

The Alcohol Sensitivity Questionnaire: Evidence for Construct Validity

Kimberly A. Fleming, Bruce D. Bartholow, Joseph Hilgard, Denis M. McCarthy, Susan E. O'Neill, Douglas Steinley, and Kenneth J. Sher

Background: Variability in sensitivity to the acute effects of alcohol is an important risk factor for the development of alcohol use disorder (AUD). The most commonly used retrospective self-report measure of sensitivity, the Self-Rating of the Effects of Alcohol (SRE) form, queries a limited number of alcohol effects and relies on respondents' ability to recall experiences that might have occurred in the distant past. Here, we investigated the construct validity of an alternative measure that queries a larger number of alcohol effects, the Alcohol Sensitivity Questionnaire (ASQ), and compared it to the SRE in predicting momentary subjective responses to an acute dose of alcohol.

Methods: Healthy young adults (N = 423) completed the SRE and the ASQ and then were randomly assigned to consume either alcohol or a placebo beverage (between-subjects manipulation). Stimulation and sedation (Biphasic Alcohol Effects Scale) and subjective intoxication were measured multiple times after drinking.

Results: Hierarchical linear models showed that the ASQ reliably predicted each of these outcomes following alcohol but not placebo consumption, provided unique prediction beyond that associated with differences in recent alcohol involvement, and was preferred over the SRE (in terms of model fit) in direct model comparisons of stimulation and sedation.

Conclusions: The ASQ compared favorably with the better-known SRE in predicting increased stimulation and reduced sedation following an acute alcohol challenge. The ASQ appears to be a valid self-report measure of alcohol sensitivity and therefore holds promise for identifying individuals at-risk for AUD and related problems.

Key Words: Alcohol Sensitivity, Level of Response, Subjective Alcohol Effects, Alcohol Challenge, Model Comparison.

SUBSTANTIAL EVIDENCE SUGGESTS that risk for alcohol use disorder (AUD) is conferred via sensitivity to the effects of alcohol (Newlin and Thompson, 1990; Quinn and Fromme, 2011; Schuckit, 1994). Alcohol sensitivity is defined as the amount of alcohol one must consume in order to experience a given effect, or the extent to which a given alcohol dose influences subjective feelings (Pollock, 1992) and physiological (e.g., hormonal, neural) responses (Schuckit et al., 1987). Since the first demonstration that low sensitivity (LS) at age 20 is associated with substantially greater likelihood of developing an AUD by age 30 (Schuckit, 1994), empirical work on the correlates of alcohol sensitivity has proliferated (for reviews, see Morean and Corbin, 2010; Quinn and Fromme, 2011). Evidence suggests that LS-associated risk is dissociable from other AUD predictors,

including alcohol expectancies, externalizing behavior, comorbid psychiatric disorders, and personality (Schuckit et al., 2004; Trim et al., 2009).

Given these considerations, the ability to easily and reliably measure sensitivity is very important. Ideally, alcohol sensitivity would be assessed through a combination of subjective (e.g., self-reported intoxication) and objective (e.g., standing ataxia; physiological) responses to a laboratory alcohol challenge (Schuckit, 1994). However, this mode of assessment is cost-prohibitive and is inappropriate for certain populations who cannot be ethically administered alcohol, such as underage drinkers, individuals with active AUDs, and individuals taking certain medications (Wood and Sher, 2000). Furthermore, laboratory-based assessment is untenable for large-scale epidemiological studies that rely on broadly generalizable and relatively brief instruments.

Self-Rating of the Effects of Alcohol Form

To meet these challenges, Schuckit and colleagues (1997) developed the Self-Rating of the Effects of Alcohol (SRE) form. The SRE asks respondents to indicate the number of drinks required to experience up to 4 effects from drinking alcohol (recognition of "any effect"; dizziness or slurred speech; stumbling gait; passing out) during 3 different time periods (their first 5 drinking episodes,

From the Department of Psychological Sciences (KAF, BDB, JH, DMM, SEO, DS, KJS), Midwest Alcoholism Research Center, University of Missouri, Columbia, Missouri.

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Reprint requests: Bruce D. Bartholow, Department of Psychological Sciences, Midwest Alcoholism Research Center, University of Missouri, 210 McAlester Hall, Columbia, MO 65211; Tel.: 573-882-1805; Fax: 573-882-7710; E-mail: bartholowb@missouri.edu

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period of heaviest drinking in their lives, and most recent consecutive 3-month period in which they drank) and to respond only to effects that were actually experienced in a given time frame. The SRE has demonstrated good internal consistency ($\alpha > 0.90$) and test–retest reliability (r = 0.82; Schuckit et al., 1997). Concurrent validity has been established by correlating SRE scores with subjective effects during laboratory alcohol challenge (Schuckit et al., 1997) and with scores on AUD diagnostic instruments (Ray et al., 2011). SRE scores also predict development of AUD and problems prospectively (Schuckit and Smith, 2001; Schuckit et al., 2006, 2007, 2011).

Thus, the SRE has been important in advancing understanding of the role of alcohol sensitivity in the etiology of AUD. Nevertheless, the SRE suffers from some limitations. First, the scope of effects assessed by the SRE is small and consists primarily of sedation-like symptoms generally associated with large alcohol doses. Although its brevity likely reduces subject burden, this factor also likely limits the range of individuals for whom SRE scores fully reflect drinking experiences. This situation can result in fewer endorsed effects for some individuals than for others, which can produce skewed estimates of sensitivity level due to an inherent correlation between the number of effects endorsed and the number of drinks needed to experience them (Lee et al., 2015). On the other end of the severity spectrum, "feeling any different" is a relatively vague item that could be open to numerous interpretations, potentially limiting its utility (Clark and Watson, 1995).

Another limitation of the SRE is that it requires respondents to recall experiences that may have occurred many years in the past, or that in any case might be difficult to remember. Given the problems associated with accurately recalling alcohol use experiences (Del Boca and Darkes, 2003; Parra et al., 2003), it is likely that the retrospective reports queried by the SRE are less accurate than those related to more proximal experiences.

Alcohol Sensitivity Questionnaire

To address these limitations, O'Neill and colleagues (2002) created the Alcohol Sensitivity Questionnaire (ASQ). In creating the ASQ, O'Neill and colleagues (2002) aimed to sample a wide range of effects that could be experienced across numerous contexts on both the ascending and descending limbs of the blood alcohol concentration curve. Like the SRE, the ASQ asks respondents to indicate the number of drinks they must consume in order to experience alcohol-related effects. Specifically, the ASQ contains 15 items (Table 1), of which 9 tap effects typically associated with

lower doses and stimulation (e.g., feeling more talkative; more flirtatious) and 6 tap effects typically associated with heavier doses and sedation (e.g., feeling nauseous, passing out). For each item, respondents indicate whether or not they have experienced the effect from drinking alcohol; for each endorsed effect, they estimate the *minimum* number of drinks they must consume to experience the effect (for lower dose/light-drinking effects) or the *maximum* number of drinks they could consume without experiencing the effect (for larger dose/heavy-drinking effects). These differing referents are designed to provide estimates of limits on sensitivity across the spectrum of common alcohol effects.

High ASQ scores (indicating LS) are associated with heavy alcohol use (Bartholow et al., 2003, 2007, 2010) and alcohol-related negative consequences (Bartholow et al., 2010; Fleming and Bartholow, 2014). Other evidence linking ASQ scores with AUD risk has come from research showing that ASQ scores uniquely predict heavy drinking prospectively, beyond the influence of baseline alcohol involvement (Bartholow et al., 2007). Moreover, high ASQ scores are associated with enhanced brain responses to alcohol-related images (Bartholow et al., 2007, 2010; Shin

Table 1. Alcohol Sensitivity Questionnaire (ASQ) Items and Their Factor Loadings

ASQ Items	Factor 1	Factor 2
Do you ever experience a hangover after drinking alcohol? ^H	0.671	
Do you ever pass out after drinking alcohol? ^H	0.885	
Do you ever throw up (vomit) after drinking alcohol? ^H	0.934	
Do you ever feel nauseated after drinking alcohol? ^H	0.944	
Do you ever forget part of an evening (i.e., blackouts) after drinking alcohol? ^H	0.938	
Do you ever feel dizzy or feel things spinning after drinking alcohol? ^H	0.831	
Do you ever become more talkative after drinking alcohol? ^L		0.857
Do you ever become more flirtatious after drinking alcohol? ^L		0.842
Do you ever feel high or "buzzed" after drinking alcohol? ^L		0.765
Do you ever feel more socially at ease after drinking alcohol? ^L		0.865
Do you ever feel more relaxed after drinking alcohol? ^L		0.714
Do you ever feel sluggish after drinking alcohol? ^L		0.684
Do you ever feel less inhibited after drinking alcohol? ^L		0.772
Do you ever feel that your driving would be affected after drinking alcohol? ^L		0.513
Do you ever feel sedated or sleepy after drinking alcohol? ^L		0.499

For each item to which respondents indicate "yes," they are asked to respond to a follow-up question to indicate the number of drinks associated with experiencing the effect in question. Items marked with superscript "L" comprise the lighter drinking factor; follow-up questions are structured: "IF YES, what is the *minimum* number of drinks you could consume before. .." Items marked with superscript "H" comprise the heavier drinking factor; follow-up questions are structured: "IF YES, what is the *maximum* number of drinks you could consume without ...".

¹The first version of the ASQ (O'Neill et al., 2002) contained 16 items. However, in subsequent (unpublished) analyses, it was determined that 1 of those items, "Have you ever felt any effects from drinking alcohol?", provided little discriminative information for identifying levels of alcohol sensitivity, and therefore, it was dropped.

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et al., 2010) but not to other appetitive stimuli (Bartholow et al., 2010).

To date, no study has examined whether ASQ scores predict responses to alcohol challenge, an essential component of the measure's construct validity. Further, the ASQ has not been compared directly with the SRE to determine its performance relative to this better-known measure. This was the purpose of this study, for which 3 primary hypotheses were advanced. First, consistent with the modified differentiator model (King et al., 2011), we predicted that higher ASQ scores would be associated with increased feelings of stimulation following alcohol consumption. Given that the ASQ contains items specifically tapping stimulation-related effects, which are largely unassessed by the SRE, we predicted that a model based on ASQ lighter drinking items would be preferred (in terms of model fit) over an SRE-based model of these effects. Second, we predicted that higher ASQ scores would predict reduced feelings of sedation postconsumption. Further, because the ASQ assesses a broader range of sedating effects, we predicted that a model based on ASQ heavy-drinking items would be preferred over an SRE-based model in predicting sedation. Finally, we predicted that higher scores on the ASQ and SRE would be associated with decreased feelings of subjective intoxication.

MATERIALS AND METHODS

Participants

Four hundred and fifty-eight adults aged 21 to 34 (M age = 23.31; 49% female, 88% Caucasian) were recruited from the Columbia, MO community for a study examining effects of alcohol on cognition. Study announcements were placed in mass email blasts and in online classifieds. Interested individuals were instructed to contact the laboratory. Potential participants were interviewed via telephone; individuals reporting conditions contraindicating participation in an alcohol challenge (abstention; history of alcohol or drug abuse treatment or other serious mental or physical illness; deliberate attempts to cut down on drinking; prescription medication other than oral contraception; pregnancy) or that would impede completion of laboratory tasks (color-blindness; a primary language other than English) were excluded from the sample. In addition, to ensure that the alcohol dose received in the study would be within participants' normal range of experience, naïve drinkers (<2 drinks/wk on average) and very heavy drinkers (≥25 drinks/wk on average) were excluded from the sample. Eligible individuals were scheduled for the first of 2 laboratory sessions. Participants received \$35 for the baseline session and \$14/hour for participation in the second (beverage administration) session.

Self-Report Measures

Means and SDs of the measures described in this section, as a function of beverage group assignment, are reported in Table 2.

Alcohol Sensitivity Questionnaire. The first 9 of the ASQ's 15 items query effects of alcohol often associated with lighter drinking. For each of these items, respondents are asked to indicate whether they have ever experienced the effect as a result of drinking alcohol, and if so, to estimate the *minimum* number of drinks they need to

Table 2. Means (and SDs) of Demographic Characteristics, Alcohol Sensitivity, Alcohol Use, and Alcohol Problems Variables, and Drink Estimates as a Function of Experimental Group

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	Group		
Variables	Alcohol	Placebo	Mean comparisons
Age Sex (% male) AlcQF Neg. Con. AUD SRE 3-mo. ASQ-Heavy ASQ-Light Estimated drinks	23.4 (2.7) 52 7.72 (6.9) 4.39 (6.3) 2.01 (3.3) 6.29 (2.2) 8.79 (2.9) 3.43 (1.3) 4.03 (1.3)	23.2 (2.6) 46 7.09 (7.0) 3.84 (5.9) 1.79 (2.8) 6.07 (2.1) 8.51 (2.9) 3.35 (1.3) 2.57 (1.4)	t(421) = -0.62, p = 0.532 t(421) = -0.90, p = 0.369 t(421) = -0.91, p = 0.361 t(420) = -0.88, p = 0.382 t(421) = -1.02, p = 0.301 t(421) = -1.01, p = 0.312 t(421) = -0.65, p = 0.516 t(420) = -10.56, p < 0.001

AlcQF = quantity \times frequency of alcohol use; Neg. Con. = alcohol-related negative consequences; AUD = alcohol-related negative consequences that resemble symptoms of alcohol use disorder; SRE 3-mo. = average of Self-Rating of the Effects of Alcohol form, "most recent consecutive 3-month period in which you drank" items; ASQ-Heavy = average of Alcohol Sensitivity Questionnaire heavy-drinking factor items; ASQ-Light = average of ASQ light-drinking factor items; Estimated drinks = the number of standard alcoholic drink equivalents participants believed were contained in the drinks they consumed in the laboratory session. For both the SRE and ASQ, means shown here represent the average number of drinks associated with the experience of queried alcohol effects. See the text for explanations of how variables reported in the table were calculated.

consume in order to feel the effect. The remaining items, assessing effects most associated with heavier drinking, are structured similarly, except that respondents are asked to estimate the *maximum* number of drinks they can consume without experiencing the effect.²

Confirmatory factor analysis was used to compare a 1-factor model of the ASQ to a 2-factor model (9 lighter drinking items, 6 heavier drinking items). The 2-factor model represented a significant improvement in fit, $\chi^2(\text{Difftest}) = 881.51$, df = 1, p < 0.001. Initially, fit for the 2-factor model was fair ($\chi^2 = 374.22$, df = 89; comparative fit index [CFI] = 0.88, root mean square error of approximation [RMSEA] = 0.09). Modification indices suggested a significant correlation between the error terms of 2 items on the lighter drinking factor, "Sleepy" and "Sluggish." Given the conceptual similarity between these items, a correlation was specified between their error terms, resulting in a final version of the 2-factor model that fit adequately ($\chi^2 = 271.3$, df = 88; CFI = 0.92, RMSEA = 0.07). Internal consistency in the current sample was excellent for both factors (ASQ-Heavy $\alpha = 0.95$; ASQ-Light $\alpha = 0.89$). Factor scores were used for primary data analyses.

Self-Rating of the Effects of Alcohol (SRE) Form. Respondents indicate the number of standard drinks required to experience up to 4 different effects (recognition of "any effect"; dizziness or slurred speech; stumbling gait; passing out) over 3 different time periods (their first 5 drinking episodes; the period of heaviest drinking in their lives; the most recent consecutive 3 months in which they

²As with the SRE, scoring the ASQ begins with averaging the number of drinks a participant reports for each endorsed effect; ergo, a given item can be included in the score only if the participant reports having experienced that effect from drinking alcohol. This leads to a nonrandom pattern of missing data in which the number of endorsed items correlates with the number of drinks reported, which in turn can systematically bias sensitivity scores. See Lee and colleagues (2015) for scoring approaches to reduce this problem.

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drank). To approximate the time frame queried by the ASQ, only responses from the most recent consecutive 3 months of drinking (*SRE 3-mo*.) were used in the current analyses.³

Confirmatory factor analysis was used to estimate a single factor model of the SRE. Fit indices were mixed, with the CFI indicating a good fit, but with a high RMSEA value ($\chi^2 = 40.37$, df = 2; CFI = 0.95, RMSEA = 0.21). Internal consistency for the SRE 3-mo. items was good ($\alpha = 0.83$). As with the ASQ, factor scores were used for primary data analyses.

Alcohol Use and Consequences. Participants reported their average number of drinking occasions per week and average number of drinks consumed per occasion in the past 3 months (scored on a per week basis), using items adapted from the NIAAA Task Force recommendations (NIAAA, 2003). An alcohol quantityfrequency variable (AlcQF) was created by multiplying the number of typical weekly drinking occasions by number of drinks typically consumed per occasion. Participants indicated their experience of various alcohol-related negative consequences using the 24-item Young Adult Alcohol Problems Screening Test (Hurlbut and Sher, 1992). Nine of these items specifically query features of AUD (e.g., withdrawal; continued use despite problems). Participants indicated whether they had experienced each consequence "Never," "Yes, but not in the past year," "In the past year but not the past 3 months," "Yes, in the past 3 months: once; twice; 3 times; 4 or more times" (scored 0, 0.3, 0.5, 1, 2, 3, and 5, respectively). An overall "negative consequences" score was calculated as the sum of responses to all 24 items ($\alpha = 0.86$); a separate "AUD" score was calculated as the sum of responses to the 9 dependence-related items ($\alpha = 0.75$).

Subjective Effects of Alcohol

Stimulation and Sedation. The Biphasic Alcohol Effects Scale (BAES; Martin et al., 1993) is a self-report measure of stimulant and sedative effects of drinking alcohol. Respondents use a 10-point scale to rate the extent to which they are currently experiencing 7 states associated with sedation (e.g., down, sluggish) and 7 states associated with stimulation (e.g., up, excited). As is customary, BAES items were modified to eliminate direct attribution of feeling states to alcohol consumption. At each measurement occasion, responses to each subscale were summed to create individual sedation ($\alpha = 0.89$) and stimulation scores ($\alpha = 0.93$).

Subjective Intoxication. Similar to previous research (Earlywine and Erblich, 1996; Newlin, 1985), at each assessment participants indicated how drunk they felt ("How drunk do you feel right now?") using a 10-point scale (1 = not drunk at all; 10 = the most drunk I've ever been).

Procedure

Participants attended an initial (nondrinking) laboratory session where they completed the self-report measures as well as a battery of cognitive tasks germane to the aims of the larger study from which the current data were derived. One-to-three weeks later (M = 19.1 days) participants returned for a second (alcohol challenge) session. Participants were asked to eat a light meal 2 to 4 hours before their appointment. After providing informed consent, women were given a urine stream pregnancy test to self-administer (none tested positive); men were also asked to void the bladder. Participants completed a baseline BAES and subjective intoxication assessment and then were randomly assigned to receive an active placebo (diluted [10-proof] vodka and tonic water; 0.04 g/kg ethanol [EtOH]) or alcohol beverage (100-proof vodka and tonic water; 0.80 g/kg EtOH for men [0.72 g/kg for women]; average peak BrAC = 0.082, SD = 0.012). In both conditions, beverages were mixed in front of participants, their contents poured from Smirnoff[®] vodka and Schweppes[®] tonic bottles, and divided into 3 equalsized drinks, consumed at the rate of 1 every 8 minutes. Participants in both conditions were told that their drinks contained "a moderate amount of alcohol"; as shown in Table 2, placebo participants estimated they had consumed >2.5 standard drinks, indicating the manipulation was effective. Total beverage was isovolumic across conditions.

After beverage consumption and following a 5-minute absorption period, BrAC, BAES, and subjective intoxication measures were administered every 5 to 6 minutes until BrAC reached 0.065% for alcohol participants (or after 1 BrAC measurement for placebo participants), at which time the cognitive task battery was initiated. These measures were re-administered after every other cognitive task (approximately every 20 minutes). Upon completion of the cognitive tasks, BrAC and subjective effects were assessed every 5 minutes until BrAC descended from peak to 0.075%, at which time the cognitive battery was completed again; as during the ascending limb, BrAC, BAES and subjective intoxication were assessed after every other task. Upon completion of the second round of cognitive tasks, placebo participants were debriefed and dismissed. Participants in the alcohol condition were retained in the laboratory until they were sober (BrAC ≤ 0.02%; see NIAAA, 2004).

Analytic Approach

The primary aims of this report involve comparisons of nonnested models (i.e., whether the ASQ or the SRE affords better prediction of a given effect). Traditional null hypothesis significance testing (NHST) via *F*-ratio cannot accommodate comparison of nonnested models; therefore, model comparisons were carried out using Akaike information criterion (AIC; Akaike, 1974; Sakamoto et al., 1986). The AIC is an unbiased estimator of the amount of information lost in approximating a data set with a model (Burnham and Anderson, 2002). Thus, AIC provides a measure of goodness of fit that can be compared across several models fit to the same data (Schermelleh-Engel et al., 2003). Although formulae for AIC vary in the literature (O'Boyle and Williams, 2011), AIC can be represented simply as:

$$AIC_i = -2\log(L_i) + 2V_i$$

where L_i is the likelihood of the data given model M_i and V_i is the number of free parameters in model M_i . Lower values of AIC indicate a better fit; hence, the model with the lowest AIC is the best-fitting model. The quality of any other model M_i can be quantified by the difference in AIC between that model and the best-fitting model (i.e. Δ AIC)

To perform a pairwise comparison between 2 models, one can convert ΔAIC_i into an *evidence ratio*, which gives the odds that one model provides a better fit to the data relative to the other. Ratios of <5:1 indicate slight evidence, ratios between 5:1 and 30:1 indicate moderate to strong evidence, and ratios in excess of 30:1 indicate very strong evidence (Burnham and Anderson, 2002). Model com-

³A variety of models were tested for the current report, including some in which the SRE was represented by the average of responses to all 3 time frames. Model comparison results using that version of the SRE scoring were similar to those reported here. Other models used breath alcohol concentration (BrAC) instead of time as a predictor of postconsumption subjective effects. The pattern of conclusions drawn from models using BrAC was highly similar to models using time, unsurprising given the close association between these 2 variables. Finally, we tested models in which the 2 ASQ factors were combined to form a single predictor of subjective effects. Those models are reported in Table S1 in the Supporting information.

parison through evidence ratios is straightforward and, unlike NHST, can support continuous rather than dichotomous quantification of evidence (Wagenmakers and Farrell, 2004).

Participants varied greatly in their alcohol pharmacokinetics (Li, 2000), and due to the necessity of reaching specific BrACs to begin task sets, the number and timing of observations varied across participants. Thus, models were fit with Hierarchical Linear Modeling (HLM), which is capable of nesting repeated observations within participants and is robust to different numbers of observations per individual. HLM also can model changes in slopes over time. All models included a random intercept of subject.

Because the shape of the relationship between time and alcohol effects was expected to differ as a function of BrAC limb (Holdstock and Wit, 1998), a regression spline was included in each model. For each individual, the spline variable at time t is equal to $p_{\rm max}(0)$, time $t-{\rm time_{peakBrAC}}$). During the ascending limb, this variable is equal to 0; and during the descending limb, it is equal to the time elapsed since peak BrAC. This places a "knot" at the time of the individual's peak BrAC, allowing the trajectory of the relationship between time and outcome variables to change at that time. For placebo participants, the spline was yoked to the average time when alcohol participants achieved maximum BrAC (t=80 minutes).

To address whether ASQ scores predict interindividual variability in postconsumption alcohol responses, as well as how the ASQ's prediction of variation in response trajectories compares with the SRE, each subjective response outcome was modeled as a function of the interaction of time postconsumption, beverage group, sex, and 1 of the alcohol sensitivity measures (i.e., ASQ-Heavy, ASQ-Light, or SRE 3-mo.), as well as all lower order interactions and main effects. This model allows for an effect of time (effects varying as BrAC rises and falls), moderated by beverage group (alcohol participants should experience more change over time than placebo participants), moderated by sex (men and women might differ in their response to alcohol), and moderated by scores on the ASQ or SRE (those with higher scores should show different effect trajectories than those with lower scores). By comparing analogous ASQbased and SRE-based models, it is possible to determine whether scores on 1 measure more effectively capture the variance in the data than scores on the other measure.

AIC is valid for model comparison only when all models are fit to the same data. Therefore, participants who were missing either the entire ASQ or SRE or did not provide alcohol use data were excluded from all analyses (n = 5 placebo; n = 10 alcohol). Additionally, individuals in the alcohol group whose peak BrAC did not reach at least 0.059% (n = 9) or was >0.12% (n = 1) were excluded, as were placebo participants who did not finish their beverage

(n = 9). One participant was excluded for reporting nonzero subjective intoxication at baseline. Therefore, the final sample used for analyses included 423 individuals (ns = 219 and 204 in the alcohol and placebo groups, respectively).

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RESULTS

Bivariate correlations among primary study variables and sample demographic characteristics are given in Table 3. AIC-based comparative fit statistics and R^2 estimates for primary models are presented in Table 4. Model-derived estimated trajectories for each outcome measure are presented in Figs 1–3.

Stimulation

As shown in Table 4, when predicting postconsumption stimulation ratings the model based on ASQ-Light was strongly preferred to the SRE 3-mo. (Δ AIC = 10.61; evidence ratio = 202) and ASQ-Heavy models (\triangle AIC = 25.18, evidence ratio = 2.9×10^{5}). As depicted in Fig. 1 and consistent with our hypotheses (King et al., 2011), higher scores on the ASQ-Light factor predicted greater stimulation during ascending BrAC. In theory, individual differences in alcohol sensitivity should modulate subjective response only after alcohol has been consumed. Alternatively, ASQ scores could reflect alcohol-related expectancies or capture a generalized sensitivity to affective states. To test these alternatives, the best-fitting (ASQ-Light) model was tested without the interaction term involving beverage group. The loss of prediction caused by dropping this interaction was dramatic $(\Delta AIC = 19.7; evidence ratio = 1.90 \times 10^4)$, indicating that the effect of ASQ-Light on stimulation ratings depends on alcohol consumption.

Sedation

Next, models predicting postconsumption sedation ratings were compared. Here, ASQ-Heavy produced the best-fitting

Table 3. Correlations Among Primary Study Variables and Sample Demographic Characteristics

	1	2	3	4	5	6	7	8	9
1. Age	_								
2. Sex	0.05	_							
3. ASQ-Light	-0.18**	0.35**	_						
4. ASQ-Heavy	-0.21**	0.46**	0.57**	_					
5. SRE 3-mo.	-0.21**	0.38**	0.60**	0.70**	_				
6. Max. BrAC	0.04	0.08	0.02	0.05	0.04	_			
7. AUD	-0.14**	0.02	0.16**	0.20**	0.20**	0.06	_		
8. Neg. Con.	-0.14**	0.03	0.13**	0.22**	0.20**	0.05	0.94**	_	
9. AlcQF	-0.15**	0.24**	0.29**	0.35**	0.36**	0.04	0.48**	0.50**	_
10. Binge/wk	-0.29**	0.03	0.25**	0.29**	0.37**	0.09*	0.39**	0.44**	0.65**

^{*}p < 0.05, **p < 0.01.

ASQ-Light = Alcohol Sensitivity Questionnaire, light-drinking factor score; ASQ-Heavy = ASQ heavy-drinking factor score; SRE 3-mo. = factor score from the Self-Rating of the Effects of Alcohol form, "most recent consecutive 3-month period in which you drank" items; Max. BrAC = maximum breath alcohol concentration reached during the alcohol administration session (alcohol group participants only); AUD = alcohol use disorder specific alcohol-related negative consequences; Neg. Con. = other alcohol-related negative consequences; AlcQF = quantity × frequency of alcohol use; Binge/wk = number of binge drinking episodes per week. See the text for explanations of how these variables were calculated.

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Table 4. Fit and Model Comparison Statistics for Alcohol Sensitivity Measures Predicting Postconsumption Subjective Response Measures

Models	AIC	Δ_i	Marginal R^2	Conditional R^2	Evidence ratio		
Stimulation							
ASQ-Light	10,443	0	0.084	0.772	_		
ASQ-Heavy	10,468	25.18	0.088	0.771	>1,000:1		
SRE 3-mo.	10,454	10.61	0.086	0.772	202:1		
Sedation							
ASQ-Light	11,290	8.23	0.097	0.745	61:1		
ASQ-Heavy	11,282	0	0.096	0.747	_		
SRE 3-mo.	11,298	15.76	0.092	0.746	>1,000:1		
Subjective Intoxication							
ASQ-Light	12,031	19.94	0.355	0.695	>1,000:1		
ASQ-Heavy	12,025	13.59	0.355	0.694	893:1		
SRE 3-mo.	12,011	0	0.360	0.693	_		

ASQ-Light = Alcohol Sensitivity Questionnaire light-drinking factor score; ASQ-Heavy = ASQ heavy-drinking factor score; SRE 3-mo. = factor score from the Self-Rating of the Effects of Alcohol, "most recent consecutive 3-month period in which you drank" items. All models represent the Time \times Beverage group \times Sensitivity measure (ASQ-Light, ASQ-Heavy, or SRE 3-mo.) \times Sex interaction term. AlC = Akaike information criteria; Δ_i = difference in AlC between a given model ($_i$) and the best-fitting model within a family of models; the best-fitting model for each measure is shown in boldface. Marginal P^2 indicates the prediction of variance achieved through fixed effects alone; Conditional P^2 indicates the prediction of variance achieved through fixed and random effects (Nakagawa and Schielzeth, 2013). Evidence ratio = odds that the model in question provides a poorer fit relative to the best-fitting model.

model, which was strongly preferred over the SRE 3-mo. (Δ AIC = 15.8, evidence ratio = 2,640) and ASQ-Light models (Δ AIC = 8.23, evidence ratio = 61.3). As shown in Fig. 2, relative to lower scores, higher scores on ASQ-Heavy predicted less sedation across time, and this pattern was more apparent following alcohol than following placebo consumption. Dropping the interaction with beverage group led to a substantial loss of prediction (Δ AIC = 12.9; evidence ratio = 631).

Subjective Intoxication

Unlike both stimulation and sedation, subjective intoxication was best predicted by the SRE 3-mo. model, which was strongly preferred over the ASQ-Heavy (Δ AIC = 13.6; evidence ratio = 893) and ASQ-Light models (Δ AIC = 19.9; evidence ratio = 21,400). Figure 3 shows that higher scores on SRE 3-mo. were associated with lower subjective intoxication throughout the postdrinking period, and this difference was more pronounced following alcohol relative to placebo consumption. The loss of prediction caused by dropping the interaction with beverage group was dramatic (Δ AIC = 36.9; evidence ratio = 2.05 × 10⁶). A similar pattern is evident for the ASQ, but the score terciles appear to differentiate less clearly than for the SRE.

Sensitivity Versus Typical Alcohol Use

A common concern with measures like the SRE and ASQ is that scores may simply reflect respondents' recent alcohol

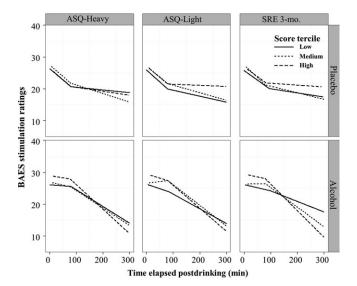


Fig. 1. BAES stimulation ratings across time as a function of score terciles on ASQ-Heavy (left panel), ASQ-Light (middle panel), and SRE 3-mo. (right panel) factors for participants in the placebo group (top row) and alcohol group (bottom row). ASQ-Heavy = Alcohol Sensitivity Questionnaire heavy-drinking factor; ASQ-Light = ASQ light-drinking factor; SRE 3-mo. = Self-Rating of the Effects of Alcohol form "most recent 3-month period in which you drank" factor. BAES = Biphasic Alcohol Effects Scale. Score terciles, where "low" represents the lower third of ASQ or SRE factor scores (i.e., high sensitivity) and "high" represents the upper third of factor scores on those measures (i.e., low sensitivity), were created for graphical representation purposes only; all analyses were carried out using continuous scores.

involvement. If so, then models including the AlcQF variable should perform just as well as models including ASQ or SRE scores. This possibility was tested by comparing additional sets of models: (i) using the AlcQF variable in place of ASQ or SRE and (ii) using both the AlcQF and ASQ or SRE in the same model.

For stimulation effects, the ASQ-Light model and AlcQF model afforded similar prediction, with only very slight evidence in favor of ASQ-Light (\triangle AIC = 1.07, evidence ratio = 1.71). However, the AlcQF model was rather strongly preferred over the SRE 3-mo. model (Δ AIC = 9.53, evidence ratio = 118). Compared to the model with AlcOF alone, the model including both AlcQF and ASQ-Light performed decidedly better $(\Delta AIC = 22.2,$ evidence ratio = 67,200), as did the SRE 3-mo. model (\triangle AIC = 13.7, evidence ratio = 951). The model including both AlcQF and ASQ-Light performed much better compared to an analogous model including AlcQF and SRE 3-mo. (\triangle AIC = 8.52, evidence ratio = 71).

For sedation effects, the ASQ-Heavy model performed far better than the AlcQF model (Δ AIC = 29.0, evidence ratio = 1.99 × 10⁶). The SRE 3-mo. model also outperformed the AlcQF model (Δ AIC = 13.2, evidence ratio = 753). Compared to the model with AlcQF alone, the model including both AlcQF and ASQ-Heavy was strongly preferred (Δ AIC = 25.5, evidence ratio > 3.4 × 10⁵), as was the model including both AlcQF and SRE 3-mo.

ALCOHOL SENSITIVITY QUESTIONNAIRE

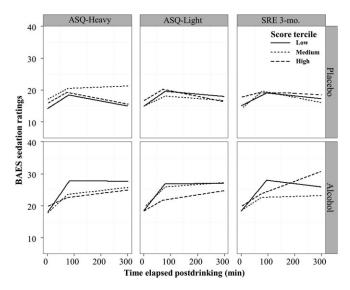


Fig. 2. BAES sedation ratings across time as a function of score terciles on ASQ-Heavy (left panel), ASQ-Light (middle panel), and SRE 3-mo. (right panel) factors for participants in the placebo group (top row) and alcohol group (bottom row). ASQ-Heavy = Alcohol Sensitivity Questionnaire heavy-drinking factor; ASQ-Light = ASQ light-drinking factor; SRE 3-mo. = Self-Rating of the Effects of Alcohol form "most recent 3-month period in which you drank" factor. BAES = Biphasic Alcohol Effects Scale. Score terciles, where "low" represents the lower third of ASQ or SRE factor scores (i.e., high sensitivity) and "high" represents the upper third of factor scores on those measures (i.e., low sensitivity), were created for graphical representation purposes only; all analyses were carried out using continuous scores.

(Δ AIC = 19.3, evidence ratio = 15,900). The model including both AlcQF and ASQ-Heavy performed better than an analogous AlcQF and SRE 3-mo. model (Δ AIC = 6.18, evidence ratio = 22).

Finally, for subjective intoxication, the SRE 3-mo. model dramatically outperformed the AlcQF model (Δ AIC = 53.1, evidence ratio = 3.4 × 10¹¹), as did the ASQ-Heavy model (Δ AIC = 39.5, evidence ratio = 3.86 × 10⁸). Compared to the model with AlcQF alone, the model including both AlcQF and SRE 3-mo. was very strongly preferred (Δ AIC = 59.0, evidence ratio = 6.62 × 10¹²), as was the model including both AlcQF and ASQ-Heavy (Δ AIC = 32.8, evidence ratio = 1.30 × 10⁷). The model including both AlcQF and SRE 3-mo. performed decidedly better compared to an analogous model including AlcQF and ASQ-Heavy (Δ AIC = 26.3, evidence ratio = 5.09 × 10⁵).

DISCUSSION

The SRE is the most widely used self-report measure of alcohol sensitivity. However, the SRE's relative utility in predicting subjective effects has never been directly tested against an alternative self-report measure. The goals of the current study were to evaluate the validity of the ASQ as such an alternative measure. We tested a family of hierarchical models in which SRE and ASQ factor scores were used to predict changes in self-reported stimulation, sedation, and intoxication over time following alcohol or placebo

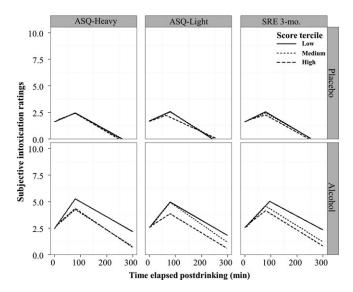


Fig. 3. Subjective intoxication ratings across time as a function of score terciles on ASQ-Heavy (left panel), ASQ-Light (middle panel), and SRE 3-mo. (right panel) factors for participants in the placebo group (top row) and alcohol group (bottom row). ASQ-Heavy = Alcohol Sensitivity Questionnaire heavy-drinking factor; ASQ-Light = ASQ light-drinking factor; SRE 3-mo. = Self-Rating of the Effects of Alcohol form "most recent 3-month period in which you drank" factor. BAES = Biphasic Alcohol Effects Scale. Score terciles, where "low" represents the lower third of ASQ or SRE factor scores (i.e., high sensitivity) and "high" represents the upper third of factor scores on those measures (i.e., low sensitivity), were created for graphical representation purposes only; all analyses were carried out using continuous scores.

consumption. We expected ASQ factor scores to reliably differentiate subjective responses over time for participants who consumed alcohol (but not placebo), such that higher ASQ scores (LS) would predict decreased sedation and subjective intoxication and increased stimulation. Moreover, due to its broader sampling of both stimulation- and sedation-related effects, we also expected the ASQ to provide better fit to the data relative to the SRE in predicting these outcomes.

Findings were largely consistent with these hypotheses, providing the first direct evidence for the construct validity of the ASQ. Several lines of evidence support this conclusion. First, trajectories of subjective response over time as a function of ASQ scores (Figs 1-3) showed that higher ASQ-Light scores were associated with greater stimulation, consistent with modified differentiator model predictions (King et al., 2011), whereas higher ASQ-Heavy scores predicted lower sedation and subjective intoxication ratings. Second, in models directly comparing the predictive utility of the ASQ and SRE, the ASQ afforded the best prediction of both stimulation and sedation. The SRE, in contrast, was better at predicting subjective intoxication (but see the Appendix S1 in Supporting information). Third, for each of these dependent measures, responses were strongly affected by interactions involving beverage group and sensitivity scores, indicating that ASQ and SRE scores reflect sensitivity to the pharmacological effects of alcohol, as opposed to expectancy-based effects or affective fluctuations more broadly.

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Incremental validity evidence for the ASQ was obtained in models comparing ASQ scores and typical alcohol use (AlcQF) as predictors of subjective effects. In each of these models, ASQ scores outperformed AlcQF and contributed substantially to model prediction over AlcQF alone, providing direct evidence that the ASQ assesses meaningful variability in alcohol sensitivity beyond what is accounted for by alcohol involvement. Interestingly, AlcQF provided better prediction of stimulation compared to the SRE, likely reflecting the lack of stimulation-related items on that measure.

The current study had numerous strengths, including a large sample, sophisticated methodological design, and the measurement of multiple domains of subjective response under both ascending and descending BrAC, but it also suffered from some limitations. Notably, participants were alone and engaged in a number of cognitive tasks over the course of the alcohol challenge session. Participants' social isolation (Doty and de Wit, 1995), coupled with fatigue due to completing the cognitive tasks, could help to explain the overall low levels of stimulation (and decline in stimulation throughout the session) observed here.

An additional limitation is that alcohol response was measured only with self-report; objective measures used in some previous research (e.g., body sway, cortisol, heart rate) were not included here. However, given that the SRE was validated using self-report responses to the Subjective High Assessment Scale (Judd et al., 1977), it is unlikely that this limitation poses a serious threat to the validity of the findings. Future research will benefit from the use of various objective measures and by querying stimulant and sedative effects that are both positive and negative (Morean et al., 2013). Also, it should be stressed that effects of initial sensitivity and effects associated with changes in sensitivity that can occur with drinking experience (i.e., tolerance) cannot be disentangled with the current data. Finally, characteristics of the current sample differed somewhat from samples used to initially validate the SRE, in that we did not conduct diagnostic interviews to exclude individuals meeting criteria for AUD, and we did exclude very light drinkers and nondrinkers.

In summary, the current study provides the first evidence that the ASQ is a reliable predictor of a variety of subjective effects of alcohol measured in the lab. Moreover, the current data suggest differing strengths for the ASQ and SRE. While both ASQ and SRE scores reflect sensitivity to pharmacological effects of alcohol beyond what is accounted for by typical alcohol use, model comparisons indicated that the ASQ outperforms the SRE in predicting postconsumption changes in stimulation and sedation but the SRE is preferred for predicting a simpler subjective intoxication index. The current results go beyond previous findings by assessing the validity of both the SRE and the ASQ in the same sample, using a statistical technique well suited for this purpose and appropriate for the structure of the data. These findings have implications for research into the risk profile characterized by differential sensitivity to acute effects of alcohol. Wide use of this instrument will allow researchers to understand how sensitivity to both stimulant and sedative effects work dynamically to indicate risk for AUD and related problems.

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REFERENCES

Akaike H (1974) A new look at the statistical model identification. IEEE Trans Autom Control 19:716–723.

Bartholow BD, Henry EA, Lust SA (2007) Effects of alcohol sensitivity on P3 event-related potential reactivity to alcohol cues. Psychol Addict Behav 21:555–563

Bartholow BD, Lust SA, Tragesser SL (2010) Specificity of P3 event-related potential reactivity to alcohol cues in individuals low in alcohol sensitivity. Psychol Addict Behav 24:220–228.

Bartholow BD, Pearson M, Sher KJ, Wieman LC, Fabiani M, Gratton G (2003) Effects of alcohol consumption and alcohol susceptibility on cognition: a psychophysiological examination. Biol Psychol 64:167–190.

Burnham KP, Anderson DR (2002) Model Selection and Multimodel Inference: A Practical Information-Theoretic Approach. 2nd ed. Springer, New York.

Clark LA, Watson D (1995) Constructing validity: basic issues in objective scale development. Psychol Assess 7:309–319.

Del Boca FK, Darkes J (2003) The validity of self-reports of alcohol consumption: state of the science and challenges for research. Addiction 98:1–12

Doty P, de Wit H (1995) Effect of setting on the reinforcing and subjective effects of ethanol in social drinkers. Psychopharmacology 118: 19–27

Earlywine M, Erblich J (1996) A confirmed factor structure for the biphasic alcohol effects scale. Exp Clin Psychopharmacol 4:107–113.

Fleming KA, Bartholow BD (2014) Alcohol cues, approach bias, and inhibitory control: applying a dual process model of addiction to alcohol sensitivity. Psychol Addict Behav 28:85–96.

Holdstock L, Wit H (1998) Individual differences in the biphasic effects of ethanol. Alcohol Clin Exp Res 22:1903–1911.

Hurlbut SC, Sher KJ (1992) Assessing alcohol problems in college students. J Am Coll Health 41:49–58.

Judd L, Hubbard R, Janowsky D (1977) The effect of lithium carbonate upon affect, mood and personality of normal subjects. Arch Gen Psychiatry 34:355–357.

King AC, de Wit H, McNamara PJ, Cao D (2011) Rewarding, stimulant, and sedative alcohol responses and relationship to future binge drinking. Arch Gen Psychiatry 68:389–399.

Lee MR, Bartholow BD, McCarthy DM, Pedersen SL, Sher KJ (2015) Two alternative approaches to conventional person-mean imputation scoring of the Self-Rating of the Effects of Alcohol Scale (SRE). Psychol Addict Behav 29:231–236.

Li T-K (2000) Pharmacogenetics of responses to alcohol and genes that influence alcohol drinking. J Stud Alcohol 61:5–12.

Martin CS, Earleywine M, Musty RE, Perrine MW, Swift RM (1993) Development and validation of the biphasic alcohol effects scale. Alcohol Clin Exp Res 17:140–146.

Morean ME, Corbin WR (2010) Subjective response to alcohol: a critical review of the literature. Alcohol Clin Exp Res 34:385–395.

Morean ME, Corbin WR, Treat TA (2013) The Subjective Effects of Alcohol Scale: development and psychometric evaluation of a novel assessment

- tool for measuring subjective response to alcohol. Psychol Assess 25:780–795
- Nakagawa S, Schielzeth H (2013) A general and simple method for obtaining R^2 from generalized linear mixed-effects models. Methods Ecol Evol 4:133–142.
- Newlin DB (1985) The antagonistic placebo response to alcohol cues. Alcohol Clin Exp Res 9:411–416.
- Newlin DB, Thompson JB (1990) Alcohol challenge with sons of alcoholics: a critical review and analysis. Psychol Bull 108:383–402.
- NIAAA (2003) Task Force on Recommended Questions of the National Council on Alcohol Abuse and Alcoholism: Recommended Sets of Alcohol Consumption Questions, October 15–16. Available at: http://www. niaaa.nih.gov/research/guidelines-and-resources/recommended-alcoholquestions. Accessed September 9, 2009.
- NIAAA (2004) Administering Alcohol in Human Studies. Available at: http://niaaa.nih.gov/Resources/ResearchResources/job22.htm. Accessed January 18, 2008.
- O'Boyle EH Jr, Williams LJ (2011) Decomposing model fit: measurement vs. theory in organizational research using latent variables. J Appl Psychol 96:1–12.
- O'Neill SE, Sher KJ, Bartholow BD (2002) Alcohol susceptibility and tolerance in young adults. Alcohol Clin Exp Res 26:119A.
- Parra GR, O'Neill SE, Sher KJ (2003) Reliability of self-reported age of substance involvement onset. Psychol Addict Behav 17:211–218.
- Pollock VE (1992) Metaanalysis of subjective sensitivity to alcohol in sons of alcoholics. Am J Psychiatry 149:1534–1538.
- Quinn PD, Fromme K (2011) Subjective response to alcohol challenge: a quantitative review. Alcohol Clin Exp Res 35:1759–1770.
- Ray LA, Hart EJ, Chin PF (2011) Self-Rating of the Effects of Alcohol (SRE): predictive utility and reliability across interview and self-report administrations. Addict Behav 36:241–243.
- Sakamoto Y, Ishiguro M, Kitagawa G (1986) Akaike Information Criterion Statistics. Springer, New York.
- Schermelleh-Engel K, Moosbrugger H, Müller H (2003) Evaluating the fit of structural equation models: tests of significance and descriptive goodness-of-fit measures. Methods Psychol Res 8:23–74.
- Schuckit MA (1994) Low level of response to alcohol as a predictor of future alcoholism. Am J Psychiatry 151:184–189.
- Schuckit MA, Gold E, Risch C (1987) Plasma cortisol levels following ethanol in sons of alcoholics and controls. Arch Gen Psychiatry 44: 942–945.
- Schuckit MA, Smith TL (2001) The clinical course of alcohol dependence associated with a low level of response to alcohol. Addiction 96:903–910.

- Schuckit MA, Smith TL, Anderson KG, Brown SA (2004) Testing the level of response to alcohol: social information processing model of alcoholism risk—a 20-year prospective study. Alcohol Clin Exp Res 28:1881–1889.
- Schuckit MA, Smith TL, Danko GP, Pierson J, Hesselbrock V, Bucholz KK, Kramer J, Kuperman SL, Dietiker C, Brandon R, Chan G (2007) The ability of the Self-Rating of the Effects of Alcohol (SRE) Scale to predict alcohol-related outcomes five years later. J Stud Alcohol Drugs 68:371–378.
- Schuckit MA, Smith TL, Tipp JE (1997) The Self-Rating of the Effects of Alcohol (SRE) form as a retrospective measure of the risk for alcoholism. Addiction 92:979–988.
- Schuckit MA, Smith TL, Trim RS, Allen RC, Fukukura T, Knight EE, Cesario EM, Kreikebaum SA (2011) A prospective evaluation of how a low level of response to alcohol predicts later heavy drinking and alcohol problems. Am J Drug Alcohol Abuse 37:479–486.
- Schuckit MA, Smith TL, Waylen A, Horwood J, Danko GP, Hibbeln JR, Davis JM, Pierson J (2006) An evaluation of the performance of the self-rating of the effects of alcohol questionnaire in 12- and 35-year-old subjects. J Stud Alcohol Drugs 67:841–850.
- Shin E, Hopfinger JB, Lust SA, Henry EA, Bartholow BD (2010) Electrophysiological evidence of alcohol-related attentional bias in social drinkers low in alcohol sensitivity. Psychol Addict Behav 24:508–515.
- Trim RS, Schuckit MA, Smith TL (2009) The relationship of the level of response to alcohol and additional characteristics to alcohol use disorders across adulthood: a discrete-time survival analysis. Alcohol Clin Exp Res 33:1562–1570.
- Wagenmakers E-J, Farrell S (2004) AIC model selection using Akaike weights. Psychon Bull Rev 11:192–196.
- Wood MD, Sher KJ (2000) Risks of alcohol consumption in laboratory studies involving human research participants. Psychol Addict Behav 14:328–334

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Additional models.

Table S1. Predicting postconsumption subjective response measures with ASQ factors, their combination, and the SRE.