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Alcohol cues impair learning inhibitory signals in beer drinkers

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Abstract

Background—Models of drug addiction emphasize the reciprocal influence of incentive-motivational properties of drug-related cues and poor impulse control resulting in drug use. Recent studies have shown that alcohol-related cues can impair response inhibition. What is unknown is whether these cues also disrupt learning of inhibitory associations.

Methods—Participants performed a Conditioned Inhibition (CI) task and were required to learn that a neutral image was a conditioned inhibitor when presented in the context of either an alcohol image intended to draw their attention away from the to-be-trained inhibitor, or a control condition in which the alcohol image was absent. After training, subjects in each condition rated the likelihood that the neutral image would signal the outcome. Eye tracking was used to verify that attention to the neutral image was in fact reduced when the alcohol image was present.

Results—Compared with controls those trained in the alcohol image condition reported a greater likelihood that the presence of the inhibitor would be followed by the outcome and thus were less able to acquire CI. Measures of eye-tracking verified that attention to the alcohol cue was associated with this maladaptive behavior.

Conclusions—When alcohol cues are present, there is a reduced ability to learn that such information is irrelevant to an outcome, and this impairs ones' ability to inhibit perseveration of a response. This has implications for persistence of a drinking episode.

Keywords

alcohol; beer drinkers; inhibition; impaired learning; attentional bias

Introduction

The ability of alcohol-related cues to evoke behavioral and physiological reactions in drinkers has long been considered an important mechanism in the development and maintenance of alcohol dependence (Niaura et al., 1988; Drobles, 2002). Indeed, decades of “cue reactivity” research have shown that exposure to alcohol cues can lead to subjective

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Disclosure

Dr. Fillmore and Jennifer Laude designed the study, and Jennifer Laude wrote the protocol. Jennifer Laude ran subjects and oversaw the data collection and coding. Jennifer Laude managed the literature searches and summaries of previous related work, and undertook statistical analyses. Jennifer Laude and Dr. Fillmore wrote the manuscript. Both authors contributed to and have approved the final manuscript.

and physiological changes in an individual that are generally assumed to underlie increased craving for alcohol. Theoretical models of addictive behavior suggest that drug seeking is at least partially controlled by external stimuli. According to the incentive-sensitization theory, drug cues come to be associated with drug taking and the rewarding effects of the drug (Robinson and Berridge; 1993, 2001). Consequently, cues become increasingly salient, motivating drug-taking. These salient drug cues are preferentially processed in favor of other non-drug cues in the situation. Such attentional bias (AB) to alcohol-related cues has been demonstrated in the laboratory by visual probe tasks in which alcohol-related images compete with other images for the participant's attention (Field and Cox, 2008). With the use of eye-tracking technology in these paradigms, AB is indexed by greater dwell time to alcohol versus neutral images. Studies have found AB in light drinkers (e.g. Miller and Fillmore, 2010).

Recent models of drug addiction have begun to emphasize the reciprocal influence of incentive-motivational properties of drug-related cues and impaired control over drug taking (Feil et al., 2010; Dawe et al., 2004). These models cite neuroanatomical evidence implicating frontostriatal circuitry dysfunction in salience attribution and response inhibition, and propose that the motivation elicited by drug-associated cues serve to directly impair control mechanisms necessary to inhibit the cue-induced impulse to use a drug.

To assess the hypothesis that alcohol-associated cues could impair control mechanisms, Weafer and Fillmore (2012) tested whether alcohol cues could impede the ability to inhibit responses in light drinkers. Inhibitory control was measured using a cued go/no-go reaction time task that measures the subject's ability to inhibit pre-potent responses to the sudden presentation of a no-go target stimulus. The study also measured the degree of AB subjects displayed toward alcohol versus neutral cues. It was found that drinkers were less able to withhold a pre-potent response (i.e. were more disinhibited) in the context of alcohol cues as compared to when a neutral cue was presented. Further, heightened AB to alcohol was associated with greater response activation in the presence of alcohol images. Thus, behavioral control was reduced in the context of alcohol cues and appeared related to their biased attention to the alcohol cues. Similar results have since been reported from other laboratories using similar cued go/no-go tasks (e.g. Kreusch et al., 2013). Taken together, these findings provide preliminary evidence for a disruptive effect of alcohol-related stimuli on the ability to inhibit pre-potent responses.

Evidence that the presence of alcohol cues can impair response inhibition to no-go signals, raises the possibility that alcohol cues could also impede the drinker's ability to learn other associations among environmental stimuli in the situation. One form of learning that could be disrupted by the presence of alcohol-related cues is inhibitory conditioning. Learning accounts of addiction, like incentive salience, focus on excitatory conditioning in which the drug cue elicits an overt response. However, drug cues might also reduce the ability to acquire basic associations that inform an individual to suppress unwanted behaviors. The learned association between two stimuli that informs an individual to withhold a response is known as conditioned inhibition (CI). One should withhold responding upon presentation of such a stimulus because it signals the absence of a reward. CI is important because it provides information about when a response is not adaptive and may result in an

unfavorable outcome. Further, given that attention is limited in capacity (Broadbent, 1958; Treisman and Gelade, 1980; Wolfe et al., 1989) and myriad irrelevant cues exist in the environment, the ability to learn these kinds of associations would enable one to dismiss irrelevant information (Reeves and Sperling, 1986; Sperling and Weichselgartner, 1995; Smith and Ratcliff, 2009), allowing for cognitive resources to be reserved for processing signals that are relevant to ones' goals. That is, conditioned inhibitors inform one to suppress perseveration of a response. Thus, it stands to reason that failure to acquire these associations in the context of alcohol cues could result in persistence of behaviors, and possibly even drinking behavior.

A stimulus is conceptually referred to as a conditioned inhibitor when it signals that an otherwise expected outcome will not occur. Studies of CI in humans use contingency learning paradigms and require participants to make causal judgments to indicate their ability to learn conditioned associations between stimuli in the laboratory (Dickinson, 2001; De Houwer and Beckers, 2002). Such models are likely conducive to studying the effect of alcohol cues on inhibitory conditioning.

In the current study, inhibitory learning was examined in beer drinkers and tested whether the presentation of an alcohol cue would impede the ability to learn that an accompanying cue fails to predict an outcome (i.e., is a conditioned inhibitor). Using a between-groups design, participants were required to learn that the accompanying "neutral" image was a conditioned inhibitor when presented in the context of either an alcohol image intended to draw attention away from the to-be-trained inhibitor, or another condition in which the alcohol cue was absent. Participants' eye movements were also measured to determine if their attention would be reduced to the to-be-trained inhibitor when alcohol-related content was present. It was hypothesized that drinkers would show an impaired ability to acquire CI when an alcohol cue was present owing to reduced attention to the to-be-trained inhibitor.

Methods and Materials Participants

Twenty-four drinkers (12 women, 12 men) between the ages of 21 and 34 years who drank beer *at least* twice per month over the past three months were recruited. Screening measures determined medical history and current and past drug and alcohol use. Volunteers who self-reported any psychiatric disorder were excluded from participation. Dependence risk was determined by a score of 5 or higher on the Short Michigan Alcoholism Screening Test (Selzer et al., 1975). Individuals who reported other high-risk indicators of dependence (e.g., prior treatment for an alcohol use disorder) were not invited to participate. Demographic information is presented in Table 1. Volunteers were recruited via university advertisements. The University of Kentucky Institutional Review Board approved the study. Participants received \$35 for their participation.

Procedure

Participants were asked to abstain from drinking alcohol or using any other psychoactive substances at least twenty-four hours prior to the experimental session- no participants were disqualified for this reason. Upon arriving to the laboratory, participants provided informed consent. They then completed the assessment battery which included the questionnaires that

measured their alcohol and drug use. Volunteers who did not meet criteria for participation in the study were paid \$10 and discontinued. Those who met inclusion criteria then completed the CI task, the visual-probe task, and the updating memory task in that fixed order. Upon completion of the session, participants were paid and debriefed. Task descriptions are provided below.

Conditioned Inhibition Task

We used a CI procedure (see Table 2; adapted from Urcelay et al., 2008) wherein the presumed conditioned inhibitor (CS2) was presented in compound with a second stimulus (CS1) and was followed by the absence of reinforcement (no outcome). In a later stage of training, CS1 was followed by an outcome- it was at this point that participants should have learned that CS2 signaled the absence of the outcome, rendering it a conditioned inhibitor. After this training, in test, the question was whether participants learned that CS2 functioned as a conditioned inhibitor. We manipulated the type of cue that was presented in compound with CS2: in one group, CS1 was an alcohol cue (*alcohol cue* condition) and in a second group, a neutral cue was presented (CS4; *control cue* condition). By comparing the *alcohol cue* condition and *control cue* condition, the task measures the degree to which alcohol-related cues disrupt the ability to acquire CI.

Equal numbers of participants were assigned to the two treatment groups: *alcohol cue* (n = 12) vs. *control cue* condition (n = 12). Group assignment was random with the constraint that equal numbers of men and women were assigned to each group.

Stimuli and Task Parameters—The cues consisted of various realistic images: 1) beer being poured into a glass (CS1), 2) an open cardboard box (CS2,) 3) an open book (CS3) and 4) milk being poured into a glass (CS4). Pilot testing revealed that subjects self-reported that an image of a girl with oversized glasses giving the “thumbs up” was funny (reinforcing) and thus served as an outcome in the task. Throughout training and testing, stimuli were presented for a 2000 ms duration and were 90mm × 80mm. The outcome was presented for a 1500ms duration and was 110mm × 100mm. A variable intertrial interval (mean = 3000 ms) separated the trials. Trial types were presented in a pseudorandom order within the training phases. Participants were not explicitly told to learn associations.

Training—Figure 1 presents a schematic of the two phases of training necessary for the establishment of CS2 as a conditioned inhibitor. Note that the training described herein is with regard to the *alcohol cue condition*. The *only* difference between the alcohol and neutral cue conditions was whether the alcohol (CS1) or milk cue (CS4) was presented in training (see Table 2).

Phase 1—Compound cue conditioning: CS1 CS2. The purpose of this phase was to train participants that the compound of CS1 and CS2 predicted the absence of an outcome. The cues were presented side-by-side (CS1 CS2; 10 trials).

Phase 2—Excitatory conditioning: CS1+, CS3+. The primary purpose of this phase was to establish CS2 as a conditioned inhibitor. Thus, CS1 underwent excitatory conditioning (C1+), which should establish CS2 as a conditioned inhibitor. Two trial types were

presented: 1) CS1 was paired with the outcome and 2) CS3 was paired with the outcome. Each trial type was presented 5 times (10 total trials).

Test Phase—The purpose of this phase was to assess the degree to which CS2 functioned as a conditioned inhibitor owing to training. To accomplish this, two test types were presented: 1) CS3 and 2) the compound of CS3 and CS2 (CS3 CS2). For each test type, participants were to rate the likelihood that the outcome would follow ranging from 0% to 100% (see Figure 1). The order of the test type was counterbalanced across participants.

Eye tracking—We were also interested in whether an impaired ability to acquire CI would be due to increased attention to the alcohol cue during Phase 1 training. Thus, we measured ocular fixation time to the compound of cues in Phase 1 using a Tobii T120 Eye Tracking Monitor (Tobii Technology, Sweden). The Tobii Monitor had dual embedded cameras and tracked participants' gaze locations to each respective cue in the compound for both the alcohol and control cue groups. Gaze locations were sampled at 120 Hz and fixations were defined as gazes with standard deviations less than 0.5 degrees of visual angle (durations 50 ms). For each trial in Phase 1 of compound conditioning, we calculated the total duration of all fixations directed towards each image in the *alcohol cue* and *control cue* conditions. These values were averaged across the ten trials to produce a mean fixation time for each image in each compound of cues.

Visual-probe Task

To check that the sample had an AB to alcohol cues and groups were comparable on this measure, an independent measure of AB was obtained. A visual-probe task was used to measure AB towards alcohol-related images. Two stimuli were presented on-screen (1000ms) on each trial and subjects were told to scan both images. The task included 40 “alcohol” trials and 40 “filler” trials; included to reduce the likelihood of habituation to the alcohol stimuli (for procedural details see Weafer and Fillmore, 2013). Fixations were measured the using a Tobii eye tracker. Total fixation time to each image was measured per trial and averaged across trials to produce a mean fixation time for each image type.

Updating Memory Task

The means by which CI was trained in this experiment involves learning associations between sequentially presented stimuli and thus, information needs to be held in working memory. To ensure that working memory was comparable across groups, a letter memory task was administered (Morris and Jones, 1990). Several letters from a list of variable length (5, 7, 9, or 11) were serially presented (2000 ms per letter) in a pseudorandom order. Participants were to recall the last 4 letters presented. Participants performed 16 trials for a total of 64 letters recalled. The dependent measure was the number of letters recalled correctly out of 64- higher numbers indicated better performance.

Drinking Habits

The Timeline Follow-back calendar (TLFB; Sobell and Sobell, 1992) was used to assess daily patterns of alcohol use over the past 90 days. This measure uses a structured calendar

anchored with notable dates to facilitate recall of past drinking. The TLFB provided a measure of drinking days (total number of days that alcohol was consumed).

Trait Impulsivity

It has been demonstrated that impulsivity is associated with an impaired ability to acquire simple associations (e.g. Corr et al., 1995). To assess whether groups in the study had comparable levels of impulsivity, and its relationship to CI, participants completed the Barratt Impulsiveness Scale (BIS; Patton et al., 1995). Participants indicated how typical each of 30 statements (e.g., “I am self-controlled”) was for them on a 4-point Likert scale. Higher scores indicated greater total levels of impulsiveness.

Results

Demographics, Drinking and Other Substance Use, and Trait Impulsivity

See Table 1. Independent sample *t* tests revealed that groups did not differ significantly in age, BIS scores, or alcohol consumption over the past 90 days as reported on the TLFB, $ps > 0.05$. The sample reported frequent drinking (over one-third of the days assessed) and on average drank more than the criteria set forth for inclusion in the study. All participants reported use of caffeine; some reported use of nicotine ($n = 7$), other stimulants ($n = 2$), marijuana ($n = 8$), PCP ($n = 1$), and opiates ($n = 1$) in the past 30 days.

Visual-Probe and Updating Memory Tasks

The bottom of Table 1 lists dwell time to alcohol and neutral cues for *alcohol cue* and *neutral cue* conditions for the visual-probe task. A 2 (group) $\times$ 2 (cue type) mixed model ANOVA of dwell time to cues obtained a significant main effect of cue wherein greater dwell time was maintained to the alcohol image, $F(1, 23) = 4.24$, $p = 0.05$, indicating that the sample showed AB. No other terms in the model were significant and thus, AB did not significantly differ across the *alcohol* and *control cue* groups.

The bottom of Table 1 shows scores on the working-memory task. An independent samples *t* test revealed that the *alcohol* and *control cue* groups did not significantly differ in terms of their working memory, $t(22) = 1.21$, $p = 0.24$.

Cue Effects on Conditioned Inhibition

The degree of CI to CS2 in the test phase was measured by assessing the degree to which CS2 together with the excitator CS3, decreased subjects' estimated likelihood of the outcome compared to when CS3 was presented alone (see summation test, Rescorla, 1971). CI scores were computed as one less the inhibition ratio ($1 - (CS2/CS3)/CS3$). Inhibition ratios were defined as subjects' likelihood estimate of the outcome when CS3 was presented in compound with CS2, divided by subjects' likelihood estimate of the outcome when CS3 was presented alone. *Higher values indicated greater CI*. Figure 2 displays the CI scores for each group. The figure shows that the *alcohol cue* group displayed less CI as compared to the *control cue* group and this was confirmed by an independent *t* test, $t(22) = 2.59$, $p = 0.02$, $d = 1.05$.

Attention Allocation to Cues in Phase 1—To test the prediction that subjects would display greater attention to the alcohol cue compared with the control cue during Phase 1 training, fixation times in Phase 1 were analyzed by a 2 (group) $\times$ 2 (cue type) mixed-model analysis of variance (ANOVA). A main effect of group and cue was obtained which was qualified by a significant group by cue interaction, $F(1, 23) = 4.36, p = 0.04$. Table 3 reports mean fixation time to the cues for each group and shows that the interaction occurred because subjects allocated less attention to CS2 (the to-be-inhibitor) when it was accompanied by the alcohol cue compared to when it was accompanied by the milk cue (control cue). Indeed, a priori t tests confirmed that less fixation time was allocated to CS2 versus alcohol ($p < 0.05$), but not CS2 versus milk ($p > 0.05$).

Relationship of Conditioned Inhibition to Alcohol Consumption and Impulsivity—In order for CI to be meaningful in terms of alcohol-related problems, it should be related to drinking behavior. It was found that a greater number of drinking days were associated with reduced CI in the *alcohol cue* group, $r(11) = -0.75, p < 0.01$, but not the *neutral cue* group, $r(11) = -0.25, p = 0.43$. Another possibility is that heightened impulsivity is associated with a reduced ability to acquire CI in the context of alcohol cues. Such an idea was supported by a significant negative correlation between greater BIS scores and less CI in the *alcohol cue*, $r(11) = -0.77, p < 0.01$, but not the *neutral cue* group, $r(11) = -0.06, p < 0.83$.

Discussion

This study examined the degree to which an alcohol cue served to disrupt acquisition of CI. The theoretical rationale for such an effect was that increased attention to the alcohol image and subsequent decreased attention to the to-be-trained inhibitor in the *alcohol cue* condition would result in a reduced ability to acquire the critical association. Results showed that drinkers were less able to acquire CI when an alcohol cue was in the context relative to when a neutral cue was present. Furthermore, the *alcohol cue* group fixated on alcohol content longer than the *control cue* group fixated on the milk image in the compound of cues. As such, the study provides some corroborating evidence that the reduced ability to acquire CI might have been due to subjects' heightened attention to the alcohol cue in the situation. It was also found that impaired learning in the context of alcohol cues was most pronounced in more impulsive individuals, as well as heavier drinkers.

It is well established that heightened AB is *associated* with greater alcohol consumption (Field and Cox, 2008). However, causal mechanisms by which a bias towards alcohol cues might generally result in dysregulated behaviors are not well understood. This study demonstrates that alcohol cues can impede drinkers' ability to learn to suppress behaviors that are unlikely to be reinforced and are therefore no longer adaptive to the situation. As such, this could result in perseveration of behaviors that no longer yield positive outcomes. Among the myriad behaviors this may influence, one of these may be actual drinking behavior. The interaction between heightened AB to alcohol-related content and a reduced ability to learn about signals that could serve to cue inhibition of a response could explain persistence of a drinking episode as a result of being under the stimulus control of alcohol cues. This is because conditioned inhibitors that would otherwise cue the drinker to inhibit

unwanted behavior would receive less attention and thus less consideration in the decision-making process.

Though other studies have shown a disruptive effect of alcohol-related images on learning basic associations (e.g. Freeman et al., 2013), this study breaks much new ground as we have tested a population of drinkers with regard to the formation of basic associations using a novel paradigm. Furthermore, this study assessed an associative learning process never assessed in a drug-using population. This is important as it should not be assumed that drug-related cues generally impair acquisition of all associations equally. Our procedure also has the added benefit of employing direct measures of attention while further controlling for the fact that an alcohol image is a primary reinforcer by using an image of another consumable reinforcer in the control condition. However, one could argue that there are potential limitations to the study. The between-subjects design is a potential limitation as it is possible that the groups differed in the extent to which other characteristics that were not controlled could disrupt learning of CI which could provide an alternative account to the effect observed. However, we obtained comprehensive measures of relevant attributes, such as drinking habits, trait levels of impulsivity, AB, and working memory and we were able to demonstrate that the groups did not differ on any of these key characteristics.

One could also argue that alcohol cues are more salient and interesting than the other stimuli used in this task. If inherent cue differences in associability are responsible for a reduced ability to acquire CI within this paradigm, these stimuli should acquire greater conditioned value and hence, subjects should report greater likelihood estimates upon their presentation. However, control tests were presented: test 1) compound of cues seen in Phase 1 (alcohol/box in the experimental condition; milk and box in the neutral condition), test 2) alcohol alone in the experimental group; milk alone in the control group, and revealed that groups did not differ significantly in their likelihood estimates on these tests, $ps > 0.05$. These data refute accounts based on inherent cue differences in associability on impairing learning of the critical association. Although task stimuli were equated on aspects such as degree of detail, discriminability between the object and background and amount of negative space, future research should equate stimuli for general interest.

That the disruptive effect of an alcohol cue on CI is especially pronounced in heavy drinkers suggests that the more semantically meaningful a stimulus is to an individual, the greater the behavioral impairment. There is empirical support for this idea beyond the results of this study in other drug using populations (e.g. Freeman et al., 2013). However, there is evidence to the contrary. For instance, food-associated stimuli induce comparable impairments in behavioral control in those with a history of overeating (obese) and normal weight controls (Loeber et al., 2011).

It is also possible that in the alcohol cue condition, the to-be-trained conditioned inhibitor was imbued with excitatory properties which may have interfered with the expression of its inhibitory value in test (Williams et al., 1986; Williams and Overmier, 1988). The alcohol cue was associated with increased incentive salience as (as demonstrated by AB towards the cue in Phase 1) and in phase 2, the alcohol cue was likely associated with greater conditioned reinforcing properties than the excitatory cue in the control condition. As a

result of this training, the presumed conditioned inhibitor could have taken on some of the excitatory value of the alcohol cue by virtue of generalization. This kind of interpretation would require further testing. However, it would have important implications for how cues associated with incentive salience or conditioned reinforcing properties could promote alcohol consumption in that non-alcohol-related cues can take on some of the excitatory value of alcohol cues in the situation. This would result in the drinker being under the stimulus control of a variety of signals in the environment beyond the alcohol cue itself.

Another possibility is that our results could be interpreted in terms of a conditioned stimulus (CS) pre-exposure effect. The CS-pre-exposure effect (i.e. latent inhibition, Lubow and Moore, 1959; Lubow, 1976) is the finding that repeated nonreinforced presentations of a CS prior to its being paired with an unconditioned stimulus (US), impairs later acquisition of responding to that CS. Some accounts of the CS-pre-exposure effect attribute the phenomenon to an attentional decrement accrued to the CS as a consequence of the stimulus predicting the absence of an outcome during the pre-training exposure treatment (Lubow et al., 1976; Lubow et al., 1981; Mackintosh, 1975; Pearce and Hall, 1980; Wagner, 1981). The underlying assumption is that the resultant decrease in attention paid to the pre-exposed CS as a result of pre-training exposure hinders the subsequent formation of a strong CS-US association during conditioning. Results of this experiment can be interpreted in such a framework as less attention to CS2 in the alcohol cue condition resulted in a failure to pass a summation test but in the control cue condition, when there was a relatively greater attention to CS2, it passed the summation test. Future work should include control groups to allow for a clear differentiation between CI and latent inhibition accounts.

In addition to associative learning concepts, such human behavioral phenomena can also be accounted for by cognitive concepts, and this was recognized by early associative learning theorists (e.g. the addition of the expectancy construct, Bolles, 1972). As such, a more cognitive explanation could account for the results; that what is being learned is the predictive power that a stimulus will be followed by some outcome. AB can be thought of as a behavioral measure of pre-occupation with alcohol, as a result of poor attentional control. Attentional control would be evidenced by equal allocation of attention amongst stimuli presented in the context of alcohol cues. Thus, one interpretation of the data is that for the experimental group, pre-occupation with alcohol may have interfered with processing of information to be obtained from other stimuli in the situation, while no such interference occurred in the control group. Further, it is known that poor attentional control is asymptomatic of impulse control disorders, including alcohol abuse (de Wit, 2009) and as such, particularly impulsive individuals may show a pronounced impairment in their ability to acquire basic predictive relationships when alcohol cues are present in the situation. This hypothesis was supported in that greater impulsivity as measured by the BIS was related to a reduced ability to acquire CI in the context of alcohol cues. Additionally, heavier drinking was related to a reduced ability to acquire CI in the alcohol cue condition.

The findings of this study add to a small but emerging body of evidence showing that AB to drug-related cues can disrupt behavior and learning. The ability of AB to alcohol to impede the acquisition of CI is related to heavy drinking and could contribute to the appearance of perseveration and impulsive behavior, possibly promoting continued drinking or other

maladaptive behaviors. That CI can be acquired in the absence of alcohol cues, even in heavy drinkers, suggests that a previously established conditioned inhibitor may be presented in the context of alcohol-related content to suppress such perseverative responding. Pre-clinical research suggests that the presentation of conditioned inhibitors may reduce drug administration. Further, it is known that conditioned inhibitors are resistant to extinction and are durable across contexts (Boakes & Halliday, 1972). As such, conditioned inhibitors may provide a new means of both stopping a binge episode before it begins or reducing consumption after drinking has been initiated.

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Figure 1.

Schematic of the two training phases and the test phase in the CI task for the *alcohol cue condition* displayed in the left panel, and *control cue condition* in the right panel. Trial types within each of the respective phases are depicted. Phase 1 includes conditioning of the compound of cues that is followed by the absence of the outcome (*alcohol cue condition*: CS1 CS2; *control cue condition*: CS4 CS2). In Phase 2, two trial types are successively presented: 1) either CS1 (*alcohol cue condition*) or CS4 (*neutral cue condition*) is now followed by an outcome and 2) CS3 is also followed by the outcome. The two groups only differ in that Phase 1 and Phase 2 training. In the test phase, subjects are presented with two test trial types: 1) CS3 and 2) the compound of cues CS3 CS2. They are asked to rate the likelihood of the outcome after each respective test type is presented on a scale from 0% to 100%.

Figure 2.

The graph displays conditioned inhibition scores ($1 - (CS2/CS3)/CS3$) for the *alcohol cue* and *control cue conditions*. *Capped vertical lines* represent standard errors of the mean.

Table 1

Participants' Demographic Characteristics, Drinking Habits, Questionnaire scores and Task Performance.

	<u>Alcohol Cue Condition</u>		<u>Control Cue Condition</u>	
	<u>Mean</u>	<u>SD</u>	<u>Mean</u>	<u>SD</u>
Age	23.8	2.3	24.3	3.4
TLFB Total Days	34.2	16.1	29.1	15.0
BIS	59.4	9.2	58	7.3
Visual-Probe Task				
Alcohol dwell time (ms)	355.0	60.5	360.3	48.1
Neutral dwell time (ms)	324.0	54.5	326.2	55.7
Updating-Memory Task	56.3	6.0	58.9	4.4

Note. TLFB is the Timeline Follow-Back. BIS is the Barratt Impulsiveness Scale. Visual-Probe task provides an index of attentional bias to alcohol. Updating-Memory Task provides a measure of working memory.

Table 2

Phase 1, Phase 2 and Test by Cue Condition in the Conditioned Inhibition Task.

	<u>Alcohol Cue Condition</u>	<u>Control Cue Condition</u>
Phase 1	(CS1 CS2)	(CS1 CS4)
Phase 2	CS1+/CS3+	CS1+/CS3+
Test	CS3/(CS3 CS2)	CS3/(CS3 CS2)

Note: For both groups, in Phase 1, a compound of cues CS1 and CS2 (*alcohol cue condition*) or CS1 and CS4 (*neutral cue condition*) were presented followed by the absence of the outcome. In Phase 2, there were two trial types: 1) CS1 was followed by an outcome 2) CS3 was followed by the same outcome. This was followed by two tests in which participants were to rate how likely it was that the outcome would follow given the presentation of the stimulus onscreen: 1) CS3 2) the compound of cues CS3 and CS2. Participants in the *alcohol cue condition* differed from the *control cue condition* in one way: CS1 was an alcohol stimulus rather than a neutral stimulus (referred to later as CS4).

Table 3

Fixation times separated by picture type.

	Picture Type	
	Alcohol	Box
Alcohol Cue Group	785 (355.5)	455.5 (216.4)
	Milk	Box
Control Cue Group	743.4 (132.6)	691.1 (143.7)

Reported values are mean (SD) fixation time for each picture type in the conditioned inhibition task. Greater attention was allocated towards the alcohol cue when presented in compound with the box (*alcohol cue condition*) than when the milk image was presented in the compound (*control cue condition*). Less attention was maintained to the to-be-trained conditioned inhibitor (box) when it was presented in compound with the alcohol cue (in the *alcohol cue condition*) than when accompanied by another neutral cue (*control cue condition*).