rohsenow & Monti, 1999). Craving for alcohol generally is a strong correlate of alcohol use disorder (AUD) severity, quantity of alcohol consumed, and the experience of drinking-related adverse consequences (see Casey et al., 2012; MacKillop et al., 2010; Murphy et al., 2014).[1] Such evidence has led many to suggest craving as a candidate endophenotype for AUD (see Hines et al., 2005; Ray, Mackillop, & Monti, 2010).

Craving is a key construct in the incentive sensitization theory of addiction (ISTA; Berridge & Robinson, 2003, 2016; Robinson & Berridge, 1993, 2000, 2001). ISTA posits that repeated drug use sensitizes the mesocorticolimbic dopamine system's response to cues that signal the availability of drug reward, such that these cues take on the motivational properties of the drug itself. As a result, drug reward-predictive cues (e.g., the sight or smell of alcoholic beverages) are transformed into "motivational magnets" that attract attention, evoke craving, and arouse approach responses (Berridge & Robinson, 2003; Everitt & Robbins, 2005).

Cue-induced craving has been elicited in human lab studies via exposure to alcoholic beverages (e.g., Manchery et al., 2017; Monti et al., 1993; Ramirez et al., 2015a, 2015b) or pictures of alcoholic beverages (see Litt & Cooney, 1999), exposure to alcohol odors (Bragulat et al., 2008; Cyders et al., 2014; Fleming et al., 2021; Kareken et al., 2004, 2010), and guided imagery (see Erblich et al., 2009; Seo et al., 2013). Interindividual variation in cue-induced craving is associated with *in vivo* alcohol consumption in the lab, supporting the utility of cue-induced craving as a proximal indicator of motivation to drink (e.g., MacKillop & Lisman, 2005; O'Malley et al., 2002). Other work shows that laboratory-measured cue-induced craving predicts alcohol use and problems outside of the lab (e.g., Papachristou et al., 2014; Ramirez & Miranda, 2014), and that cue exposure in the natural environment is associated with increased craving in daily life (e.g., Fatseas et al., 2015; Kuerbis et al., 2020; Miranda et al., 2014; Trela et al., 2018; Treloar Padovano & Miranda, 2021).

Research examining the effect of alcohol consumption (i.e., priming doses) on craving indicates that, rather than slaking the desire to drink, alcohol exposure appears to increase craving (e.g., Chutuape et al., 1994; de Wit, 1996, 2000; de Wit & Chutuape, 1993; Duka et al., 1999; Hodgson et al., 1979; Kirk & de Wit, 2000; Rose & Duka, 2006; Schoenmakers et al., 2008). As implied by the term, priming dose studies have focused on effects of initial consumption and/or small alcohol exposures on craving. However, at least one study (Schoenmakers & Wiers, 2010) reported a linear association between alcohol exposure level (as indicated by breath alcohol concentration, up to 0.16%) and craving in the natural environment, suggesting this effect might hold for larger exposures.

In theory, whereas the effect of cue exposure on craving (in the absence of alcohol exposure) is relevant to determining whether a drinking episode is initiated, priming effects (via initial exposure) are relevant to determining the heaviness of a drinking episode, that is, whether a first drink leads to additional drinks. Together, the combination of cue- and priming-induced craving may have additive or synergistic effects that promote heavier drinking within an episode, and thereby, negative consequences. Yet, few studies have tested the independent and combined effects of cue exposure and priming on craving. Available evidence suggests these two variables do not have synergistic effects. Schulze and Jones (1999) reported that a priming dose did not exacerbate the effect of visual cue exposure on craving. Both Bragulat et al. (2008) and Kareken et al. (2010) reported that exposure to olfactory cues (or combined olfactory/visual cues) increased craving, but this effect was not moderated by intravenous alcohol infusion (i.e., exposure). Similarly, Courtney et al. (2015) found that two "interoceptive" cues—a priming dose and a taste cue—increased craving, but their effects were independent.

No prior investigation has examined craving in the natural environment as a function of both cue exposure (i.e., whether visual cues are present) and alcohol exposure (i.e., whether drinking has been initiated, implying priming). Results of field studies might differ from those of laboratory studies. Most lab studies combining cue and alcohol exposure have used relatively impoverished visual (e.g., beverage photos) or olfactory cues (e.g., alcohol odors delivered via nasal canula), and/or have used intravenous infusion, which is devoid of typical consumption-related kinesthetic, olfactory, and gustatory cues. Relatedly, compared to a lab setting in which cues are selected by an experimenter, everyday cue exposures are more likely to represent beverages and beverage-specific cues for which incentive-motivational responses have become conditioned (see Robbins & Ehrman, 1992). Finally, unlike the conditions in most lab experiments, cue exposure in natural settings is more likely to occur in typical drinking contexts (which also act as cues; see Martins et al., 2019; Nees et al., 2012; Trela et al., 2018) and to signal alcohol availability. Numerous studies (e.g., Carter & Tiffany, 2001; Papachristou et al., 2012; Wertz & Sayette, 2001) have shown that perceived substance availability can modulate cue-elicited craving (also see Simon et al., 2020). Thus, the combination of visual cues and alcohol exposure in the natural environment represents a much richer, more immersive set of experiences than exist in the lab, which could produce stronger craving.

The propensity to attribute incentive salience to reward-related cues varies considerably between individuals (Flagel et al., 2010; Robinson et al., 2014). Consistent with this notion, in some studies, only 50%–60% of participants reported increased craving following cue exposure (Litt & Cooney, 1999). Identifying alcohol-use phenotypes associated with susceptibility to incentive salience sensitization (ISS) is an important translational goal. Evidence from both rodents (e.g., Beckstead & Phillips, 2009; Murphy et al., 2002; Risinger et al., 1994) and humans (see Cofresí et al., 2019, 2021; Fleming et al., 2021) suggests low sensitivity (LS) to alcohol's acute effects (i.e., requiring a larger dose to experience various effects)—a heritable, biobehavioral trait (Heath et al., 1999; Ray, Miranda, et al., 2010; Viken et al., 2003) linked to increased AUD risk (e.g., Schuckit, 1994; also see King et al., 2014, 2021, for evidence that higher sensitivity to alcohol's stimulating effects predicts AUD onset)—as a promising candidate phenotype associated with ISS susceptibility.

To the extent that ISS susceptibility plays a role in linking LS with AUD risk (Cofresí et al., 2019), LS individuals also should experience more cue-elicited craving than their higher-sensitivity (HS) counterparts. Two recent studies tested this idea. In a sample of underage drinkers, Fleming et al. (2021) found that exposure to

[1] Some studies have failed to capture a relationship between craving and alcohol use outcomes, but this apparent inconsistency appears largely attributable to methodological and measurement differences (see de Wit, 2000; Sinha & O'Malley, 1999, for discussion).

alcoholic beverage odors in the lab increased self-reported alcohol craving among LS but not HS individuals. Trela et al. (2018) used ecological momentary assessment (EMA) to measure alcohol craving in young adult drinkers' natural environments, finding that craving during nondrinking moments increased when respondents were in contexts (e.g., bar/restaurant) often associated with drinking, and that craving increased more in such contexts among LS drinkers.

The data reported in the present article are drawn from an ongoing, prospective study aimed at increasing understanding of AUD etiology by characterizing associations between changes in alcohol use and changes in incentive-motivational responses, including craving, during emerging adulthood—a period in which pathological drinking patterns are established (Swendsen et al., 2012). Prior research has shown the importance of craving for AUD risk in this population (Bollen et al., 2020; Ramirez et al., 2015b; Rosenberg & Mazzola, 2007) and that college attendance significantly increases AUD risk (Carter et al., 2010; Slutske et al., 2004).

The analyses reported here extend prior craving research in two ways. First, to permit examination of the independent and combined effects of cue exposure and alcohol consumption on craving in the natural environment, we examined associations between visual cue exposure and alcohol craving both when participants were not drinking (i.e., nondrinking moments) and when they reported having initiated a drinking episode (i.e., postdrinking moments). Based on existing research, we predicted that craving would be higher when cues are present than when cues are absent (Hypothesis 1) and during postdrinking than during nondrinking moments (Hypothesis 2). In addition, we tested the exploratory prediction that cue exposure would be associated with stronger craving during postdrinking than during nondrinking moments (Hypothesis 3). This prediction was based on the idea that cues present during drinking episodes are more likely to be encountered in typical drinking contexts that directly signal alcohol availability.

We also examined whether cue exposure and consumption-related effects on craving were moderated by individual differences in alcohol sensitivity, as reflected in scores on a validated, retrospective self-report measure (Fleming et al., 2016). Based on findings of our prior lab-based (e.g., Fleming et al., 2021) and naturalistic studies (Trela et al., 2018), we predicted that the magnitude of cue-induced craving reactivity during both nondrinking and postdrinking moments would be greater among LS than HS drinkers (Hypothesis 4).

Method

The University of Missouri Institutional Review Board reviewed and approved all procedures used in this study. Variable selection and analyses were planned prior to data collection as part of the grant application (R01 AA025451) that funded this study. However, the analyses were not formally preregistered. Data and data processing scripts are available upon request from corresponding authors.

Participants

Participants were 177 healthy emerging adults (ages 18–20; 59% women; 95% White/Caucasian) enrolled in a longitudinal parent study aimed at characterizing associations between alcohol sensitivity, laboratory-based alcohol cue reactivity, and craving and alcohol use in the natural environment among underage drinkers.

Participants were recruited via weekly mass email announcements to the University of Missouri community, flyers posted around the Columbia, MO community, introductory Psychology classes at the University of Missouri, and advertisements on social media. Study candidates completed an initial screening survey to determine eligibility. Candidates were eligible if they (a) were age 18–20 years at recruitment, (b) consumed alcohol at least monthly over the past year with at least one binge-drinking experience in the past 6 months, (c) could read and write English, and (d) had normal or corrected-to-normal visual acuity. Study candidates were deemed ineligible if they reported (a) a history of unsuccessful attempts to quit or reduce alcohol use, (b) a history of neurological disease, or (c) head injuries that resulted in loss of consciousness for >2 min.[2]

Participants were paid up to $150 for completing at least 85% of prompted assessments (see Supplemental Materials for details). The study is ongoing; the present analyses are limited to data collected prior to an interruption caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) lockdowns in March 2020. Participants were excluded from analyses if no drinking moments were reported across the EMA period (n = 16) or if estimated blood alcohol concentration (eBAC) could not be computed due to missing anthropometric data (n = 6). Demographic and other participant characteristics for the final analytic sample (n = 155) are reported in Table 1. The primarily undergraduate sample (95%) was majority White (95%) and mostly women (59%). The sample comprised a range of drinking patterns; the mean Alcohol Use Disorders Identification Test (AUDIT-C) score (M = 5.9, SD = 2.0; Bush et al., 1998) indicated moderate–high risk, and nearly half of the participants met criteria for AUD based on the mini neuropsychiatric interview (MINI; Sheehan et al., 1998).

Procedure

Each participant attended one laboratory session prior to the 21-day EMA study period. Upon providing informed consent, participants completed a battery of self-report measures and underwent a diagnostic interview (the MINI) to assess for common psychiatric disorders. Participants also downloaded the electronic diary application (Morrison et al., 2018) to their personal smartphone and were instructed on how to complete prompted reports and initiate first-drink reports. The 21-day EMA period began the following day.

Participants completed four types of reports. A prompted *morning report* (n = 2,175) at typical rising time was completed daily upon awakening but no later than noon. Participants also received approximately four *random prompts* (n = 5,993) per day, stratified to occur randomly during four equally spaced time periods from 8:00 a.m.–11:00 p.m. Participants were instructed to initiate a *first-drink report* (n = 366) after finishing the first drink of a drinking episode. *Drinking follow-up reports* (n = 969) were automatically triggered to occur at 30, 60, 90, and 120 min following the first drink. To catch drinking

[2] The larger prospective study from which the data for this article were acquired included a laboratory visit in which the electroencephalogram (EEG) was measured. Accordingly, history of neurological disease or serious head injuries were included as exclusionary criteria, as these conditions contraindicate EEG recording.

Table 1
Characteristics of Final Sample Used for the Present Analyses (N = 155)

Variable	*N* (%)	*M* (*SD*)
Age	—	19.42 (.75)
Undergraduate student status	148 (95)	
Biological sex (female)	91 (59)	
Hispanic/Latinx	10 (6.5)	
Race		
White/Caucasian	147 (95)	
Black/African American	4 (3)	
Asian	3 (2)	
Native American Indian	1 (<1)	
TLFB past-month drinking episodes per week	—	1.8 (1.0)
TLFB past-month drinks per drinking episode	—	5.2 (2.6)
TLFB past-month binge-drinking episodes	—	2.3 (2.6)
ASQ raw score	—	4.4 (1.9)
AUDIT-C total score (0–12)	—	5.8 (2.0)
DSM-5 AUD diagnosis		
None	71 (47)	
Mild	44 (29)	
Moderate	27 (18)	
Severe	8 (5)	
EMA report characteristics		
Nondrinking moments per user		51.8 (23.4)
Postdrinking moments per user		9.5 (8.4)
Weekly drinking episodes per user		1.3 (0.8)
Drinks per drinking episode		4.0 (3.1)
Cue exposures per user		
Postdrinking moments		7.8 (7.3)
Nondrinking moments		3.3 (4.6)
Total prior night alcohol-related consequences per user		4.6 (4.2)
Momentary cigarette use prior 2 hr		
Postdrinking moments	24 (1.6)	
Nondrinking moments	50 (.6)	
Momentary cannabis use prior 2 hr		
Postdrinking moments	64 (3.2)	
Nondrinking moments	253 (4.3)	

Note. TLFB = timeline follow-back; ASQ = Alcohol Sensitivity Questionnaire; AUDIT-C = Alcohol Use Disorder Identification Test (sum of first 3 items, assessing typical quantity and frequency of alcohol use and frequency of binge drinking in the past year); DSM-5 = Diagnostic and Statistical Manual of Mental Disorders (fifth edition); AUD = Alcohol Use Disorder.

events not reported by the participant, both *random prompts* and *morning reports* asked whether alcohol had been consumed since the last report. If yes, and if this occurred within the past 2 hours, the *drinking follow-up prompts* were triggered (28.5% of recorded drinking episodes began in this manner).

Person-Level Measures

Alcohol Sensitivity

The 15-Item Alcohol Sensitivity Questionnaire (ASQ; Fleming et al., 2016; O'Neill et al., 2002) was administered as part of the eligibility screener to assess for individual differences in self-reported sensitivity to alcohol. Nine items query effects of alcohol that are often experienced from lighter drinking/low exposures (e.g., feeling buzzed; feeling flirtatious; feeling more at ease socially). For these items, respondents indicate whether they have experienced the specified effect after drinking alcohol, and if so, to estimate the *minimum* number of drinks they require to experience the effect. The remaining six items inquire about effects of alcohol often experienced from heavier drinking/higher exposures (e.g., vomiting; passing out; experiencing a hangover). For these items, respondents indicate whether they have experienced the specified effect after drinking alcohol, and if so, to estimate the *maximum* number of drinks they can consume *without* experiencing the effect. Higher scores on either subscale indicate lower sensitivity to alcohol (i.e., requiring more drinks to experience alcohol's effects). The ASQ has been validated in research (Fleming et al., 2016) showing that ASQ scores predict subjective responses to alcohol challenge in the lab and correlate strongly with scores on a more widely used retrospective self-report measure, the self-rating of the effects of alcohol (SRE) form (Schuckit et al., 1997).

Because the number of ASQ items endorsed (i.e., number of distinct effects experienced) correlates with heaviness of drinking, missing data are not missing at random, which can produce a downward bias in scores. To remedy this, ASQ scores were computed using a standardized person-mean imputation approach (Lee et al., 2015). The number of drinks endorsed for each item was standardized across participants prior to creating individual summary scores. Standardization was computed separately for males and females due to well-documented biological sex differences in alcohol sensitivity (see Sutker et al., 1983; Thomasson, 2002). Higher standardized ASQ scores indicate lower alcohol sensitivity relative to same-sex peers. Internal consistency reliability for the ASQ was very good ($\alpha = .93$).

Recent Alcohol Use

A computer-administered timeline follow-back (TLFB; Sobell & Sobell, 1992) was used to measure the frequency and quantity of past-month drinking. Participants were instructed to indicate the days they consumed alcohol, the quantity of alcohol consumed on each drinking day, and the length of each drinking episode using a calendar spanning the 30 days prior to their laboratory visit.

EMA Measures

Alcohol Craving

Craving for alcohol over the past 15 min was assessed in every diary report using the mean of two items ("urge to drink" and "craving a drink"; $\alpha = .98$) adapted from measures used in prior EMA research (Piasecki et al., 2011). Participants responded to each of the two items using a visual analogue scale anchored at 1 (*not at all*) and 7 (*extremely*). Except for one analysis (reported in the Supplemental Materials), analyses in the present study used the mean of the two items as a measure of momentary craving. Test–retest reliability, as captured by the intraclass correlation coefficient (ICC), was .27, indicating that 27% of total variance in momentary craving was attributable to stable between-person differences. The remaining 73% reflected within-person fluctuations in momentary craving across the EMA period.

Alcohol Cue Exposure

Participants indicated their exposure to alcohol cues in the past 15 min by selecting whether alcohol was "visible directly - bottle, glass,

etc." (coded 1) or "no, not visible" (coded 0) (Ramirez & Miranda, 2014).[3] This item was not administered in *first-drink reports*; direct exposure to visual alcohol cues was coded "1" in these records because participants were instructed to initiate these reports immediately after consumption of a first drink, assumed to inherently involve the presence of alcohol cues. However, cue exposure was queried in time-based *drinking follow-ups* where momentary drinking is not required and, thus, cue exposure cannot be assumed. For instance, participants may have ceased drinking, moved to another location, or paused drinking by the time of the follow-up prompt. For this reason, not all postdrinking reports occurred with cues present.

Contextual Covariates

Several contextual factors are associated with craving for alcohol (Trela et al., 2018). Time of day and day of the week were automatically recorded when each report was submitted. These timestamps were used to create a dummy-coded variable partitioned into 4-hr time blocks and a dichotomous weekend/weekday variable. The weekend was liberally defined as 6:00 p.m. Thursday to 6:00 p.m. Sunday, with weekdays spanning from 6:00 p.m. Sunday to 6:00 p.m. Thursday. These segments were chosen because they represent times and days of heavy drinking for emerging adults (Del Boca et al., 2004; Trela et al., 2018; Waddell et al., 2021; Wood et al., 2007). Locations (bar or restaurant, home, work or school, vehicle, and other) were all treated as separate, dummy-coded variables because participants were instructed to select all that apply at each report. If the participant indicated they had used cigarettes or cannabis since their last entry, time since last use was recorded. Responses from these pairs of items were combined to form "recent cannabis use" and "recent cigarette use" variables, reflecting use in the past 2 hr.

Estimated Blood Alcohol Concentration (eBAC)

If participants indicated they had consumed alcohol in the past 2 hr (i.e., Morning Reports, Random Prompts), since their last entry (i.e., Drinking Follow-Ups), or in a first-drink report, drink quantity and time since consumption were assessed. Following a commonly used formula (Matthews & Miller, 1979), these data were combined with body weight (assessed at baseline) and sex to calculate eBAC—shown to correlate well with breath alcohol content (BrAC; Hustad & Carey, 2005). A minority of the resultant eBAC values were negative (7.0% of drinking moments) and were recoded to zero. Rarely (4.7% of postdrinking moments), momentary eBAC exceeded 0.20 g/dl. Such data points were excluded from analyses because such high estimates were rare and possibly due to error in reporting or incomplete physiological absorption (e.g., emesis).

Prior studies (Piasecki et al., 2012, Trela et al., 2016) show that LS individuals achieve higher peak eBAC during self-paced, real-world drinking episodes, consistent with the notion that LS drinkers must consume more alcohol to achieve desired effects. The resulting positive association between ASQ score and person-mean eBAC ($r = .26$, $p < .001$) complicates the use of eBAC as a covariate because excess consumption "validly" overlaps with alcohol sensitivity, and therefore attempts to "partial out" consumption level may produce a residual ASQ score that no longer represents the original construct (Meehl, 1971; Miller & Chapman, 2001). Accordingly, we person-mean centered eBAC to remove systematic between-person variance in consumption. The resulting score represents within-person variation in alcohol exposure relative to one's mean level of exposure over the 21-day EMA period. Additionally, all recorded moments outside of drinking episodes were assigned an eBAC value of zero subtracted by that individual's mean level of eBAC, as it is their mathematical lower bound and a true representation of zero alcohol in the blood.

Postdrinking Moments

Reports were considered having taken place during a postdrinking moment if a participant indicated they had consumed alcohol in the past 2 hr via a *random prompt* or *morning report*, or they initiated a *first-drink report*. Subsequent moments logged during *drinking follow-up reports* were also considered having taken place during a postdrinking moment. However, especially in light-drinking episodes (e.g., one drink), eBAC can return to zero well before the final drinking follow-up. Since consecutive eBACs of zero signify the end of a drinking episode, *drinking follow-up* reports where both eBAC and ΔeBAC from the previous moment = 0 (1.5% of drinking moments) were removed.

In some iterations of the diary smartphone app, *drinking follow-up reports* remained available to participants and were sometimes completed the morning after drinking. To ensure accurate representation of the drinking episode, all follow-up entries that occurred outside of 3 hr after the reported first drink were discarded (5.0% of all postdrinking moments).

Data Analysis

Preliminary inspection of the data indicated that the dependent variables were positively skewed. Therefore, data were modeled using generalized linear mixed models (GLMM) using a nonzero-inflated gamma distribution computed using glmmTMB (Brooks et al., 2017) in R (R Core Team, 2020). Gamma distributions are useful for modeling extreme skewness with continuous positive values and are often used for analyses with similarly patterned substance use data (Neal & Simons, 2007).

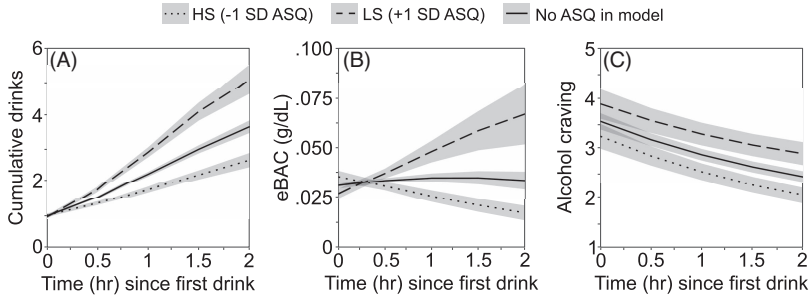
To provide context for the main analyses, we first conducted a series of descriptive analyses characterizing mean trends over time during drinking episodes for cumulative number of drinks consumed, eBAC, and craving intensity (see Figure 1). To investigate whether these trajectories differed as function of alcohol sensitivity, we ran additional models using ASQ score as a moderating variable.

Primary analyses used two-level GLMMs where moments (Level 1) were nested within participants (Level 2). A random intercept for participant and random slopes for cue exposure and drinking episodes were included in the model because doing so significantly improved fit. Follow-up comparisons of model-derived marginal means (i.e., orthogonal contrasts, pairwise comparisons, tests of second-order differences) were computed using emmeans in R (Lenth, 2020). The key predictors for our hypotheses were cue exposure, postdrinking (vs. nondrinking) moments, and their interaction. In separate models, ASQ scores (and all possible

[3] A third response option was to indicate if alcohol cues were visible indirectly (e.g., on television). Due to infrequent endorsement (1.9% of all diary records), moments where this option was selected were excluded from analyses for this report.

Figure 1

Model-Estimated Cumulative Drinks, eBAC, and Alcohol Craving During Drinking Episodes as a Function of Time Since First Drink and Alcohol Sensitivity Levels



Note. eBAC = estimated blood alcohol concentration; ASQ = Alcohol Sensitivity Questionnaire scores; HS = high sensitivity (ASQ score Mean −1 *SD*); LS = Low sensitivity (ASQ score Mean +1 *SD*). Lines inside each plot depict back-transformed, model-estimated means; the gray area around each line shows ±1 *SE*. Models were generalized linear mixed models (GLMMs) using a nonzero-inflated gamma distribution. The GLMMs used a three-level structure where moments (Level 1) were nested within drinking episodes (Level 2) nested within participants (Level 3). Random intercepts were included for participant and episode number along with a random slope for the effect of time, as model fit was significantly better with their inclusion. All models included sex, time, and time^2 as additional parameters; models including ASQ scores also included ASQ × Time interaction terms. To make the eBAC variable appropriate for use with the gamma distribution, .0001 was added to all eBAC values because all values must be nonzero and positive. Although excluded in the main analyses, reports where both eBAC and ΔeBAC from the previous moment = 0 (i.e., where alcohol exposure has returned to zero) were included in these descriptive analyses as they represent valid time points in the 2-hr postdrinking assessment window.

interactions) were added to test moderator hypotheses. All models included covariates associated in prior work with craving (see Table 2). Within-person eBAC was included as a covariate because we anticipated that alcohol exposure would account for substantial variation in craving intensity; analyses including raw eBAC as a covariate are in the Supplemental Materials.

The focal predictor related to drinking was the indicator variable classifying EMA reports according to whether they were made in the postdrinking (coded 1) or nondrinking state (coded 0). With very few exceptions, this postdrinking indicator variable is characterized by the presence of some elevation or priming of eBAC (96.8% of postdrinking moments were associated with nonzero eBAC). This variable likely also serves as a proxy for additional unmeasured psychological processes (e.g., expectancies) and contextual features that differ between drinking and nondrinking occasions. Owing to the time-based follow-up EMA assessments (Piasecki, 2019) used in this study, postdrinking moments do not necessarily reflect concurrent alcohol consumption per se. We use the terms "postdrinking moment," "postdrinking status," and "during drinking episodes" when referring to findings associated with this focal indicator variable. This terminology is slightly awkward but is more accurate than attributing effects to "drinking" or "alcohol consumption."

Results

Descriptive Analyses

The final data set included 155 participants with 9,053 moments [M = 61.3 (SD = 27.5) moments per participant] containing 1,481 drinking reports (2 *morning reports,* 144 *random* prompts, 366 *first-drink reports,* 312 *30-min follow-up reports,* 263 *60-min follow-up reports,* 223 *90-min follow-up reports,* and 171 *120-min follow-up reports*) from 512 drinking episodes. Participants reported alcohol cue exposure in 6.5% (n = 519) of nondrinking moments and 81.8% (n = 1,211) of postdrinking moments.

Characteristics of Drinking Episodes

Participants reported consuming M = 4.0 (SD = 3.1) drinks per episode. Momentary mean eBAC was marginally higher during drinking episodes when alcohol cues were present (M = .055 g/dL) than when they were absent (M = .049 g/dL), $t(1479) = 1.92$, p = .06. For each postdrinking report, successive differences in momentary eBAC values were calculated to estimate the limb of the eBAC curve (e.g., ascending limb = increased eBAC relative to the prior observation); most postdrinking reports (77.3%) occurred on the ascending limb. Additionally, participants were more likely to report visual cue exposure when eBAC was rising (92.3% cue-present) compared to falling (46.4% cue-present), OR = 18.97 (95% CI [12.98–27.70]), $p < .001$ (see Table S1).[4]

During drinking episodes, cumulative drinks (Figure 1a) and eBAC (Figure 1b) had a curvilinear relationship with time

[4] Given this rather large imbalance in cue exposures as a function of eBAC limb, it is possible that postdrink craving reports are driven primarily by effects experienced during ascending eBAC. We tested this possibility by including a Cue exposure × Limb interaction term in a model examining postdrink craving reports (see Supplemental Materials). Limb was a strong predictor of craving, with more intense craving reported on the ascending versus descending limb ($p < .001$). However, the Cue exposure × Limb interaction was not significant (see Table S2), suggesting the relation between cue exposure and craving was similar during ascending and descending eBAC.

Table 2
Fixed and Random Effects From Multilevel Regression Analyses Predicting Momentary Craving for Alcohol

Predictors in the GLMM	Estimate	*SE*	*p*
Intercept	0.157	.038	<.001
Covariates			
Within-person eBAC	0.839	.235	<.001
Biological sex	0.048	.043	.269
Locations			
Home	0.010	.023	.680
Bar/restaurant	0.080	.027	.002
School/work	0.032	.028	.176
Vehicle	0.034	.028	.213
Other	0.009	.024	.709
Time			
8 a.m.–12 p.m.	(Ref)		
12 p.m.–4 p.m.	0.048	.010	<.001
4 p.m.–8 p.m.	0.112	.011	<.001
8 p.m.–12 a.m.	0.161	.011	<.001
12 a.m.–8 a.m.	−0.035	.021	.086
Weekend	0.059	.009	<.001
Cigarette use prior 2 hr	0.110	.044	.013
Cannabis use prior 2 hr	−0.018	.023	.435
Hypothesized predictors			
Cue exposure	0.317	.033	<.001
Drinking status	0.331	.044	<.001
Cue exposure × Drinking status	0.163	.036	<.001
Random effects			
Dispersion estimate	0.120		
Random intercept *SD*	0.258		
Random slope *SD*s	$0.301_{\text{cue | participant}}$		
	$0.365_{\text{Drinking status | participant}}$		
Random intercept–slope correlations	$-0.04_{\text{cue exposure | participant}}$		
	$-0.07_{\text{Drinking status | participant}}$		
Random slope–slope correlations	$-0.20_{\text{cue | drinking moment}}$		
ICC	.436		
Fixed effects R^2/total R^2	0.33/0.61		

Note. eBAC = estimated blood alcohol concentration; GLMM = generalized linear mixed models; ICC = intraclass correlation coefficient. Because a generalized linear mixed model (GLMM) with the gamma distribution uses the log link function, the coefficients are on the log scale. Cue exposure was coded 0 (no visible alcohol cues) or 1 (visible alcohol cues); drinking status was coded 0 (nondrinking moment) or 1 (postdrinking moment). The model is based on 9,503 observations.

($\text{Time}^2_{\text{Drinks}}$: $b = -.176$, $p < .001$; $\text{Time}^2_{\text{eBAC}}$: $b = -.079$, $p = .01$). These trajectories were each moderated by alcohol sensitivity, such that higher ASQ scores (i.e., lower sensitivity) were associated with a steeper but decelerating rise in cumulative drinks ($\text{Time}^2 \times$ ASQ interaction: $b = -.102$, $p < .001$) and a steeper linear increase in eBAC over the course of an episode (Time × ASQ interaction $b = .495$, $p < .001$). Full results from these models are provided in Tables S3–S6. Craving (Figure 1c) decreased linearly over the course of a drinking episode (Time: $b = -.231$, $p < .001$, see Table S7); the rate of decrease was not moderated by ASQ scores ($p = .190$; see Table S8).

Effects of Cue Exposure and Alcohol Exposure on Craving

Results of the covariate-adjusted GLMM predicting craving from alcohol cue exposure, postdrinking versus nondrinking moments, and their interaction are given in Table 2; model-estimated mean levels of craving as a function of these variables are shown in Figure 2. Consideration of the effects of the covariates shows that craving increased as within-person eBAC increased, in bar/restaurant locations, on weekends (vs. weekdays), during afternoon/evening hours (vs. the morning), and following recent cigarette use.

Of greater interest, cue exposure, drinking status (nondrinking vs. postdrinking moments), and their interaction also were significantly associated with craving. Specifically, although cue exposure was associated with increased craving during both nondrinking ($\Delta M = 0.45$) and postdrinking moments ($\Delta M = 1.23$), the magnitude of this effect was larger during postdrinking moments $t(9, 478) = 4.52$, $p < .0001$ (Figure 2). Individual contrasts among these conditions are provided in Supplemental Materials.

Tests for Moderation by Alcohol Sensitivity

Results of the GLMM including ASQ scores (and interactions) are given in Table 3, and model-adjusted slopes depicting the association between ASQ scores and craving are given in Table 4 and depicted in Figure 3. Specific tests of our moderator hypotheses were carried out using planned comparisons of model-adjusted slopes of ASQ scores on craving under relevant conditions (see Table 4). The first prediction under Hypothesis 4—that the presence of cues would have a larger effect on craving as a function of increasing ASQ scores (i.e., lower sensitivity) during nondrinking moments—was tested by subtracting the slope predicting craving by ASQ scores when cues were visible from the corresponding slope when cues were not visible. The resulting slope difference was significant, but the direction was not as expected. As shown in Figure 3, during nondrinking moments the difference between ASQ score slopes (cues visible vs. not visible) was larger as a function of *decreasing* ASQ scores (i.e., higher sensitivity). In other words, during nondrinking moments the presence of cues had a stronger effect on craving among HS than LS participants.

The second prediction under Hypothesis 4 was tested with a parallel comparison of slopes during postdrinking moments. This contrast was not significant (see Table 4). As depicted in Figure 3, during postdrinking moments craving increased as a function of increasing ASQ scores to roughly the same degree whether cues were visible or not.

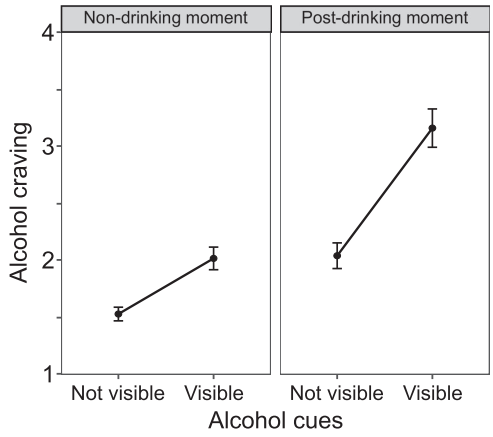
To further explore the data as relevant to Hypothesis 4, we also tested whether craving in the presence of cues was differentially associated with ASQ scores during nondrinking versus postdrinking moments, that is, comparing the slopes of the solid lines (alcohol cues visible) in Figure 3. This contrast was significant (see Table 4), providing partial support for Hypothesis 4.

Additional Models

Additional analyses tested the extent to which the patterns reported here are robust to exclusion of first-drink reports, when craving was highest overall (Figure 2) and when cue exposure was assumed rather than measured. Supplemental analyses (see Tables S13 and S14; Figure S1) indicated that retrospectively rated, predrink urges were marginally lower before compared to after a first drink, suggesting that craving levels in first-drink reports represent slight increases from predrinking states rather than (or in addition to) simple carry-over or expectancy effects. Tests of focal hypotheses

Figure 2

Model-Estimated Craving Levels During nondrinking and postdrinking Moments as a Function of Alcohol Cue Visibility



Note. $M \pm 1$ *SE* values (capped vertical bars) are back-transformed from the log scale and averaged over levels of within-person estimated blood alcohol concentration (eBAC), biological sex, location, time of day, weekend (vs. weekday), cannabis use in the past 2 hr, and cigarette use in the past 2 hr.

reported in Tables 2–4 were effectively unchanged when first-drink reports were excluded from analyses (see Tables S15–S17).

Trajectories shown in Figure 1c, which describe craving as a function of postdrinking time (and ASQ scores), give the impression that craving was highest during first-drink reports and decreased thereafter. However, craving in that model is strongly influenced by the variable duration of drinking episodes. To better understand how craving changes over the course of drinking episodes, and to characterize pharmacological effects of alcohol on craving levels, we ran additional models in which postdrinking craving was estimated from eBAC (and its quadratic term, $eBAC^2$) and ASQ scores during both ascending and descending eBAC moments (see Figure 4; Tables S9–S12). For moments on the ascending limb of the eBAC curve (Figure 4a), craving was higher as a function of increasing ASQ scores, $b = 0.12$, $p = .042$. However, craving did not differ as a function of eBAC level (or $eBAC^2$) or the interaction between eBAC and ASQ scores ($ps > .344$, see Tables S9 and S10). For moments on the descending limb (Figure 4b), there were no significant main effects of eBAC or $eBAC^2$ on craving ($ps > .126$, see Table S11), but the relationship between eBAC and craving was moderated by ASQ scores ($b = 3.45$, $p = .003$, see Table S12). During descending eBAC moments, individuals with higher ASQ scores (i.e., lower sensitivity) experienced greater levels of craving at higher eBACs, whereas individuals with lower ASQ scores (i.e., higher sensitivity) experienced overall lower levels of craving that decreased as a result of higher eBACs.

Discussion

The present study aimed to (a) examine synergistic effects of cue exposure and alcohol exposure (i.e., postdrinking status) on craving in the natural environment and (b) test the extent to which these effects are moderated by individual differences in sensitivity to alcohol's effects (Fleming et al., 2021; Trela et al., 2018). Consistent with findings from prior laboratory (e.g., de Wit & Chutuape, 1993; Kirk & de Wit, 2000; Litt & Cooney, 1999; Manchery et al., 2017; Monti et al., 1993; Ramirez et al., 2015a, 2015b) and field-based studies (Fatseas et al., 2015; Kuerbis et al., 2020; Miranda et al., 2014; Ramirez & Miranda, 2014; Schoenmakers & Wiers, 2010; Trela et al., 2018; Treloar Padovano & Miranda, 2021), craving in the natural environment was increased after cue exposure and during drinking episodes.

In contrast to prior laboratory studies (Bragulat et al., 2008; Courtney et al., 2015; Kareken et al., 2010; Schulze & Jones, 1999), the effects of cue exposure and drinking status interacted such that craving was particularly elevated when cues were visible during postdrinking moments (Figure 3). This pattern emerged despite accounting for the effects of contextual (e.g., time of day;

Table 3

Fixed and Random Effects From Multilevel Regression Analyses Predicting Momentary Craving for Alcohol Including ASQ Scores

Predictors in the GLMM	Estimate	*SE*	*p*
Intercept	0.160	.038	<.001
Covariates			
Within-person eBAC	0.855	.234	<.001
Biological sex	0.048	.043	.257
Locations			
Home	0.009	.023	.699
Bar/restaurant	0.078	.027	.003
School/work	0.032	.023	.172
Vehicle	0.034	.028	.214
Other	0.009	.024	.719
Time			
8 a.m.–12 p.m.	(Ref)		
12 p.m.–4 p.m.	0.048	.010	<.001
4 p.m.–8 p.m.	0.112	.011	<.001
8 p.m.–12 a.m.	0.162	.011	<.001
12 a.m.–8 a.m.	−0.035	.021	.094
Weekend	0.058	.009	<.001
Cigarette use prior 2 hr	0.112	.044	.011
Cannabis use prior 2 hr	−0.019	.023	.412
Hypothesized predictors			
Cue exposure	0.317	.033	<.001
Drinking status	0.326	.043	<.001
ASQ	0.067	.030	.024
Cue exposure × ASQ	−0.100	.047	.034
Drinking status × ASQ	0.072	.057	.208
Cue exposure × Drinking status	0.167	.036	<.001
Cue exposure × Drinking status × ASQ	0.093	.052	.076
Random effects			
Dispersion estimate	0.120		
Random intercept *SD*	0.253		
Random slope *SD*s	0.296 $_{\text{cue \| participant}}$		
	0.347 $_{\text{drinking status \| participant}}$		
Random intercept–slope correlations	−0.03 $_{\text{cue \| participant}}$		
	−0.11 $_{\text{drinking status \| participant}}$		
Random slope–slope correlations	−0.21 $_{\text{cue \| drinking status}}$		
ICC	0.427		
Fixed effects R^2/total R^2	0.33/0.61		

Note. eBAC = estimated blood alcohol concentration; ASQ = Alcohol Sensitivity Questionnaire (*z*-scores); GLMM = generalized linear mixed models; ICC = intraclass correlation coefficient. Because a generalized linear mixed model (GLMM) with the gamma distribution uses the log link function, the coefficients are on the log scale. Cue exposure was coded 0 (no visible alcohol cues) or 1 (visible alcohol cues); drinking status was coded 0 (nondrinking moment) or 1 (postdrinking moment). The model is based on 9,503 observations.

Table 4

Estimated Marginal Slopes of ASQ Scores on Craving as a Function of Report Types

Report types	ASQ score slope	*SE*	*t*-test ratio	*p* value
Nondrinking moments				
Alcohol cues not visible (1)	.067	.030	2.254	.024
Alcohol cues visible (2)	−.033	.054	−0.609	.542
Postdrinking moments				
Alcohol cues not visible (3)	.138	.061	2.245	.025
Alcohol cues visible (4)	.131	.054	2.446	.014
ASQ score slope comparisons				
2–1	−.10	.047	−2.123	.034
4–3	−.01	.055	−0.118	.906
4–2	.164	.053	3.107	.010*

Note. ASQ = Alcohol Sensitivity Questionnaire. Model-estimated slopes are adjusted for within-person estimated blood alcohol concentration (eBAC), biological sex, location, time of day, weekend (vs. weekday), cannabis use in the past 2 hr, and cigarette use in the past 2 hr. *df* for all comparisons = 9,474. ASQ score slope comparisons refer to differences in the slopes of ASQ scores on craving in the conditions enumerated in parentheses.

*Given the exploratory nature of the final contrast, the *p* value for this comparison was adjusted (Tukey's method) for multiple comparisons to control family-wise error rate.

day of the week; physical location) and pharmacologic factors (eBAC; Supplemental Materials) that also had robust effects on craving and that often distinguish natural and laboratory environments. Still, several other differences between natural and lab environments, including cue exposures occurring in typical drinking contexts (Nees et al., 2012; Simon et al., 2020; Trela et al., 2018) and the potential for cues to signal alcohol availability (Papachristou et al., 2012; Wertz & Sayette, 2001), might account for the apparently more potent combination of effects seen here. This finding suggests the potentiation of the cue-signaled incentive value as one mechanism by which drinking episodes can be self-perpetuating (also see Treloar et al., 2015). Future studies could more directly examine this possibility by testing whether the association between consumption-induced increases in craving and the likelihood of continued consumption during a drinking episode is strengthened by the presence of alcohol cues.

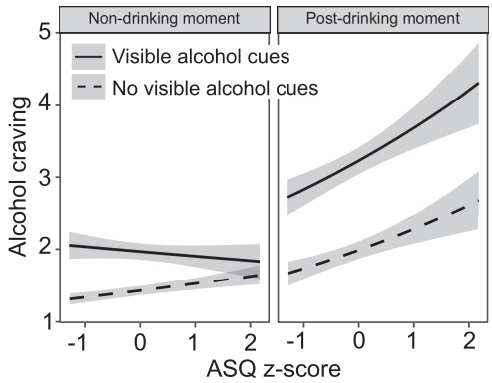
We predicted that cue-associated craving would be stronger as a function of lower alcohol sensitivity during both nondrinking and postdrinking moments (Hypothesis 4). Neither of these predictions was supported. During nondrinking moments, the presence (vs. absence) of alcohol cues increased craving more as a function of higher alcohol sensitivity (Figure 3). In part, this effect was driven by significantly stronger tonic craving among lower-sensitivity participants, which did not increase when cues were present. This finding is inconsistent with previous work showing that cue-elicited craving tends to be stronger among higher-risk drinkers (e.g., Kuerbis et al., 2020; Ramirez & Miranda, 2014) and with our prior finding that drinking-related contexts potentiated craving among LS young adults in daily life (Trela et al., 2018).

During postdrinking moments, craving was much stronger among LS than HS participants overall, and although there was no indication that ASQ scores moderated the effect of cue exposure (vs. cue absence) on craving in the postdrinking state (Hypothesis 4), ASQ scores did moderate the effect of postdrinking (vs. nondrinking) state on craving in the presence of alcohol cues. That is, comparison of craving levels across nondrinking and postdrinking moments when cues were visible (i.e., the solid lines in Figure 3) provided partial support for the idea that the combination of alcohol exposure and cue exposure differentially impacts craving for lower-sensitivity drinkers. Craving experienced during drinking episodes is a potentially pivotal factor determining continuation a drinking episode (Green et al., 2019). Although craving tended to decrease over time during postdrinking episodes regardless of alcohol sensitivity levels (Figure 1c), there was a strong—and probably bidirectional—association between craving and eBAC during drinking episodes (e.g., Table 2), indicating that individuals who experienced stronger craving consumed more alcohol. Given that LS drinkers consumed more alcohol during drinking episodes than their HS peers (Figure 1a), and that LS individuals' craving remained relatively elevated during descending eBAC (Figure 4b), these findings suggest that craving might play a larger role in prolonging drinking episodes among LS compared to HS drinkers.

Findings from preclinical studies (e.g., Beckstead & Phillips, 2009; Murphy et al., 2002; Risinger et al., 1994) and laboratory-based work in humans (Bartholow, et al., 2007, 2010; Cofresí et al., 2021; Fleming & Bartholow, 2014; Fleming et al., 2021; Martins et al., 2019; Shin et al., 2010) suggest that low alcohol sensitivity is a biobehavioral trait associated with susceptibility to sensitization of appetitive-motivational responses to alcohol-related cues (see Cofresí et al., 2019). Although discussions of the ISTA often focus on the incentive salience of exteroceptive cues (e.g., self-administration devices), the ISTA explains drug "priming" effects on drug seeking and consumption via the incentive salience of

Figure 3

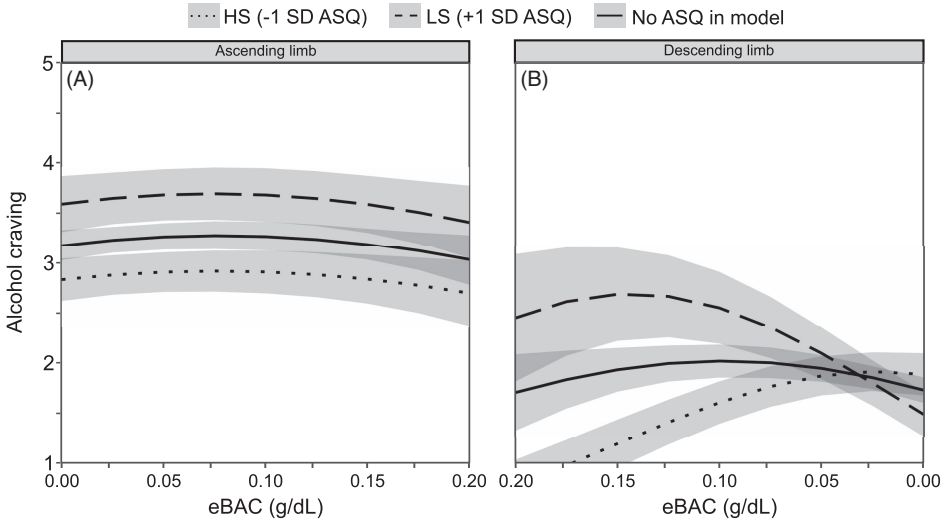
Model-Estimated Craving Levels as a Function of Alcohol Cue Visibility, Nondrinking Versus Postdrinking Status, and Alcohol Sensitivity Levels



Note. ASQ = Alcohol Sensitivity Questionnaire. More positive ASQ *z*-scores represent lower self-reported alcohol sensitivity. Lines inside each plot show the back-transformed generalized linear mixed models (GLMM)-predicted value of craving at different ASQ scores. The gray area around each line shows ±1 *SE*. Values are estimated controlling for levels of within-person estimated blood alcohol concentration (eBAC), biological sex, location, time of day, weekend (vs. weekday), cannabis use in the past 2 hr, and cigarette use in the past 2 hr.

Figure 4

Model-Estimated Craving Levels during Postdrinking Moments as a Function of Limb of the eBAC Curve and Alcohol Sensitivity Levels



Note. eBAC = estimated blood alcohol concentration; ASQ = Alcohol Sensitivity Questionnaire scores; HS = high sensitivity (ASQ score Mean −1 *SD*); LS = low sensitivity (ASQ score Mean +1 *SD*). Lines inside each plot show back-transformed model-estimated means. Gray area around each line shows ±1 *SE*. Models were generalized linear mixed models (GLMMs) using a nonzero-inflated gamma distribution. The GLMMs used a three-level structure where moments (Level 1) were nested within drinking episodes (Level 2) nested within participants (Level 3). Random intercepts were included for participant and episode number, as model fit was significantly better with their inclusion. All models included sex, eBAC, and $eBAC^2$ as additional parameters; models including ASQ scores also included an ASQ × eBAC interaction term. HS individuals' apparent increase in craving as eBAC decreases on the descending limb (Panel B) is largely an artifact of too few observations at high levels of descending eBAC in this group; of 139 reports made by individuals with ASQ scores −1 *SD* from the mean, only 4 (<3%) occurred while descending eBAC = 0.15–0.20 g/dL.

interoceptive cues (e.g., sensations resulting from the act of self-administration; see Flagel et al., 2009; Robinson et al., 2014; Saunders & Robinson, 2013). Interoceptive cues produced by alcohol self-administration are strongly associated with alcohol reward (Besheer et al., 2012; McDonald & Siegel, 2004; Saunders & Robinson, 2011; Tomie et al., 2002). Through incentive sensitization, the impact of these naturally conditioned internal cues could become amplified, transforming them into signals for wanting and further consumption among lower-sensitivity drinkers.

Another plausible interpretation of the presentfindings is that lower-sensitivity drinkers experience less intense feelings of intoxication at a given level of eBAC (Fleming et al., 2016; Trela et al., 2016). Perceived intoxication may serve as a satiety signal for stopping alcohol intake. A diminished capacity for sensing this internal feedback could contribute to persistence of drinking—and craving—once consumption has been initiated (cf. Krystal et al., 2003).

The present study suffered from several limitations that should be addressed in future research. Most critically, the EMA method limits the ability to draw causal inferences. Our participants self-selected "levels" of cue exposure and alcohol consumption, and between- and within-person variation in craving intensity likely determines when alcohol is consumed. Not surprisingly, visible alcohol cues were reported much more frequently during postdrinking than nondrinking moments. Furthermore, individuals with lower initial craving may be more likely to stop drinking and move away from cue-rich contexts, potentially contributing to a bias toward lower craving in postdrinking reports when cues were not visible. In addition, craving might be both a cause and a consequence of cue exposure in the natural environment. We view the present findings as complementing experimental studies, perhaps better describing what happens in "real-world" conditions but requiring more caveats concerning causal inference. In future EMA work, researchers could deliver experimentally manipulated pictorial cue exposures (e.g., Wray et al., 2011) to probe the degree to which self-selected and researcher-controlled cue exposures might influence craving patterns.

Related to this issue, the overall frequency of cue exposures cannot be controlled in EMA studies. Exploratory analyses (see Table S18) showed a marginal association ($p = .052$) between ASQ scores and the likelihood of endorsing cue exposure in diary reports. Lower-sensitivity drinkers show attention biases for alcohol-related cues in the laboratory (see Bailey & Bartholow, 2016; Shin et al., 2010), suggesting they might be more likely to notice such cues in the natural environment. Alternatively, they might more frequently self-select environments containing alcohol cues. This also complicates interpretation of the present findings.

Craving assessed under naturalistic conditions invariably reflects a combination of pharmacologic influences and alcohol expectancy effects. Indeed, our descriptive time course analyses (Tables S13 and S14; Figure S1) indicated that craving prior to the first drink was similar to craving reported just after the first drink, suggesting

the possibility that carry-over effects of anticipated consumption may contribute to the effects seen in postdrinking moments. Experimental designs in which beverage contents and instructions are independently manipulated are needed to complement EMA investigations that feature good ecological validity but cannot disaggregate causal components.

We inferred that cue exposure, particularly during postdrinking moments, was an indicator of immediate alcohol availability. However, diary surveys did not assess alcohol availability per se, and therefore the veracity of this inference cannot be verified. Future studies could incorporate direct assessment of drinking opportunity along with cue exposure.

To limit response burden, postdrinking follow-up reports ended 2 hr after a first-drink report. Even so, some participants might have failed to log some drinks to avoid triggering follow-up surveys. This likely resulted in our failing to capture the complete number and full extent of participants' drinking episodes, thereby limiting our ability to fully describe associations among consumption, cue exposure, and craving. Indeed, comparison of the number of drinks per drinking episode reported in EMA reports and past-month TLFB (Table 1) shows that fewer drinks were reported during the EMA period. Future studies could randomize the number of drinking follow-up surveys across drinking episodes within persons to reduce the additional burden triggered by logging first-drink reports.

In addition, assessment of cue exposure was limited here, in that participants could only indicate whether they had seen alcohol cues during the past 15 min; they could not indicate the complexity (e.g., visual vs. visual and olfactory), duration (a fleeting glance vs. prolonged exposure), or intensity of these exposures. Differing levels of these experiences likely impact subjective experiences of craving (Perkins et al., 2003). Moreover, since most drinking moments involve alcohol consumption and take place in environments containing numerous alcohol cues (e.g., peers drinking), there is an inherent imbalance in cue exposure across postdrinking and nondrinking moments in the natural environment. This imbalance underscores the need to complement EMA studies with laboratory experiments, particularly those conducted in naturalistic settings (e.g., bar labs) where cue density, alcohol pharmacology, and alcohol expectancies can be controlled or manipulated.

Alcohol sensitivity was indexed by a single administration of the ASQ, which likely reflects combined effects of heritable/constitutional differences in level of alcohol response and acquired tolerance (see Corbin et al., 2013; Morean & Corbin, 2008). Disentangling these components and separately testing their relations to alcohol cue reactivity is an important topic for future research. The data reported here are drawn from an early phase of a prospective study that aims to relate drinking patterns to changes in self-reported alcohol sensitivity and determine whether changes in cue reactivity and alcohol-related approach motivation change in tandem with acquired tolerance.

Finally, the lack of ethnic and racial diversity in our sample limits the generalizability of the findings to other groups. Replication of these findings in more diverse samples will be important for developing inclusive and effective prevention strategies. Additionally, given the moderate drinking in the present sample, these findings may not generalize to a clinically more severe drinking population.

In summary, the present study provided the first examination of alcohol craving in the natural environment as a function of alcohol cue exposure, postdrinking status, and their combination. Results suggest that the presence of cues has a stronger effect on craving during drinking episodes than during nondrinking moments. Some predicted effects were moderated by individual differences in alcohol sensitivity, but generally not as we expected. Yet, the study identified conditions under which lower-sensitivity drinkers reported elevated craving relative to their HS peers—mainly once drinking was underway. These findings contribute to understanding potential differences in the role of cue-induced craving in the natural environment across AUD risk phenotypes, an important step toward developing targeted, evidence-based AUD prevention strategies.

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