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EFFECT OF POSITIVE AND NEGATIVE AFFECTIVE STIMULI AND BEVERAGE CUES ON MEASURES OF CRAVING IN NON TREATMENT-SEEKING ALCOHOLICS

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Abstract

Rationale—Laboratory paradigms are useful for investigating mechanisms of human alcohol cue reactivity in a highly controlled environment. A number of studies have examined the effects of beverage exposure or negative affective stimuli on cue reactivity independently, but only a few have reported on interaction effects between beverage cue and affective stimuli, and none have evaluated the effects of positive stimuli on beverage cue reactivity.

Objectives—To assess independent and interactive effects of both positive and negative affective stimuli and beverage cue on psychophysiological and subjective measures of reactivity in alcohol dependence.

Methods—A total of 47 non treatment-seeking paid volunteers with current alcohol dependence participated in a within-subjects trial where each was exposed to a standardized set of pleasant, neutral, or unpleasant visual stimuli followed by alcohol or water cues. Psychophysiological cue reactivity measures were obtained during beverage presentation, and subjective reactivity measures were taken directly following beverage presentation.

Results—Mixed-effect models revealed a significant main effect of beverage and positive (but not negative) affective stimuli on subjective strength of craving, and significant main effects of both positive and negative affective stimuli on ratings of emotionality. Despite the power to detect relatively small interaction effects, no significant interactions were observed between affect and beverage conditions on any reactivity measure. A key finding of this study is that positive affective stimuli commonly associated with drinking situations can induce craving in the absence of alcohol cues.

Conclusions—Main effects of beverage cue replicated results from previous studies. In addition, positive affective stimuli influenced craving strength. Beverage and affective cues showed no interaction effects.

Keywords

Alcohol dependence; affective stimuli; cue reactivity; craving

Alcohol cue reactivity models attempt to recreate in the laboratory risk conditions for relapse similar to those experienced by alcoholics in their natural environment (Niaura et al. 1988; Litt and Cooney 1999). These paradigms link exteroceptive (e.g. the sight and smell of alcohol) and/or interoceptive (e.g. mood) cues with a hypothesized internal motivational state to drink alcohol (Carter and Tiffany 1999; Litt and Cooney 1999), a state typically referred to as craving. Craving is often a target of pharmacological and cognitive-behavioral therapeutic interventions for alcoholics based on evidence suggesting that it may increase the likelihood of relapse among alcoholics following treatment (Monti et al. 1993a; Monti et al. 1993b; Rohsenow et al. 1994; Monti et al. 1995). Laboratory models are particularly well-suited to studying mechanisms of craving, alone or in combination, given the immediacy of effects obtained under relatively well-controlled conditions (Litt and Cooney 1999).

Alcohol exposure followed by various measures of craving has been a standard component of laboratory cue reactivity studies (Monti et al. 1987; Cooney et al. 1997; Sayette 1999). Such exposure typically involves showing subjects their favorite beverage in their usual serving container, allowing them to smell it, and in some cases, to taste it or to consume a “priming” drink.

Cue reactivity theories have also predicted an important role for emotional state as a risk factor for relapse, based on evidence from both naturalistic (Marlatt and Gordon 1985; Vuchinich and Tucker 1996) and laboratory studies (Litt et al. 1990; Cooney et al. 1997; and see the review by Baker et al. 1987). For instance, laboratory studies by Litt, Cooney and colleagues have employed individualized imagery scripts, sometimes combined with hypnotic techniques, as a way to examine the impact of mood states on craving (e.g. Cooney et al. 1997). These manipulations have been largely confined to negative mood states (Litt et al. 1990; Cooney et al. 1991; Rohsenow et al. 1991; Rubonis et al. 1994; Cooney et al. 1997) based on reports of negative mood precipitants of relapse among alcoholics in treatment (Marlatt and Gordon 1985; Vuchinich and Tucker 1996).

Although a number of laboratory studies have examined the effect of alcohol exposure or mood induction on cue reactivity in humans, only a few have examined these conditions both alone and together, allowing assessment of independent and moderating (interactive, or synergistic) effects. Animal studies show that stress greatly increases previously-extinguished alcohol-seeking behavior in response to an alcohol cue, and that, more generally, stress potentiates the effects of other environmental cues previously linked to alcohol seeking and self-administration (Breese et al. 2005). Studies of related interactions in human populations are rare, and the results inconsistent. Rubonis et al. (1994) found no effects in the total sample but found subjective urge to drink was increased by prior exposure to scripts evoking negative mood in secondary analyses of a small subgroup of women who initially showed heightened reactivity. Litt et al. (1990) reported no interactions between beverage cue exposure and negative mood induction across three measures: rating of desire for alcohol, rating of difficulty to resist alcohol, and blood pressure, in a sample of 8 participants. In a much larger study, Cooney et al. (1997) also found no interactions between beverage cues and negative affective stimuli on subjective measures of desire to drink.

Both theory and prior empirical research have concentrated more on the impact of negative than positive affective stimuli on craving (e.g. Vuchinich and Tucker 1996; Cooney et al. 1997; Koob 2000). For instance, Koob (2000) proposes that a suitable definition of craving in

an animal model may be a motivation to ingest ethanol "... superimposed upon a negative affective state or the memory of the pleasant rewarding effects of ethanol superimposed upon a negative affective state." For human alcoholics, conditioning theory (Ludwig and Wikler 1974; Poulos et al. 1981) conceptualizes the motivation to drink as a conditioned response to the positive, pleasurable effects of alcohol, or as an antidote to their absence. Hence, in alcoholics, it is expected that the abstinent state will be characterized by negative affect because of the absence of the previously pleasure-inducing alcohol, with a corresponding change in neurotransmitter activity. On the other hand, studies in which participants report their most relapse-prone moods usually find some for whom this mood state is positive, e.g., during exciting sports events (Marlatt and Gordon 1985). Baker et al. (1987) concluded from a careful literature review of early cue reactivity studies that the relevance of positive affect could not be denied, and that negative and positive affect are involved in two "mutually inhibitory" or incompatible urge-related neural networks. Arguing from a cognitive social-learning perspective, Niaura (2000) also provided a theoretical basis for the role of positive affect in a feedback loop in which expectation of reward and intent to use may spiral upwards, leading to relapse. Thus our study was designed to investigate moderating effects of a priming exposure to both positive and negative affective stimuli on beverage cue-induced craving.

METHODS AND MATERIALS

Subjects

This study was conducted at the University of Miami School of Medicine, Miami, FL, and approved by the hospital's Institutional Review Board as conforming to the ethical standards of the 1964 Declaration of Helsinki. Subjects provided written informed consent prior to participation. Subjects were non treatment-seeking paid volunteers recruited primarily through advertisements, meeting DSM-IV criteria for current alcohol dependence, and abstinent from alcohol on the day of the study, as verified by Breath Alcohol Concentration (BAC), and not in acute withdrawal as verified by a Clinical Institute Withdrawal Assessments for Alcohol (CIWA-Ar; Sullivan et al. 1989) score of <8. Exclusionary criteria consisted of clinically significant medical or psychiatric disorders including depression, anxiety, or dependence on substances other than alcohol and nicotine.

Study Overview and Experimental Design

The 4-hour study included a baseline evaluation, followed by the cue reactivity procedures, and subsequent debriefing. A 3 (affective stimuli: positive, neutral, negative) $\times$ 2 (beverage cue: alcohol, water) within-subjects, block-factorial design (6 repeated measures; Kirk 1995) was employed for the cue reactivity manipulation. Thus, the 6 affect-beverage trial types were: positive-alcohol, neutral-alcohol, negative-alcohol, positive-water, neutral-water, negative-water. All six mood-beverage cue combinations were presented to each subject (with order varying systematically across subjects) during the course of a single afternoon. Since order effects of cue presentation have been observed in previous studies (Monti et al. 1987; Cooney et al. 1997), subjects were systematically assigned one of six cue order combinations, in the order they were enrolled in the study¹.

¹The six possible permutations of Positive (P), Neutral (U), and Negative (N) affective images were randomly but independently assigned to the first three and the last three exposures of a subject's total sequence. Then alcohol (A) or water (W) cues were assigned in random order to each distinct affective ordering. These procedures generated the final set of six orders, to which consecutive subjects were systematically (rotationally) assigned: (P/W,N/A,U/W—P/A,U/A,N/W), (N/A,U/A,P/W—N/W,P/A,U/W), (U/A,P/W,N/W—P/A,N/A,U/W), (P/A,U/W,N/A—U/A,P/W,N/W), (N/W,P/A,U/A—N/A,U/W,P/W), and (U/W,N/W,P/A—U/A,N/A-P/W). This approach thus takes account of the orderings of affective cues and the orderings of beverage cues, but not all possible sequences of these orderings. Note that even if we had included all $6 \times 6 = 36$ possible sequences, with 47 subjects we could not have had more than two observations per sequence and balance would have been impossible (requiring multiples of 30 subjects).

MEASURES

Baseline Assessments

Standardized measures were collected prior to cue exposure to characterize the sample, ensure admission criteria were met, and provide pre-manipulation baseline ratings of craving and affect. Alcohol dependence criteria were ascertained with the Structured Clinical Interview for DSM-IV (SCID), which was also used to exclude individuals with depressive, anxiety, or other drug use disorders. A protocol-specific standardized questionnaire was used to obtain significant drinking and substance use history, including age of first use and total years of heavy drinking (5 drinks/day for males, 4/day for females). The Timeline FollowBack Interview (TLFB; Sobell and Sobell 1992) was used to determine recency, quantity and frequency of drinking in the 90 days prior to testing. The Alcohol Dependence Scale assessed dependence severity (ADS; Skinner and Horn 1984; score range 0–47) and the Beck Depression Inventory (BDI) assessed severity of sub-syndromal depressive symptomology (Beck et al. 1961; range 0–63). The BAC was measured by breathalyzer to confirm abstinence prior to cue exposure.

To verify a safe return to a baseline state following the cue exposure trials, the Alcohol Craving Questionnaire (ACQ; Singleton et al. 1994; score range 12–84) was administered both at baseline and following the cue reactivity procedure to ensure that the trials had not resulted in increased subjective urge to drink. Similarly, the Positive and Negative Affect Scale (PANAS; Watson et al. 1988; score range 10–50) was administered at baseline and again after the experimental session, to ensure that subjects had been adequately debriefed and returned to their normal emotional state.

Cue Reactivity: Subjective Measures

Alcohol craving in response to each affect-beverage condition was assessed using four individual Visual Analog Scale items (VAS; endpoints were marked with a 0 on the left indicating no craving, and a 20 on the right indicating severe craving) adapted from ACQ (Singleton et al. 1994)². The items represented expectancy for positive reinforcement (“Having a drink would make things just perfect”), strength of craving (“How strong is your craving to drink alcohol”), intent (“If I could drink alcohol now, I would drink it”), and lack of control (“It would be hard to turn down a drink right now”). In addition to examining cue reactivity effects on each separate item, a composite craving index was formed as the average of the four items (Cronbach’s $\alpha = 0.70$).

Emotional reactivity was assessed using a computerized version of the Self-Assessment Manikin (SAM; Bradley and Lang 1994). SAM is a cartoon figure used to assess three dimensions of affect; valence (how happy or unhappy one is), arousal (excitement, possibly anxiety), and dominance (subjective sense of control). Subjects were instructed to indicate “how you are feeling right now.” Anchors for the valence dimension included “happy, satisfied, contented” versus “unhappy, sad, bored.” Arousal anchors included “stimulated, excited, jittery” versus “relaxed, calm, sluggish.” Dominance anchors included “powerful, strong, controlling” versus “powerless, submissive, controlled.” Potential responses were marked with 0 (least strong) on the left end to 20 (strongest) on the right end. Two additional VAS ratings were used to provide manipulation checks on the experimental conditions. These questions represent beverage preference (“How much did you like the beverage just given to you”) and

²In an effort to minimize response burden and attendant fatigue, a subset of the full ACQ was substituted for the entire instrument. The four items selected were the highest-loading on four factors in an analysis presented by Singleton et al. (1994). These items were not specifically validated as a subscale in that study, however.

picture emotiveness (“Watching the pictures made me feel a strong emotion”). These questions also were anchored with extreme values of 0 and 20 (20 indicating strongest emotion).

Cue Reactivity: Psychophysiological Measures

Heart rate (HR), skin conductance (SC), and facial electromyogram (EMG) were monitored throughout each experimental trial as confirmatory measures of the primary subjective measures of craving and emotion. The focus of the present analyses is on the 90-second *in vivo* beverage cue exposure periods. HR was recorded using two large (8 mm) Ag-AgCl electrodes filled with Teca Electrolyte, with one on each forearm. The EKG signal was amplified with a Coulbourn S75-01 bioamplifier, and a Schmitt trigger interrupted the computer to measure each R–R interval to the nearest 1 ms. The data were edited off-line to correct for missed or extra triggers. SC was measured from a pair of large Ag-AgCl electrodes placed on the left hypothenar eminence and filled with K-Y jelly. The signal was sampled at 50 Hz and recorded using a Coulbourn S71-22 skin conductance coupler, calibrated to record a range of 0–40 μ S. Facial EMG was recorded from a pair of miniature (4 mm) Ag-AgCl electrodes filled with Teca Electrolyte. Following guidelines provided by Fridlund and Cacioppo (1986), electrodes were placed on the corrugator and zygomatic muscle regions on the left side of the face to record negative affect (frowning) and positive affect (smiling) respectively. The EMG signals were amplified using Coulbourn S75-01 bioamplifiers with bandpass settings of 90 to 1000 Hz, then filtered with Coulbourn S76-01 contour following integrators using a 500 ms time constant.

Affective Stimuli

Positive, neutral, and negative pictures were selected from the International Affective Picture System (IAPS; CSEA 1994). Two sets of equivalent images were selected for each affective category (positive, negative, neutral), in order to reduce habituation across the 2 beverage conditions. Thus, 24 pictures from each affective category were used. To verify that the affective slides were associated with the expected affective category in the present sample, a manipulation check was conducted with 21 alcohol-dependent subjects following their participation in the current study. These subjects were given 8 $\times$ 10 color copies of the 72 slides used in the study in random order, and were instructed to sort these images into 3 piles representing negative, positive, or neutral stimuli. The majority of subjects categorized all pictures accurately, with correct classification rates for negative slides ranging from 90 to 100% (mean = 98%) and positive slides ranging from 67 to 98% (mean = 87%).

Procedures

Laboratory sessions occurred at approximately 2:00 p.m. to control for effects of circadian rhythm and satiety. Subjects were required to have been abstinent the day of their session, as verified by BAC. After completing all baseline assessments, subjects were escorted to a comfortable chair located in a windowless, sound-attenuated testing room, adjacent to the control room and separated by a large one-way mirror. Electrodes for psychophysiological recordings were placed according to established guidelines, and baseline impedance for facial EMG measures were recorded to confirm adequate skin contact.

Subjects were familiarized with laboratory procedures during a practice neutral-water cue reactivity trial, followed by the six experimental trials. Each trial consisted of a set of affective pictures, followed immediately by exposure to alcohol or water beverage cues which they were instructed to not drink. The affective picture viewing procedure consisted of pictures presented on a large screen directly in front of the participant, and included pleasant (e.g. adventure sports, intimate kissing), negative (e.g. traumatic physical injuries, dangerous weapons) or neutral (e.g. household objects, mushrooms) images. For each trial, participants were exposed to a set of 12 pictures within the relevant affective condition, with each picture presented for 10-

seconds, and a 4-second interval between pictures. Subjects were instructed to look at each picture for the entire presentation time and remember the mood evoked by the pictures. Immediately following the picture sequence, the computer display went blank, and subjects were then presented with either their preferred alcoholic beverage (e.g., vodka, lager beer) or bottled water on a tray table adjusted to a height that placed the beverage under the subject's nose. The alcohol or water beverage was presented in the subject's preferred mode of consumption (e.g., small tumbler for vodka, Pilsner glass for beer) and the alcoholic bottle/can of alcohol or water bottle was placed at the left corner of the tray table for visual reference. Specific alcohol brand preferences were accommodated whenever possible, including choices of mixers (e.g. vodka would be poured into a glass along with orange juice if the favorite drink were a screwdriver). Subjects were instructed to "focus on the sensation you have while smelling the alcohol or water beverage and continue to feel the mood stirred up in your imagination by the pictures you have just viewed." The beverage cue exposure period lasted for 90-seconds³. Following the beverage exposure period, the beverage was removed. Subjects then completed all subjective ratings by making selections from the computer screen with a computer mouse. Presentation and timing of all affective images and timing of beverage cue exposure, as well as time-locked collection of all psychophysiological measures and ratings, was controlled by a computer running VPM software (Cook et al. 1987).

Upon completing all 6 cue reactivity trials, a debriefing period commenced, all electrodes were removed and relevant baseline assessments were repeated to ensure that affect and urge to drink had returned to baseline levels. Subjects received monetary compensation of \$100.00 before leaving. Table 1 presents the schedule of events for the laboratory session.

Statistical Analysis

Mixed-effects modeling (Laird and Ware 1982; Gueorguieva and Krystal 2004) with MLwIN software (Rasbash et al. 2000) was used for statistical analysis. Beverage (alcohol or water) and affective stimuli (positive, neutral, or negative) were treated as within-subject fixed factors. Of the 47 participants, 42 provided complete data over all fixed conditions for all outcome variables. Of the total of 282 subject-condition combinations (47×6), 40 observations were missing for one subjective response measure (about 14%), and no more than 15 were missing for any of the others (5%). The missing data were a result of software deficiencies in the data collection apparatus (for example, failing to prevent a participant from clicking the mouse button twice in quick succession, inadvertently skipping over a response), and could safely be treated as missing at random (MAR)⁴.

RESULTS

Subjects were 47 non treatment-seeking paid volunteers with current alcohol dependence, who were abstinent on the day of testing. Table 2 shows detailed demographic, substance use, and clinical characteristics of the sample.

Manipulation Checks

Validity of beverage and affective manipulations were tested primarily by examining their effects on ratings of beverage-liking and feeling strong emotion. We found a statistically

³This somewhat shorter exposure time than employed in some studies (e.g. Monti et al. 1993a; Rubonis et al. 1994) was adopted in part to keep the entire protocol as brief as possible, an issue because of the repeated measures design. Pilot testing (not reported) had suggested that 90 seconds was a sufficient length of time for subjects to experience responses to presented beverages similar to what had been found with longer exposures, and subsequent results (reported below) suggest this decision was reasonable.

⁴These difficulties were addressed in later versions of the software, so this was mainly a problem with cases collected early in the study. The subject pool was the same throughout, however, so this difficulty is not likely to have created outcome-related bias in the partially missing cases.

significant main effect of beverage cue on beverage-liking (more liking for alcohol, compared to water), and also statistically significant main effects of both positive and negative images relative to neutral images on feeling strong emotion, as shown in Table 3a. The latter finding suggests that the images served their intended purpose. Further, since the validity check was performed following the presentation of affective stimuli and subsequent beverage presentation, results are consistent with the interpretation that the affective response lasted through the period of beverage presentation. As an additional check, we examined within-subject correlations (Snijders and Bosker 1994) between psychophysiological measures (heart rate, skin conductance, zygomatic, and corrugator averages calculated during vivo beverage exposure) and all subjective arousal measures including the four craving questions, three SAM questions, beverage liking, and feeling strong emotion. While these correlations were all small and most were non-significant, skin conductance was consistently positively associated with the four subjective craving ratings, with correlations ranging from 0.097 to 0.155. The latter was statistically significant ($p < .05$), and two others showed a trend towards significance ($p < .10$). Skin conductance also showed a trend association with feeling strong emotion (0.125, $p < .10$). Additionally, zygomatic (smiling) response showed a significant positive correlation with SAM Valence (0.145, $p < .05$) and beverage liking (0.133, $p < .05$), and a trend towards significance for feeling strong emotion (0.117, $p < .10$). Heart rate and corrugator (frowning) response were not associated with any subjective measure. Taken together, these results suggest that the experimental conditions had effects that differed within subjects as expected.

Random Effects

Tests for variation from the standard ANOVA covariance structure $\sigma^2\mathbf{I}$ were routinely conducted at both the between and within-individual levels. Departures from this structure were not observed for any of the mixed-effect models reported below.

Effects of Beverage and Affective Cues on Craving

Table 3a presents results of mixed-effect analyses of subjective outcome measures. The models associated with each row contain three within-subject main effect terms, dummy-coded to represent beverage cue (0=water, 1=alcohol), positive affective stimuli (0=neutral, 1=positive), and negative affective stimuli (0=neutral, 1=negative), and two interaction terms, beverage cue by positive affect, and beverage cue by negative affect. This parameterization implies that all effects presented below are compared to a water-neutral affect condition. Model-predicted means are based on effect estimates. Actual cell means and standard deviations for the subjective measures are shown in Table 3b.

Statistically significant main effects of alcoholic beverage cue were found on three of four individual craving questions, and on the mean of the four items (Table 3a). The effect size for alcoholic beverage cue on subjective craving measures (Cohen's d^5 ; Cohen 1988; Dunlap et al. 1996) ranged from 0.58 (strength of craving), to 0.22 (difficult to turn down); the composite effect size was 0.45.

Positive affect independent of beverage cue significantly ($p < .01$) increased craving strength and showed a trend for a significant ($p < .08$) increase in the composite craving scale. Effect sizes for positive affect ranged from 0.55 (difficult to turn down) to nearly zero (make things perfect). For negative affect, the largest effect size was 0.18 (strength of craving), and none of the effects of negative affective stimuli on measure of craving were statistically significant.

⁵Effect size calculations reported here reflect the difference in the predicted mean of the outcome variable Y for a dummy predictor = 1 vs. 0. The denominator for this calculation is typically the standard deviation σ_Y . In multilevel analyses, σ_Y may be partitioned by level. But in this study it is of substantive interest to determine how much of the total variability in Y is generated by cue exposures, and this would imply that σ_Y is the appropriate denominator.

No interaction effects were detected between alcoholic beverage cue and affective stimuli on any outcome measure of craving.

Effects of Beverage and Affective Cues on Measures of Emotion

Of the three SAM measures, only arousal was found to be significantly affected by alcoholic beverage cue, indicating more arousal for alcohol than water (1.94, $p < .01$; $d = 0.29$).

Both SAM valence and SAM arousal were significantly associated with negative affective stimuli ($d = 0.42$ and 0.31 , respectively, $p < .01$ for each). The negative affective condition resulted in generally lower positive valence and greater arousal compared to the neutral condition. Positive affect was not associated with any SAM measures.

Finally, no interaction effects were observed between alcoholic beverage cue and affective stimuli on any outcome measure of emotion.

DISCUSSION

The purpose of this study was to investigate moderating effects of positive and negative affective stimuli on alcohol beverage cue reactivity. Alcohol beverage cues elicited significantly greater subjective craving responses than did water beverage cues, with effect sizes comparable to previous studies (Cooney et al. 1997; Carter and Tiffany 1999). Similarly, validity checks verified both positive and negative visual affective cues had induced a strong emotional response. However, only positive and not negative affective stimuli were associated with increased craving strength. No affect $\times$ beverage interaction effects were found, despite sufficient (0.80) power to detect even small ($d = 0.20$) moderating effects of induced affect on beverage cue⁶.

The few previous laboratory studies addressing interactions between beverage and affective cues on alcohol cue reactivity (Litt et al. 1990; Rubonis et al. 1994; Cooney et al. 1997) were also largely negative across a range of mood induction methods. Taking the results of these studies and our own at face value, in the context of naturalistic relapse studies linking negative affect to relapse, one may speculate that if an internal negative affective state such as dysphoria, anxiety, tension or irritability is strongly enough linked to drinking (e.g., conditioned), then a beverage cue may not be necessary to elicit a craving response. Conversely, the negative affective stimuli used in the present study, e.g., pictures of accident victims or dangerous situations, although rated as having greater arousal and less happy valence than neutral pictures, may not have increased craving because they may never have been strongly linked (i.e., conditioned) to drinking.

The inclusion of positive affective stimuli is a novel component of this study. The significant relationship found between positive affective stimuli and strength of craving for alcohol is consistent with clinical relapse data for some individuals (Marlatt 1985; Lowman et al. 1996). Baker et al. (1987) argued that the direct, appetitive effect of alcohol may serve as an unconditioned stimulus that can condition a variety of situational cues typically associated with drinking, including positive affect. The circumstances portrayed in the positive stimuli of this study, such as peak sporting achievements or romantic/sexual encounters, are designed to produce positive emotion, which in turn may be associated with alcohol consumption and decreased inhibitory control, for many individuals.

⁶The study design produced this level of power to detect affect $\times$ beverage cue interactions for two reasons: first, within-subject correlation of craving measures was modest (about .35), and second, because of random assignment, the interacting variables were stochastically independent. See McClelland and Judd (1993) for a full discussion.

Despite the effects noted above on craving, exposure to positive affective cues did not affect SAM measures. Conversely, despite the significant effect of negative affect on SAM Valence, negative affect as induced in this study was not found to predict any craving measures. Taken together, these results suggest that reporting an effect of affective stimuli on one's mood is neither a necessary nor a sufficient condition for the emotion-inducing stimulus to cause alcohol cue reactivity or craving.

Furthermore, given the significant effect of positive cues on "feel strong emotion" and the directional increase in SAM valence in the positive cue conditions, it is most likely that subjects actually did experience increased positive affect, in some sense, in positive cue conditions, and that this feeling mediated the observed craving effect. Reported responses to positive cues may be less dramatic (and hence less sensitive, from a measurement perspective) than to negative cues because negative cues tend to be more personally salient. Humans are descended from risk-averse hominids. Any threat is potentially personally relevant, as it may be an immediate matter of life or death. The same is not typically true of any positive stimulus. But despite the less attention-grabbing effect of positive (vs. negative) affective cues, the positive cues may still link to alcohol urges through strong prior conditioning (see the discussion of positive cues in Baker et al. 1987).

The negative affective image cues in the standard IAPS set could be characterized as "negative-aversive", including photos of a snake about to strike, someone being assaulted, and so on; but not negative in a way that is typically associated with drinking. In contrast, interview studies that explored the nature of cues associated with relapse to drinking among alcoholics attempting abstinence (e.g. Marlatt and Gordon 1985) reported negative experiences in which the subject is personally involved, such as social pressure, interpersonal conflict, or personally costly situations, like losing one's job. Arguably, such cues arouse a somewhat different set of negative emotions than aversive images. It may be that negative stimuli of the type that is typically associated with drinking are required to induce alcohol cue reactivity in craving, e.g. several studies have found effects of negative affect induced by personalized scripts (Litt et al. 1990; Cooney et al. 1997; Niaura et al. 1998). The Niaura et al. (1998) study is the only published direct comparison of several different approaches; however its focus was on craving for tobacco, a drug with quite different addictive properties than alcohol (Carter and Tiffany 1999). One of the unique benefits of laboratory studies is their ability to investigate effects of very specifically-operationalized cues, and given the considerable scientific value of alcohol cue reactivity, further investigation of the effect of variability in affect induction methods is warranted.

A possible limitation of the present study relative to others reported in the literature is the subject pool. The present study included only non treatment-seeking alcohol-dependent paid volunteers, who were required to refrain from drinking on the day of their cue reactivity session. Other studies of mood and alcohol cue reactivity (Litt et al. 1990; Rubonis et al. 1994; Cooney et al. 1997; Jansma et al. 2000; Rohsenow et al. 2001; Ooteman et al. 2006) recruited subjects from treatment programs or treatment-seeking populations. It is possible that cue exposure is more salient for individuals who are motivated to remain abstinent. Thus, having established in the present study that craving returns to baseline following our cue exposure procedures, a future direction may be to now further evaluate these procedures for mood x beverage interaction effects in a treatment-seeking sample.

A key finding of this study is that positive affective stimuli commonly associated with drinking situations can induce craving in the absence of alcohol cues. This finding may represent another important focus for human laboratory studies and clinical relapse prevention strategies, in addition to the more established association of negative affective state with relapse.

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The experiments comply with the current laws of the country in which they were performed (USA).

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Table 1
Schedule of Procedures for Cue Reactivity Session

<i>Pre-Test Period</i>	
1:00 p.m.	Subject arrives; vital signs, BAC, urine toxicology screen for illicit drug use, date and time of last drink obtained, and clinical and laboratory assessments completed ^a
2:00 p.m.	Subject prepped for cue session; electrodes attached, impedance checked
2:20 p.m.	Subject given instructions and cue-reactivity practice trial
<i>Cue Reactivity Trials</i>	
2:40 p.m.	Step 1 - Mood Induction: Subject exposed to block of 12 affective images (pleasant, unpleasant or neutral), psychophysiological recording
2:45 p.m.	Step 2 - <i>In Vivo Beverage Cue</i> : alcohol or water beverage placed in front of subject for 90-sec while recalling picture-induced mood, psychophysiological recording
2:50 p.m.	Step 3 - Ratings: Complete VAS craving, SAM, and manipulation check ratings in presence of beverage, beverage removed from testing area after ratings completed
2:55 p.m.	Repeat Steps 1–3 for remaining affect-beverage trial combinations (6 trials total)
<i>Post-Test Period</i>	
3:55 p.m.	Electrodes removed, debriefing and relaxation period, post-cue session assessment of craving and affect to verify return to baseline, subject paid
5:00pm	Subject leaves

^aClinical assessments included: Clinical Institute Withdrawal Assessments for Alcohol (CIWA-Ar), Structured Clinical Interview for DSM-IV (SCID), Alcohol Dependence Scale (ADS), Alcohol Craving Questionnaire (ACQ), Positive and Negative Affect Scale (PANAS), Timeline FollowBack (TLFB)

Table 2
Demographic and Clinical Characteristics of the Sample (N=47)

Demographics		N
Age, yrs	44.3 ± 9.5	47
Sex, male (%)	74	47
Ethnicity (%)		
White	47	47
African American	37	
Latino	16	
<i>Drinking Characteristics</i>		
Age of first drink	14.9 ± 4.0	43
Years of heavy drinking ^a	17.5 ± 10.7	43
Most typical heavy drinking occasion (%)		
Evenings or weekends	46	41
Binges	14	
All day long	10	
Other	30	
Prior alcohol detox or treatment (%)	25	45
Alcohol Dependence Scale	13.1 ± 7.6	45
One or more days abstinent before day of cue testing (%)	68	47
<i>Pre and Post Cue Testing: Craving and Affect Measures</i>		
Alcohol Craving (ACQ)		
Before cues	41.5 ± 14.6	46
After debriefing [*]	39.8 ± 13.4	
PANAS-Positive		
Before cues	31.1 ± 8.3	46
After debriefing ^{**}	29.1 ± 8.5	
PANAS-Negative		
Before cues	15.5 ± 6.0	46
After debriefing ^{***}	13.5 ± 4.9	

* Before-after difference: N.S. (p>.05)

** Before-after difference: p<.05

*** Before-after difference: p<.01.

^a“Heavy drinking” is defined as 5+ drinks/day for males, 4+ drinks/day for females.

Table 3

Table 3a. Mixed-Effect Analysis Summary for Outcome Measures

Outcome	Pct ^a	Intercept	Beverage Cue	-----Estimated Model Coefficients-----			
				Induced Affect +	Induced Affect -	Bev x Aff+	Bev x Aff-
Reactivity Check							
Like beverage:	97	6.17 [*]	7.22 [*]	0.99	0.09	-0.82	-0.52
Feel strong emotion	96	10.75 [*]	-0.71	3.05 [*]	3.14 [*]	1.67	0.66
Craving							
Strength	95	8.31 [*]	3.68 [*]	3.52 [*]	1.17	-1.68	-0.72
Drink Now	96	9.41 [*]	2.68 [*]	0.55	0.20	-0.35	-0.23
Difficult to turn down	96	2.27 [*]	1.30	0.67	-0.76	-0.05	
Make things perfect	97	8.86 [*]	1.53 ^{**}	0.33	-0.56	-0.49	1.07
Composite	97	8.80 [*]	2.58 [*]	1.02	0.18	-0.84	0.08
Subjective Emotional Reaction							
SAM Valence	95	13.09 [*]	-0.29	0.97	-2.20 [*]	-0.79	1.23
SAM Arousal	95	7.05 [*]	1.94 ^{**}	0.23	2.08 ^{**}	1.66	-0.48
SAM Dominance	96	11.24 [*]	-0.29	0.22	-0.11	-0.55	-0.08

Table 3b. Means (Standard Deviations) for Dependent Measures, by Beverage and Affective Cue Conditions

Beverage: Affect:	-----Water-----			-----Alcohol-----		
	Neutral	Positive	Negative	Neutral	Positive	Negative
<i>Measure</i>						
Reactivity Check						
Like beverage:	6.3(6.3)	7.2(6.3)	6.3(5.9)	13.4(5.9)	13.6(5.5)	13.1(6.0)
Feel strong emotion	10.6(6.4)	13.8(4.8)	13.9(5.1)	10.0(6.9)	13.8(4.5)	14.6(5.0)
Craving						
Strength	8.3(5.7)	10.2(5.9)	8.7(6.6)	11.9(6.8)	12.2(6.2)	11.6(6.2)
Drink Now	9.3(5.8)	10.0(5.4)	9.6(6.4)	12.1(6.4)	12.3(5.9)	11.9(6.1)
Difficult to turn down	8.6(5.3)	10.2(5.7)	9.3(6.1)	11.0(6.2)	11.5(5.9)	11.4(5.5)
Make things perfect	8.7(5.9)	9.2(5.7)	8.3(6.0)	10.4(6.8)	10.3(6.5)	10.7(6.5)

Table 3b. Means (Standard Deviations) for Dependent Measures, by Beverage and Affective Cue Conditions

Beverage: Affect:	-----Water-----			-----Alcohol-----		
	Neutral	Positive	Negative	Neutral	Positive	Negative
Composite	8.7(5.4)	9.8(5.3)	9.0(5.5)	11.4(6.0)	11.6(6.0)	11.6(5.8)
Subjective Emotional Reaction						
SAM Valence	13.2(5.0)	14.1(4.1)	10.8(5.9)	12.7(5.0)	13.0(5.3)	11.9(6.0)
SAM Arousal	7.0(6.3)	7.3(6.4)	9.0(6.5)	9.0(6.6)	10.9(6.8)	10.6(6.6)
SAM Dominance	11.2(5.1)	11.5(5.6)	11.1(5.1)	10.9(4.8)	10.6(5.3)	10.8(4.8)

^aPercent of subject-by-repeated-measure non-missing observations (out of $47 \times 6 = 282$ possible).

* $p < .01$

** $p < .05$.

NOTE: Potential responses for all craving measures ranged from 0 (least strong) to 20 (strongest). Responses on SAM Valence ranged from 0 (unhappy), Arousal from 0 (relaxed) to 20 (stimulated), and Dominance from 0 (powerless) to 20 (controlling).