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Craving and Subjective Responses to Alcohol Administration: Validation of the Desires for Alcohol Questionnaire in the Human Laboratory

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ABSTRACT. Objective: The abbreviated Desires for Alcohol Questionnaire (DAQ) is a self-report assessment of craving comprising the following subscales: (a) strong desires/intentions to drink, (b) negative reinforcement, and (c) positive reinforcement and ability to control drinking. Although the DAQ is sensitive to changes in alcohol craving precipitated by alcohol administration and/or cue exposure, no studies to date have examined the relationship between DAQ scores and subjective responses to alcohol. This study addresses this gap in the literature by testing the relationship between subjective responses to alcohol during alcohol administration and DAQ scores assessed 1 month later. **Method:** Individuals with alcohol dependence (n = 32) completed a randomized, single-blinded, intravenous alcohol administration in the laboratory in which subjective responses to the alcohol were measured, followed by a visit to the laboratory 1 month later to complete the DAQ. **Results:** Analyses revealed robust associations between DAQ scores and alcohol craving during alcohol administration (partial correlations: r = .43–.50, ps < .01), with the exception of the positive reinforcement subscale (r = .20, p = .30). Subjective intoxication and sedation were only associated with the negative reinforcement subscale of the DAQ (r = .38, p < .05 and r = .33, p < .05, respectively). **Conclusions:** Craving, captured by the DAQ, is reliably and positively associated with alcohol-induced craving. The DAQ is also associated with specific dimensions of subjective responses to alcohol. These results support the clinical utility of the DAQ, particularly in large samples where experimental manipulations may not be feasible. (*J. Stud. Alcohol Drugs, 74,* 797–802, 2013)

CRAVING FOR A SUBSTANCE is defined as a strong desire to consume that substance, which, in turn, has been associated with the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV; American Psychiatric Association, 1994), symptom of loss of control over substance use. Craving itself represents a criterion for substance dependence in the current version of the *International Statistical Classification of Diseases and Related Health Problems* (ICD-10; World Health Organization, 1992), and a longitudinal study found that alcohol craving was associated with the highest relative severity of all ICD-10 alcoholism symptoms (de Bruijn et al., 2005). Furthermore, craving has been adopted as a new symptom in the fifth edition of the DSM from the American Psychiatric Association (2013).

Although most investigators agree that craving is inherently a subjective experience best described as a state of desire or wanting, the operational definition of craving has been debated over the years (Monti et al., 2004). To that end, the subjective stimulating effects (Miranda et al., 2008) and anticipated reinforcement of alcohol (Bohn et al., 1995; Love et al., 1998) have been posited as important contributors to the development and maintenance of craving (e.g., Baker et al., 1986), with some evidence for common genetic underpinnings between subjective effects and desire for alcohol (Hutchison et al., 2008). Further, both subjective responses to alcohol and the subjective experience of craving have been reliably associated with important alcohol-related outcomes. Higher levels of craving, lower sensitivity to the aversive effects (i.e., low level of response to alcohol), and greater sensitivity to the stimulant and rewarding effects of alcohol have been individually associated with greater alcohol consumption and a greater risk of the development of alcohol use disorders (e.g., King et al., 2011; Ray et al., 2007, 2010b; Schuckit and Smith, 1996; Schuckit et al., 2004).

Craving for alcohol is typically measured in humans using the cue-exposure paradigm, which consists of systematically

presenting individuals with alcohol and control cues (e.g., visual, smell, taste cues) while recording subjective and physiological changes associated with the urge to drink. The cue-exposure paradigm is largely predicated on associative learning principles in that repeated pairing of alcohol cues with alcohol consumption, including both the positively and negatively associated subjective responses to the alcohol, produces conditioned reinforcement such that alcohol cues become conditioned stimuli capable of eliciting alcohol craving. These learned processes have been well documented in both human (O'Brien et al., 1990) and animal (Rodd et al., 2004) models.

Alcohol craving is also measured in the human laboratory during alcohol administration, or alcohol challenges, alongside the measurement of subjective responses to alcohol (Plebani et al., 2012; Ray et al., 2010a). Whereas experimental methods have been developed and validated to assess alcohol craving under controlled conditions, self-reports are also needed, particularly in the context of large-scale studies where experimental paradigms may be impractical. The abbreviated Desires for Alcohol Questionnaire (DAQ) has been developed for the assessment of alcohol craving in self-report format and has been incorporated into the Collaborative Studies on the Genetics of Alcoholism.

A principal components analysis of the abbreviated DAQ resulted in a three-factor solution, with dimensions characterized by (a) strong desires/intentions to drink, (b) negative reinforcement, and (c) positive reinforcement and ability to control drinking (Kramer et al., 2010). In addition, DAQ scores have been found to increase during cue exposure (Schoenmakers et al., 2008) and after alcohol administration in the laboratory (Rose and Duka, 2006; Schoenmakers et al., 2008). Given that the DAQ focuses on positive and negative reinforcement in addition to the craving subscale, it is especially well suited for validation using experimental methods. In particular, alcohol administration represents the gold standard for capturing subjective responses to alcohol such as positive and negative reinforcement. As such, examining DAQ scores in relation to experimentally acquired measures of subjective responses to alcohol and craving will provide construct validity and advance the DAQ as a tool for alcoholism research when experimental manipulations (i.e., alcohol administration) are not feasible.

Although the DAQ is sensitive to moment-to-moment changes in alcohol craving precipitated by alcohol administration and/or cue exposure, no studies to date have examined the relationship between DAQ scores and subjective responses to alcohol. This is particularly important because the DAQ is conceptually related to the positive and negative reinforcing effects of alcohol in the context of craving (Kramer et al., 2010; Love et al., 1998). Further, craving and subjective responses to alcohol are routinely assessed through the use of prospective/retrospective self-report questionnaires; however, little research has assessed the validity of these measurements in the context of acute alcohol intoxication. Thus, this study sought to use measures of craving and subjective responses to alcohol during a well-controlled, within-subjects, laboratory alcohol-administration paradigm to test the validity of a self-report measure of craving (DAQ) assessed 1 month later. The 1-month lag time between alcohol administration and DAQ assessment was implemented to reduce reporting bias as well as to enable the assessment of temporal and contextual stability in the measurement of craving on the DAQ.

Method

Participants and procedures

Non-treatment-seeking alcohol-dependent individuals between ages 21 and 65 years were recruited from the Los Angeles community through print and online advertisements. Exclusion criteria and general study procedures were consistent with published guidelines for conducting alcohol administration research in alcohol-dependent samples (Carter and Hall, 2008; Enoch et al., 2009; Lawson et al., 1980). Specifically, criteria for exclusion were as follows: (a) in treatment for alcohol problems or seeking treatment, (b) 21 or more days since last drink, (c) history of bipolar disorder or any psychotic disorder, and (d) Clinical Institute Withdrawal Assessment for Alcohol scale, revised (Sullivan et al., 1989), score of 10 or greater.

A total of 42 individuals met the criteria for current alcohol dependence and completed the alcohol administration (Ray et al., 2013). Of those, 32 completed the 1-month follow-up when the DAQ was administered. The average age of the sample of study completers (n = 32) was 28.75 years (SD = 9.7), and the majority were male (75%) and White (59.4%). The average years of education was 14.91 (SD = 2.1), and the average alcohol abuse plus dependence symptom count was 6.78 (SD = 2.15; range: 3–11).

After initial telephone interview, eligible participants were invited to the laboratory for a screening session. After providing written informed consent, participants completed individual differences measures. Participants then were given a physical examination and, following medical clearance, completed two randomized infusion sessions—one alcohol infusion and one saline control infusion. Alcohol administration was conducted using a single-blinded, randomized, counterbalanced, crossover design. Infusion sessions were separated by 1–2 weeks, with the mean observed time between infusions being 10.6 days. All participants were required to have a breath alcohol concentration (BrAC) of zero immediately before the alcohol administration, and the infusion was performed using a 5% ethanol intravenous solution (infusion rates were: 0.166-ml/minute × weight, in kilograms, for men, and 0.126-ml/minute × weight, for women).

Consistent with our previous work, the target BrACs were 0.02, 0.04, and 0.06 g/dl (Ray and Hutchison, 2004). Previous research has shown that the large subjective effects assessed during intravenous alcohol administration map closely to the subjective effects from oral alcohol consumption at these levels (Ray et al., 2007). BrAC levels were assessed by breath alcohol analysis in 3- to 5-minute intervals beginning at the start of the infusion. Upon reaching each of the target BrAC levels, infusion rates were reduced to half to maintain stable BrAC during testing. Participants were required to have a BrAC of .02 g/dl or less before leaving the laboratory (or BrAC = .00 g/dl if driving). Participants were invited back to the laboratory 1 month later to complete follow-up measures, at which time they had a BrAC of .00 g/dl. Given that this was a sample comprising alcohol-dependent individuals, all participants were invited for an individual session of motivational interviewing on completion of the study (34 of 42 completed the motivational interviewing).

Measures

The individual difference measures assessed at the screening visit and used to determine eligibility included (a) the 30-day Timeline Followback interview to assess alcohol use (Sobell and Sobell, 1980), (b) the Structured Clinical Interview for DSM-IV (First et al., 1995), and (c) the Clinical Institute Withdrawal Assessment for Alcohol scale, revised.

During the alcohol administration, the following measures were administered at baseline and at each target BrAC: (a) the Biphasic Alcohol Effects Scale (BAES) to assess feelings of alcohol-induced stimulation and sedation (Erblich and Earleywine, 1995; Martin et al., 1993), (b) the Subjective High Assessment Scale (SHAS) to assess subjective intoxication and loads most strongly on the aversive and sedative effects of alcohol (Ray et al., 2009), and (c) the Alcohol Urge Questionnaire (AUQ) to assess urge to drink (Bohn et al., 1995; MacKillop, 2006).

The abbreviated DAQ was administered at 1-month follow-up. As recommended by Kramer et al. (2010), three subscales were generated in addition to the total score and captured the following dimensions of alcohol craving: (a) strong desires/intentions to drink, (b) negative reinforcement, and (c) positive reinforcement and ability to control drinking. Although subjective responses to alcohol were available at each target BrAC, a composite of subjective responses across the ascending limb of the alcohol curve was created to minimize the number of comparisons.

Results

As reported elsewhere (Ray et al., 2013), manipulation checks testing the effects of Alcohol, Time, and the Alcohol × Time interaction on subjective response to alcohol demonstrated that alcohol was distinguishable from placebo (saline infusion). Only the active alcohol administration responses were used in the analyses because this study aimed to investigate subjective responses to alcohol and not placebo effects. Analyses consisted of correlations across the DAQ and its subscales (i.e., DAQ-total, DAQ-crave, DAQ-positive, and DAQ-negative) and subjective responses to alcohol during the alcohol administration (i.e., stimulation and sedation [BAES], subjective intoxication [SHAS], and alcohol craving [AUQ]). Partial correlations were used to account for baseline scores on the corresponding subjective response measures (e.g., the partial correlation between DAQ-total and AUQ, controlling for baseline AUQ). Thus, the associations between DAQ and subjective responses reflect the pharmacological effects of alcohol.

Reliability of the DAQ-total score and subscale scores were found to be adequate in this sample (DAQ-total Cronbach's α = .70; DAQ-crave α = .70; DAQ-negative α = .76; DAQ-positive α = .86). As shown in Table 1, DAQ scores were robustly associated with alcohol craving measured by the AUQ during the alcohol administration protocol (partial correlations: r = .43–.50, ps < .01), with the exception of the positive reinforcement subscale (r = .20, p = .30). The significant associations accounted for between 18% and 25% of the variance in AUQ score during the alcohol administration controlling for baseline AUQ, which is well within the large effect size range (Cohen's d = 0.94–1.15).

TABLE 1. Means, standard deviations, and partial correlations (and r^2) between abbreviated Desires for Alcohol Questionnaire (DAQ) scores and subjective responses to alcohol, controlling for baseline (pre-alcohol) scores on subjective response measures

Variable	M	SD	DAQ-total	DAQ-crave	DAQ-neg.	DAQ-pos.
DAQ-total	44.39	23.85				
DAQ-crave	17.36	6.02	.89 (.79)***			
DAQ-neg.	11.00	3.92	.88 (.77)***	.72 (.52)***		
DAQ-pos.	16.03	3.14	.69 (.48)***	.25 (.06)	.43 (.18)**	
BAES-stim.	29.58	13.83	.10 (.01)	-.03 (.001)	.25 (.06)	.10 (.01)
BAES-sed.	24.60	11.78	.27 (.07)	.28 (.08)	.33 (.11)*	.01 (.0001)
SHAS	39.97	18.78	.30 (.09)	.29 (.08)	.38 (.14)*	.04 (.002)
AUQ-crave	3.48	1.67	.48 (.23)**	.50 (.25)**	.43 (.18)*	.20 (.04)

Notes: Neg. = negative; pos. = positive; BAES = Biphasic Alcohol Effects Scale; stim. = stimulation; sed. = sedation; SHAS = Subjective High Assessment Scale; AUQ = Alcohol Urge Questionnaire.
*p ≤ .05; **p ≤ .01; ***p ≤ .001.

Subjective intoxication (measured by the SHAS) and sedation (measured by BAES) were associated with the negative reinforcement subscale of the DAQ ($r = .38$, $p < .05$ and $r = .33$, $p < .05$, respectively) but were unrelated to DAQ-total and to the other subscales. These effects also fell into the large effect size range (Cohen's $d = 0.70$–0.81). To further investigate these effects, sex and alcohol dependence symptom count were added to the partial correlation analyses, and doing so did not alter the results presented herein. DAQ-positive subscale scores were not significantly associated with any of the subjective response variables assessed ($p > .10$).

Discussion

This study sought to address gaps in the literature regarding the relationship between DAQ scores and subjective responses to alcohol. To achieve this goal, subjective responses to alcohol during alcohol administration and 1-month follow-up DAQ scores were acquired in a sample of individuals with alcohol dependence. Results revealed that the negative reinforcement subscale of the DAQ was positively correlated with sedation, subjective intoxication, and craving during alcohol administration, whereas the positive reinforcement subscale of the DAQ was not associated with any subjective response measure during alcohol administration. These findings may be interpreted as consistent with the prominent neurobiological theories of alcoholism, whereby alcohol craving in alcohol dependence is marked by negative—as opposed to positive—reinforcement (Everitt and Robbins, 2005; Goldstein and Volkow, 2002).

Additionally, craving reported during alcohol administration positively correlated with the negative reinforcement and craving subscales of the DAQ. This emphasis on the negative reinforcement and craving subscales translates well to a model of dependence in which the later stages of substance use disorders are marked by the shift from drinking for pleasure to drinking compulsively or out of habit (Everitt and Robbins, 2005). Perhaps the positive reinforcement subscale may be capturing more of the "ability to control" than the "positive reinforcement" dimension in this sample of alcohol-dependent individuals. This is consistent with Kramer et al. (2010), who found that items of control loaded highest onto the positive reinforcement and control subscale. Alternatively, this subscale may be more influential for heavy drinkers than for alcohol-dependent individuals, as evidenced by the lower positive reinforcement item loadings in the alcohol-dependent sample from the original validation study (Kramer et al., 2010).

The robust association observed between alcohol craving during alcohol administration and DAQ scores taken 1 month later provides crucial evidence in support of alcohol craving as a reliable and stable construct. The significance of this association despite differences in satiation at time of assessment (i.e., during alcohol intoxication vs. sobriety) and measurement period of each scale (i.e., the AUQ assesses phasic craving, whereas the DAQ assesses tonic craving) suggests alcohol craving is highly stable across settings and over time within alcohol-dependent samples. Because craving has been advanced as a hallmark of the transition to later stages of substance use disorders (Robinson and Berridge, 2001), the observed consistency of results across the human laboratory and clinical presentation advances craving as a translational phenotype for alcoholism.

These findings should be interpreted with regard to the strengths and limitations of the study design. Notable strengths include the combination of data obtained during an acute intravenous alcohol administration with self-report data in the absence of alcohol, and the sufficient time difference (1 month) between administrations of the craving measures, which reduces measurement biases. This time delay allowed for a much-needed within-subject validation of the DAQ with regard to subjective responses to alcohol in the human laboratory.

The well-characterized sample of alcohol-dependent individuals represents another significant strength of the study. The decision to administer alcohol to alcohol-dependent individuals was based in large part on the available research suggesting that individuals with alcoholism can—and should—be given "the same right to participate in and benefit from scientific research into their condition, as anyone afflicted by any other medical disorder" (Carter and Hall, 2008, p. 221; Enoch et al., 2009). In fact, others have argued that dependent subjects who participate in research that administers addictive drugs derive some therapeutic benefit from their participation (Montoya and Haertzen, 1994). A previous alcohol administration study with alcohol-dependent individuals followed by brief intervention found an increase in the percentage of days abstinent and a decrease in the number of drinks consumed on drinking days, at least in the 6 weeks following the study (Pratt and Davidson, 2005). However, we excluded alcohol-dependent treatment seekers and individuals suffering from severe alcohol withdrawal because of ethical and medical concerns, respectively. Thus, the results presented herein may not generalize to alcohol-dependent treatment seekers or individuals with severe alcohol withdrawal symptoms. Further, the sample size, although representative of alcohol administration studies, was insufficient to validate the factor structure of the DAQ determined by Kramer et al. (2010) in our independent sample of alcohol-dependent participants.

In sum, these analyses demonstrate that craving as determined by the DAQ is reliably and positively associated with alcohol-induced craving, thereby enhancing the clinical utility of this measure. Furthermore, analysis revealed a significant association between the negative reinforcement factor of the DAQ and alcohol-induced sedation responses or AUQ craving, whereas there were no significant relationships be-

tween study measures and the "positive reinforcement/ability to control" factor. Future studies are needed across a broader range of alcohol use patterns (from heavy drinking to severe alcohol dependence). Such studies will be positioned to test whether alcoholism progression moderates the relationship between DAQ scores and subjective responses to alcohol.

Acknowledgments

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