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### **Test-retest reliability of the underlying latent factor structure of alcohol subjective response**

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#### **Abstract**

**Rationale—**Alcohol subjective experiences are multi-dimensional and demonstrate wide interindividual variability. Recent efforts have sought to establish a clearer understanding of subjective alcohol responses by identifying core constructs derived from multiple measurement instruments.

**Objective—**The aim of this study was to evaluate the temporal stability of this approach to conceptualizing alcohol subjective experiences across successive alcohol administrations in the same individuals.

**Methods—**Healthy moderate alcohol drinkers (n=104) completed 6 experimental sessions each; 3 with alcohol (0.8g/kg) and 3 with a non-alcoholic control beverage. Participants reported subjective mood and drug effects using standardized questionnaires before and at repeated times after beverage consumption. We explored the underlying latent structure of subjective responses for all alcohol administrations using exploratory factor analysis and then tested measurement invariance over the three successive administrations using multi-group confirmatory factor analyses.

**Results—**Exploratory factor analyses on responses to alcohol across all administrations yielded four factors representing 'Positive mood', 'Sedation', 'Stimulation/Euphoria' and 'Drug effects and Urges'. A confirmatory factor analysis on the separate administrations indicated acceptable configural and metric invariance and moderate scalar invariance.

**Conclusions—**In this study we demonstrate temporal stability of the underlying constructs of subjective alcohol responses derived from factor analysis. These findings strengthen the utility of this approach to conceptualizing subjective alcohol responses especially for use in prospective and longitudinal alcohol challenge studies relating subjective response to alcohol use disorder risk.

#### **Keywords**

Subjective alcohol responses; factor analysis; test-retest reliability

#### **1. Introduction**

Subjective responses to alcohol have been investigated as an endophenotype predictive of the development of alcohol use disorder (AUD). However, subjective responses to alcohol

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are multifaceted and show high inter-individual variability. In addition, there are a number of different self-report instruments, some of which may only capture certain aspects of the subjective experience after alcohol. Thus, it is not surprising that studies examining the relationship between alcohol responses and risk for AUD have been inconsistent (Morean and Corbin 2010; Newlin and Thomson 1990; Quinn and Fromme 2011). In order to delineate a unified theory relating subjective alcohol responses to AUD risk, it is important to characterize and capture the full range of alcohol subjective responses in laboratory studies.

A number of laboratory studies have examined the relationship of subjective alcohol responses to elevated drinking and risk for AUD with mixed results. Some report that a low level of response to the intoxicating effects of alcohol is associated with future AUD (Schuckit and Smith 1996; Schuckit et al. 2004). Others, report that individuals sensitive to the stimulant-like and tolerant to the sedative effects of alcohol are most vulnerable to excessive alcohol consumption and AUD (King et al. 2014). One difficulty in comparing results across studies is that they often use different instruments to measure alcohol subjective responses, some of which may not capture the full array of alcohol experiences. Thus, there has been a recent push to identify parsimonious constructs of subjective responses to alcohol by using multiple instruments to capture a more complete range of subjective mood and drug effects.

Recently, studies conducted by Ray and colleagues (Bujarski et al. 2015; Ray et al. 2009) used an exploratory factor analytic approach to assess alcohol subjective responses measured using multiple self-report questionnaires (Subjective High Assessment Scale, SHAS (Judd et al. 1977); Biphasic Alcohol Effects Scale, BAES (Martin et al. 1993); Profile Of Mood States, POMS (McNair and Droppleman 1971); Alcohol Urge Questionnaire, AUQ (Bohn et al. 1995)). They identified four main constructs: 1) a stimulant and positive mood altering factor, 2) an unpleasant and sedative factor, 3) a tension reduction and alleviation of negative mood factor, and 4) a craving and motivation factor. This approach represents an attempt to identify more parsimonious constructs of alcohol subjective responses, however, the stability of this approach is unclear. It is important that subjective alcohol responses measured in this manner demonstrate temporal stability especially if they are to be viewed as an endophenotype for behavioral genetics (Ray et al. 2010) and as a Research Domain Criterion (Ray et al. 2016).

The aim of the current study was to explore and examine the test-retest reliability of a latent factor structure of subjective alcohol responses identified using a factor analytic approach in the same individuals. Male and female moderate non-dependent alcohol drinkers participated in multiple alcohol challenge sessions. They completed standardized questionnaires to measure mood and drug subjective effects. We hypothesized that the latent factor structure identified using factor analysis would be similar to that of previous studies and that the factors would demonstrate temporal stability across multiple alcohol administrations.

#### **2. Methods**

#### **2.1 Participants**

Healthy male ( $N=70$ ) and female ( $N=34$ ) volunteers aged 21–40 were recruited from the Chicago area and local community using advertisements and flyers. Participants attended the laboratory for an in-person screening interview and electrocardiogram (ECG). Inclusion criteria were 10–30 drinks per week and at least one binge in the past month (to avoid adverse effects of the alcohol dose to be administered). Exclusion criteria included a current or recent history (past year) of a major axis I DSM-IV disorder (APA 1994) including drug dependence, history of alcohol dependence, hypertension, abnormal ECG, use of contraindicated medications, body mass index outside of 19–26kg/m2, less than high school education or lack of fluency in English,  $> 4$  caffeinated beverages/day or  $> 5$  cigarettes per day (to avoid any effects of withdrawal), nightshift work and pregnancy or lactation in women. Eligible candidates signed a consent form which stated that they would consume beverages that may or may not contain alcohol.

#### **2.2 Experimental protocol**

The current analysis focused on subjective response data obtained from a parent study (Childs and de Wit 2016). The University of Chicago Hospital's Institutional Review Committee for the use of human subjects approved the protocol. Procedures were conducted at the Human Behavioral Pharmacology Laboratory at the University of Chicago Hospital. The parent study consisted of 8 separate sessions including an enrollment session, 6 drug administration sessions and a final testing session. The current analysis focuses on subjective responses obtained during the 6 drug administration sessions. During drug administration sessions, participants were tested individually in rooms furnished as a comfortable living area. They received an alcoholic beverage (ALC, 0.8g/kg) on 3 occasions and a nonalcoholic beverage (noALC, 0.0g/kg) on 3 occasions in a pseudo-randomized double alternating order (ALC, noALC, noALC, ALC, ALC, noALC, OR noALC, ALC, ALC, noALC, noALC, ALC).

Upon arrival, participants provided breath and urine samples to test for the presence of drugs and alcohol, and for pregnancy in women. No one tested positive. Participants then relaxed for 15 min before baseline measures of mood, heart rate and blood pressure were obtained. To mimic more naturalistic drinking, the total dose (0.8g/kg) was consumed over two separate 15 min drinking periods (0.4g/kg each) separated by a 15 min rest period. Each 0.4g/kg dose was further divided into 3 equal portions to be consumed over 5 min each. The research assistant remained in the testing room and conversed with the subject during each drinking period to mimic drinking in a social setting. The research assistant provided feedback on the time remaining in each 5 min period to ensure the dose was consumed within the allotted time. All participants consumed the total dose in each session. Dependent measures (subjective mood and drug effects, breath alcohol concentration) were collected before drinking began, and then at 20 min after drinking began (5 min after completion of the first drinking period), 60 min after drinking began, and then at 30 min intervals for 3h. At the end of the session, final measures were collected and participants were allowed to leave once breath alcohol concentration was <0.04mg% (as per NIAAA guidelines).

#### **2.3 Beverages**

ALC drinks (8% solution) were prepared with 95% alcohol (Everclear, Luxco, Inc., Saint Louis, MO) and fruit juice. Participants were allowed to choose their favorite mixer from a range of fruit juices (e.g. cranberry, orange, apple, etc.) that were equicaloric, to enhance palatability and liking of the drinks. Drink volumes for female participants were adjusted to approximately 85% of that for males to allow for differences in body composition (Sutker et al. 1983). NoALC drinks consisted of fruit juice mixer only.

#### **2.4 Dependent measures**

**2.4.1 Subjective mood and drug effects—**Standardized self-report questionnaires were used to assess mood and drug effects. The Profile of Mood States (POMS; McNair and Droppleman 1971) is a list of 72 adjectives that are rated on a 5-point Likert scale [from "not at all" (0) to "extremely" (5)] which yields 8 subscales measuring Anxiety, Depression, Anger, Vigour, Fatigue, Friendliness, and Elation. The Addiction Research Center Inventory (ARCI; Haertzen et al. 1963) is a 53 item true-false questionnaire that yields 5 empirically derived subscales that measure sedation [pentobarbital-chlorpromazine group (PCAG)], stimulant-like effects [amphetamine (A); and benzedrine group (BG)], somatic and dysphoric effects [lysergic acid (LSD)], and euphoria [morphine-Benzedrine group (MBG)]. The Drug Effects Questionnaire (DEQ; Morean et al. 2013b) consists of five visual analog scales (100mm) each associated with a question; "Do you feel any drug effect right now?" (DEQ Feel, rated from "none at all" to "a lot"), "Do you like the effects you are feeling now?" (DEQ Like, rated from "no effect" to "like very much"), "Do you dislike the effects you are feeling now?" (DEQ Dislike, rated from "no effect" to "dislike very much"), "Are you high?" (DEQ High, rated from "not at all" to "very"), and "Would you like more of what you consumed, right now?" (DEQ More, rated from "not at all" to "very much"). The Biphasic Alcohol Effects Scale (BAES, Martin et al. 1993) is a list of 14 items rated on a likert scale from 0 (not at all) to 10 (extremely) that yields 2 primary scales consisting of 7 items each: stimulantlike effects (BAES Stimulation) and sedative effects (BAES Sedation). These questionnaires are widely used in human laboratory studies of drugs and alcohol and measure multidimensional aspects of subjective mood and drug experiences.

**2.4.2 Breath alcohol concentration—**Breath samples were collected using a Breathalyzer (Alco-sensor IV, Intoximeters, Inc., Saint Louis, MO). Participants rinsed their mouth with water prior to tests to avoid contamination of samples with any alcohol residue present in saliva.

#### **2.5 Data analysis**

Descriptive statistics and demographic characteristics of the sample, including the Short Michigan Alcoholism Screening Test (SMAST, Selzer et al. 1975) and Alcohol Use Disorder Identification Test (AUDIT, Saunders et al. 1993), were compared between sexes using t-tests and chi-square tests for continuous and categorical variables respectively.

**2.5.1 Summary measures—**We calculated summary measures of subjective responses (for each subscale of the ARCI, BAES, POMS, and each item for the DEQ) across the entire session using area under the curve (AUC) relative to pre-drug baseline using the trapezoid

method (Altman 1990). We then calculated net responses ( $AUC<sub>NET</sub>$ ) by subtracting AUC<sub>noALC</sub> from AUC<sub>ALC</sub> for each successive administration (AUC<sub>NET1</sub> = AUC<sub>ALC1</sub> –  $AUC_{noALC1}$ ;  $AUC_{NET2} = AUC_{ALC2} - AUC_{noALC2}$ ;  $AUC_{NET3} = AUC_{ALC3} - AUC_{noALC3}$ ).

**2.5.2 Data analytic plan—**We conducted an exploratory factor analysis (EFA) on all  $AUC<sub>NET</sub>$  values (N=312) to determine the underlying latent factor structure. We then examined the stability of the factor solution using a multi-group (group variable = Administrations 1, 2 and 3) confirmatory factor analysis (CFA) on  $AUC<sub>NET1</sub>$ ,  $AUC<sub>NET2</sub>$  and AUCNET3 simultaneously, testing for configural, metric, and scalar invariance over time. Configural invariance evaluates the model fit of the mean EFA structure across the three administrations separately. Metric invariance evaluates whether factor loadings are equivalent for the three separate administrations. Scalar invariance evaluates whether mean subscale and item responses are equivalent for the three separate administrations.

**2.5.3 General methods for exploratory factor analyses—**We conducted EFA on the questionnaire subscales and DEQ items using principal axis factoring on the correlation matrix (as the measures use different scales) with direct oblimin (oblique) rotation (to allow factors to correlate). Subscales or items that exhibited extreme non-normal univariate distributions were omitted from the initial analysis. Given the number of observations  $(n=312)$ , subscales and items were retained if  $16\%$  of the variance was accounted for by a single factor (factor loading  $\,$  .4; Stevens 2012). The number of factors to be retained was determined by Eigenvalues >1. Factor reliability was evaluated using Cronbach's α based on standardized subscales and items (Falk and Savalei 2011).

**2.5.4 General methods for confirmatory factor analyses—**We conducted CFA using maximum likelihood estimation with AMOS (Chicago, IL). Configural, metric, and scalar invariance were evaluated in 3 steps. First, we tested for configural invariance using a three-level (administration 1, 2, and 3) CFA in which all parameters were estimated freely except for the highest loading items for each factor which were set to 1.0 and the factor means were set to 0. Second, we tested for metric invariance by constraining all factor loadings to be equal for all three levels (administration 1, 2, and 3). Factor variances were set to 1.0 in order to identify the model. Third, we tested for scalar invariance by constraining all subscale and item intercepts to be equal for all three levels (administration 1, 2, and 3).

We used absolute fit indices to evaluate model fit; the Comparative Fit Index (CFI – cutoff:  $>0.9$ ; Bentler 1990), the root mean square error of approximation (RMSEA – cutoff:  $< 0.08$ ; Hu and Bentler 1999), and standardized root mean square residual (SRMR – cutoff: <0.08; Hu and Bentler 1999). To evaluate metric and scalar invariance, we used cutoffs established by Chen (Chen 2007) on the difference in fit between the metric and the configural models and the difference in fit between the scalar and metric models. The difference in model fit between the metric and configural models ( $_{INDEX}=INDEX_{METRIC}-INDEX_{CONFIGURAL}$ ) was used to evaluate metric invariance (cutoffs:  $C_{\text{FI}}$   $-0.01$ ;  $RMSEA$   $0.015$ ;  $SRMR$ 0.03) and the difference in model fit between the scalar and metric models

 $(NDEX = INDEX_{SCALAR} - INDEX_{METRIC})$  was used to evaluate scalar invariance (cutoffs: CFI  $-0.01$ ; RMSEA  $0.015$ ; SRMR  $0.01$ ).

All analyses were conducted using SPSS® Version 24 and AMOS Version 23 for Windows (Chicago, IL).

#### **3. Results**

#### **3.1 Demographic characteristics**

One hundred and four participants (34 females and 70 males) with a mean±SD age of  $24.7\pm3.6$  completed the study (Table 1). The majority were white (73%), moderate-to-heavy drinkers (14.9±6.8 drinks/week). They reported consuming 14.9±6.8 drinks/week and 5.0 $\pm$ 3.3 binges/week. SMAST scores were low (1.7 $\pm$ 1.9) and AUDIT scores were elevated  $(10.5\pm4.1)$  consistent with a profile of alcohol abuse but not dependence. Men and women did not significantly differ on any of the demographic characteristics.

#### **3.2 Exploratory factor analysis**

Univariate distributions for combined  $AUC<sub>NET1</sub>$ ,  $AUC<sub>NET2</sub>$ , and  $AUC<sub>NET3</sub>$  scores were first evaluated for normality and most subscales approximated normal distribution albeit with relatively high kurtosis (skewness estimates <|0.97|, kurtosis estimates <3.5). POMS Depression (kurtosis = 10.7) and POMS Anger (kurtosis = 15.7) exhibited extreme levels of kurtosis (because alcohol did not significantly influence these scales) and were therefore omitted from the factor analysis. The initial principal axis factor analysis on the remaining subscales yielded a 5-factor solution that explained 64.6% of the total variance. Extracted latent factors did not account for more than 16% of the variance for POMS Confusion (highest loading = .379) and DEQ Dislike (highest loading = .393). These subscales were therefore removed from the analysis. The resultant analysis yielded a 5-factor solution that explained 68.6% of the total variance. Extracted factors did not account for more than 16% of the variance of POMS anxiety (highest loading = .272) so it was also removed from the analysis. The next analysis yielded a 5-factor solution that explained 71.6% of the total variance. The next analysis yielded a 4-factor solution that explained 64.4% of the total variance. Extracted factors did not account for more than 16% of the variance of ARCI-LSD (highest loading = .165) so it was removed from the analysis. The final analysis yielded a 4 factor solution that explained 68.5% of the total variance (Table 2). Factor 1 comprised POMS Elation, POMS Vigour, POMS Friendliness, and BAES Stimulation suggesting a component representing mood enhancing aspects of subjective responses (Positive Mood). Factor 2 comprised DEQ Like, DEQ More, DEQ Feel, and DEQ High suggesting a construct embodying overall drug effects with a component of drug-induced craving (Drug Effects and Urge). Factor 3 comprised ARCI-A, ARCI-BG, and ARCI-MBG suggesting a component representing archetypal stimulant-like and euphoric drug effects (Stimulation/ Euphoria). Finally, factor 4 was composed of BAES Sedation, ARCI-PCAG, POMS Fatigue, and ARCI-BG (negative, low cross loading) suggesting a component representing sedative effects (Sedation).

#### **3.3 Confirmatory factor analysis**

**3.3.1 Configural Invariance—**The initial model for the three-level CFA model measuring configural invariance across administrations 1, 2, and 3 showed a poor fit for 2 out of 3 fit indices ( $\chi^2(210) = 427.2$ ; CFI = .880; RMSEA = .058 [90% CI = .050–.066];

SRMR = .089). The modification index representing covariance between residuals for DEQ Like and DEQ More during administration 2 was high (MI=25.6). Thus, to improve model fit, we allowed the covariance between these 2 error terms to be freely estimated (the items load onto the same factor and are highly correlated across all administrations: r=0.672, p<0.01 for AUC<sub>NET1</sub>; r=0.653, p<0.01 for AUC<sub>NET2</sub>; r=0.529, p<0.01 for AUC<sub>NET3</sub>). The fit of the resulting model met criteria for 2 out of 3 fit indices (Table 3, Model 1;  $\chi^2(207)$  = 363.6; CFI = .914; RMSEA = .049 [90% CI = .041–.058]; SRMR = .082). In line with criteria defined by Bentler and colleagues (CFI>.900, RMSEA<.080, SRMR<.080; Bentler 1990; Hu and Bentler 1999), we conclude that the latent factor structure demonstrated configural invariance across time.

**3.3.2 Metric Invariance—**To assess metric invariance across time, we constrained the factor loadings of matching subscales and items to equality across the three administrations (e.g. factor loadings of "ARCIA" for administration 1, 2 and 3 were set to be equal). The resulting model met acceptable fit indices levels for CFI and RMSEA but not SRMR (Table 3, Model 2;  $\chi^2(237) = 416.9$ ; CFI = .901; RMSEA = .050 [90% CI = .042–.057]; SRMR = . 102). Based on model fit decrement cutoffs ( $_{\text{CFI}}$   $-0.01$ ;  $_{\text{RMSEA}}$   $0.015$ ;  $_{\text{SRMR}}$   $0.03$ ), the resulting model did not exhibit a significant decrement in fit as evidenced by 2 out of 3 indices ( $_{\text{CFI}}=-.13$ ;  $_{\text{RMSEA}} = .001$ ;  $_{\text{SRMR}} = .020$ ) when compared to the configural invariant model supporting metric invariance. Thus, we conclude that overall the model met criteria for metric invariance across time.

**3.3.2 Scalar Invariance—**To assess scalar invariance over time, we constrain intercepts of matching subscales to equality (e.g. intercepts of "ARCI-A" for administration 1, 2 and 3 were set to be equal). The resulting model met acceptable fit indices levels for one criteria (RMSEA) but not for CFI and SRMR (Table 3, Model 3;  $\chi^2(265) = 469.8$ ; CFI = .887; RMSEA = .050 [90% CI = .043–.057]; SRMR = .105). Based on model fit decrement cutoffs ( $_{\text{CFI}}$   $-0.01$ ;  $_{\text{RMSEA}}$  0.015;  $_{\text{SRMR}}$  0.01), resulted in a non-significant decrement in fit as evidenced by 2 out of 3 indices ( $_{CFI}=-.014$ ;  $_{RMSEA} = .000$ ;  $_{SRMR} = .$ 003;) when compared to the metric model supporting scalar invariance. Thus, we conclude that overall the model demonstrated scalar invariance across time.

#### **4. Discussion**

This study was designed to assess the test-retest reliability of an underlying latent structure of alcohol subjective responses derived from factor analysis in the same individuals across separate alcohol administrations in the laboratory. We found that the factor structure derived from the ARCI, POMS, BAES, and DEQ is consistent with those of previous reports (Bujarski et al. 2015; Ray et al. 2009) and was comprised of a factor representing Positive Mood, Stimulation/Euphoria, Drug Effects and Urges, and Sedation. We also found that the factor structure demonstrated adequate stability across repeated administrations as evaluated by measurement invariance. These findings support the notion that the multidimensional nature of subjective alcohol experiences can be comprehensively measured using a variety of instruments and strengthen the predictive validity of using this approach in studies relating subjective responses to risk for AUD.

EFA on responses from all sessions yielded a latent structure that was generally similar to those of previous reports (Bujarski et al. 2015; Ray et al. 2009). Unlike Ray and colleagues, we did not capture a Negative affect/Tension relief construct (Bujarski et al. 2015; Ray et al. 2009). In our analysis, scales and items (i.e., POMS Depression, Anger, Anxiety & Confusion, DEQ Dislike, ARCI-LSD) that would have formed a similar factor were removed as they exhibited extreme non-normal distributions (because alcohol did not significantly influence these scales) or low factor loadings. In addition, scales measuring positive mood (i.e. POMS Elation, Friendliness, Vigour, and BAES Stimulation) and those measuring archetypal stimulant-like drug effects and drug-induced euphoria (i.e. ARCI-A, MBG, and BG) formed distinct constructs. In the analyses by Ray and colleagues, a single domain representing stimulation/hedonia was obtained (including BAES Stimulation, POMS Vigour and Happy or Positive Mood; Bujarski et al. 2015; Ray et al. 2009). This difference between analyses is likely due to our inclusion of the ARCI questionnaire (which measures prototypical drug effects) in the current study. Indeed, in the current study, items that loaded onto the Stimulant-like/Euphoria factor were derived from the ARCI questionnaire suggesting that this instrument captures an aspect of stimulant-like alcohol experiences that is not captured by the BAES or POMS. Despite discrepancies between studies, the current results replicate in part those of Ray and colleagues' studies in an independent sample with different subjective response questionnaires. This has important implications for the field as it converges towards defining a definitive underlying factor structure for subjective responses to alcohol. Taken together, the findings from our study and those of Ray and colleagues suggest that there are several distinct domains of subjective response to alcohol. Interestingly, some of the data derived domains identified in the current study overlap with theory-driven domains proposed by Morean and colleagues in the Subjective Effects of Alcohol Scale (Morean et al. 2013a). While the overlap between the field's theoretical framework and data-driven findings is encouraging, no single instrument currently measures the full range of alcohol responses. Until an instrument is developed that measures all domains comprehensively, we suggest including several instruments to fully capture the range of alcohol responses.

This is the first study to show that the latent factor structure of subjective alcohol responses collected from a number of well-validated instruments is relatively stable across repeated alcohol administrations. This has important implications for factor analytic approaches on self-report measures of subjective responses to alcohol. Primarily it supports the reliability of this method in conceptualizing alcohol experiences (i.e. for acute alcohol administration studies) and their relation to AUD risk (i.e. for cross-sectional studies on individual differences). Moreover, temporal stability of a measure is an important prerequisite for studies using factor analysis derived constructs of subjective alcohol responses as a predictor of future drinking in prospective and longitudinal studies.

There were several strengths and limitations to the present study. Study strengths include the use of a controlled pseudo-naturalistic drinking paradigm, and administration of several standardized self-report instruments to measure subjective alcohol responses. Although this study used an adequate sample size for factor analysis (MacCallum et al. 1999), the generalizability of the findings to independent samples with differing demographics and alcohol use characteristics is uncertain. Specifically, one of the limitations of the current

study is that the sample was relatively homogenous with regards to drinking behavior (moderate-to-heavy binge drinkers) and there is evidence that subjective alcohol responses (Holdstock and de Wit 1998; Holdstock et al. 2000; King et al. 2002) and factor structure of subjective alcohol responses (Bujarski et al. 2015) differ in heavy and light drinkers. Therefore, it is not yet clear whether the factor structure is stable across repeated alcohol administrations among lighter drinkers. Indeed, subjective alcohol responses may be less stable among less experienced drinkers and this should be examined in future studies. Another limitation is that our findings pertain only to a single dose of alcohol (0.8g/kg) that produces a robust, perceptible stimulus. It is possible that the factor structure of subjective alcohol responses, and its temporal stability, is sensitive to alcohol dose. Although others have reported similar factor solutions across different orally and intravenously administered alcohol doses (Bujarski et al. 2015; Ray et al. 2009), these studies used cumulative dosing procedures and factor structures of subjective alcohol responses at different doses should be investigated in future studies with randomized dosing procedures.

In summary, the main findings of this study are that data-driven and theory-driven approaches are converging towards identifying definitive underlying domains of subjective response to alcohol. In addition, the underlying domains elucidated by factor analytic approaches are reliable over repeated administrations in the same individuals. This has important implications for how we relate subjective alcohol responses to AUD risk, and increases our confidence in factor domains derived from a single administration. Future studies are required to determine whether this approach is valid across several demographic strata such as age, genetic ancestry, and sex. Furthermore, an alcohol administration study including all of the different instruments in use (e.g. SHAS, BAES, AUQ, DEQ, POMS, ARCI, SEAS), comparing routes of administration (e.g. intravenous, oral) and doses would solidify our understanding of the underlying latent factor structure of subjective alcohol responses.

In conclusion, the current study demonstrates temporal stability of the latent factor structure of subjective responses to alcohol. This highlights the validity of this approach in conceptualizing subjective responses to alcohol and their potential value in predicting development of AUD.

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#### **Table 1**

Demographic characteristics of study participants.



Other includes American Indian, Pacific Islander, more than one race, or unknown race; SMAST: Short Michigan Alcohol Screening Test; AUDIT: Alcohol Use Disorder Identification Test

#### **Table 2**

Exploratory factor analysis solution for the all  $AUC<sub>NET</sub>$  values (N=312).



Note: Scales with factor loadings <0.4 were omitted. ARCI: Addiction Research Center Inventory (A=Amphetamine; MBG=Morphine-Benzedrine Group; BG=Benzedrine Group; PCAG=Pentobarbital-Clorpromazine-Alcohol Group); BAES: Biphasic Alcohol Effects Scale; POMS: Profile Of Mood States; DEQ: Drug Effects Questionnaire

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# **Table 3**

Evaluation of measurement invariance by AUCNET1, AUCNET2 and AUCNET3 on the exploratory factor analysis solution for combined AUCNETS. Evaluation of measurement invariance by AUC<sub>NET1</sub>, AUC<sub>NET2</sub> and AUC<sub>NET3</sub> on the exploratory factor analysis solution for combined AUC<sub>NETS</sub>.



TLI: Tucker-Lewis Index; CFI: Comparative Fit Index; RMSEA: root mean square error of approximation; SRMR: standardize root mean square residual TLI: Tucker-Lewis Index; CFI: Comparative Fit Index; RMSEA: root mean square error of approximation; SRMR: standardize root mean square residual