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A Multilevel Structural Equation Model of Within- and Between-Person Associations among Subjective Responses to Alcohol, Craving, and Laboratory Alcohol Self-Administration

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Abstract

Subjective responses to alcohol are important determinants of drinking behavior and have been linked with risk for alcohol use disorders. However, few attempts have been made to examine proximal within-person associations among state changes in subjective responses and ongoing alcohol self-administration in the laboratory. This study disaggregated within- and between-person associations among subjective responses and alcohol self-administration, while also examining the mediating role of craving and the moderating role of trait impaired control over alcohol. Sixty young heavy drinkers (mean age=19.90, *SD*=0.86) completed self-report measures including the Impaired Control Scale, then participated in a 2-hour intravenous alcohol self-administration session using the Computer-Assisted Self-infusion of Ethanol (CASE) paradigm. Repeated assessments of subjective stimulation, subjective sedation, and craving were examined in relation to ongoing in-session self-administration, as indexed by breath alcohol concentration (BrAC) assessed 15 minutes later. Multilevel structural equation modeling was used to disentangle within-person and between-person associations. The results showed few significant associations at the between-person level, except for a direct negative association between sedation and BrAC. At the within-person level, state fluctuations in stimulation were positively associated with both craving and subsequent BrAC, whereas state changes in sedation were negatively associated with craving and positively associated with BrAC. Within-person indirect associations from subjective stimulation and sedation to subsequent BrAC mediated via craving were statistically significant. Also, participants higher on impaired control showed stronger within-person associations between craving and greater subsequent BrAC. The results suggest that subjective responses to alcohol and craving have proximal associations with self-administration behavior, the strength of which is linked with trait impaired control over alcohol.

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Introduction

Heavy drinking among youth is associated with a wide range of negative outcomes (Hingson, Heeren, Winter, & Wechsler, 2005; Wechsler & Nelson, 2008). The onset of alcohol use disorders (AUD) peaks during late adolescence (Hingson, Heeren, & Winter, 2006; SAMHSA, 2015), and AUD have been conceptualized as developmental disorders (Chassin, Sher, Hussong, & Curran, 2013). Thus, it is widely believed that early intervention is crucial for curbing the vast public health impact of alcohol misuse. This objective requires an improved understanding of early processes that are associated with progression to AUD.

Subjective Responses to Alcohol

A large body of research indicates that heritable or acquired differences in sensitivity to the effects of alcohol are important risk factors for the development of AUD. Consistent with the Low Level of Response (LLR) model (Schuckit, 1980, 2009), a large number of studies have found that relatively low sensitivity to alcohol's effects confers risk for heavy drinking and AUD (Schuckit, 1984, 1994; Schuckit & Smith, 2001; for reviews, see Morean & Corbin, 2008; Quinn & Fromme, 2011; Ray, Mackillop, & Monti, 2010). Much of the research in support of the LLR model has focused on sensitivity to alcohol's sedative effects (King, Roche, & Rueger, 2011; Quinn & Fromme, 2011). Yet, alcohol also has psychomotor stimulant effects, which may play a crucial role in positive reinforcement processes relevant to addictive behavior (see Wise & Bozarth, 1987). Accordingly, researchers have found that heightened sensitivity to alcohol's stimulant effects is also associated with heavier drinking and risk for AUD. Recently, King, de Wit, McNamara, and Cao (2011) found that, in response to a bolus dose of alcohol, heavier drinkers reported greater stimulation and lower sedation relative to light drinkers across several repeated post-drinking assessments, including at peak BrAC. Among heavy drinkers, greater stimulant/rewarding effects and lower sedation predicted increases in AUD symptoms during a six-year follow up period (King, McNamara, Hasin, & Cao, 2014). Based on these and other findings, King and colleagues have suggested that theoretical models should be revised to include both reduced responses to alcohol on measures of sedation and greater responses on measures of stimulation as risk factors for heavy drinking (King, de Wit, et al., 2011; King, Roche, et al., 2011; see also Newlin & Thomson, 1990).

Despite the large literature linking subjective responses to alcohol with heavy drinking, relatively few studies have examined proximal mediators of this association at the event level (i.e., within a drinking session). Recent theorizing has invoked reward-related mechanisms in this process (Bujarski & Ray, 2014; King, Roche, et al., 2011; Ray, Mackillop, & Monti, 2010). In particular, stimulant response to alcohol may be rewarding and motivate further alcohol consumption to maintain or increase pleasurable stimulant effects; thus, craving (or desire to consume more alcohol) may mediate the association between stimulant response and heavier drinking. Consistent with this perspective, studies of

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non-dependent heavy drinkers have found associations between subjective stimulation and craving in laboratory alcohol challenge studies (Bujarski & Ray, 2014; Hendershot et al., 2015; Ray et al., 2010; Rose et al., 2010). Also, studies show that craving measured during or after alcohol administration predicts greater subsequent ad libitum alcohol consumption (De Wit, 2000; O'Malley, Krishnan-Sarin, Farren, Sinha, & Kreek, 2002; Rose et al., 2010; Walitzer & Sher, 1990). Yet, craving has rarely been examined as a mediator of the link between stimulation and alcohol self-administration.

Further, the link between sedative response to alcohol and craving is currently unclear, with most studies reporting little or no association (Bujarski & Ray, 2014; Hendershot et al., 2015; Ray et al., 2010; Rose et al., 2010). However, most of these studies have used an alcohol challenge paradigm to achieve a pre-specified BAC, which has a different motivational context than ad lib alcohol self-administration. Based on the notion that subjective responses play a role in reward-related processes, perhaps increases in sedative effects, which are often aversive, may deter further alcohol consumption by decreasing desire for alcohol (i.e., craving). However, no prior studies to our knowledge have examined the mediating role of craving in the influence of both stimulant and sedative responses on ad lib alcohol self-administration.

Within- vs. Between-Person Associations

As Curran and Bauer (2011) have noted, a common problem in psychological research is that many theories articulate within-person processes but are largely studied using between-person analyses. With respect to the association between subjective response to alcohol and laboratory alcohol self-administration, we refer to between-person associations as relationships among trait-like individual differences in level of response to alcohol and individual differences in self-administration behavior. Examples of commonly reported between-person relationships are associations of average level of stimulation and sedation across a given drinking session, or ratings assessed at a specific time point (e.g. following a priming dose of alcohol or at peak BAC), with total observed alcohol consumption during an ad lib session (e.g., Corbin, Gearhardt, & Fromme, 2008; DeWit, Pierri, & Johanson, 1989). In contrast, within-person associations refer to the link between state fluctuations in subjective responses within an individual over the course of a drinking session (independent from between-person levels) and corresponding changes in ongoing alcohol self-administration behavior.

While the vast majority of studies in this area have focused on between-person relationships, some theoretical accounts of the role of subjective response to alcohol in AUD risk either implicitly or explicitly reference within-person processes as potential mechanisms of risk. For example, it has been posited that acute, state changes in stimulation and craving while consuming alcohol have motivational significance for ongoing drinking behavior (King, de Wit, et al., 2011; King, Roche, et al., 2011; Ray et al., 2010). So, ups and downs in subjective responses while consuming alcohol – relative to an individual's average levels throughout a drinking episode – should predict ongoing alcohol self-administration behavior. Although there are a few isolated examples of within-person analyses in this literature (Bujarski & Ray, 2014; Miranda, Monti, et al., 2014), these studies have not examined

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ongoing alcohol self-administration during the course of a given drinking episode in relation to state fluctuations in subjective responses. Thus, while within-person processes might help to explain how between-person differences in subjective responses to alcohol relate to AUD risk, these processes remain largely unexamined.

Although it is possible that studies examining between-person associations can capture theorized within-person associations (i.e., aggregating repeated assessments of variables that covary within individuals over a drinking session can yield observed covariation in the variables across individuals), it is still necessary to isolate within-person from between-person associations to confirm that subjective responses to alcohol are in fact linked with drinking behavior at the within-person level. Indeed, it is conceivable that the associations between subjective responses and drinking behavior may operate simultaneously at both levels through different mechanisms. Further, if associations differ at the within-person and between-person levels, inconsistent findings across studies may emerge if these associations are not appropriately disaggregated.

Human Laboratory Self-administration Paradigms

Human laboratory paradigms of alcohol self-administration are well suited to characterizing within-person processes that may link subjective responses, craving and alcohol consumption. However, one obstacle to experimental precision in this type of research is that several factors influence the blood alcohol concentration (BAC) time course, including large individual differences in absorption and distribution kinetics (Ramchandani, Plawecki, Li, & O'Connor, 2009; Zimmermann et al., 2008; Zimmermann, O'Connor, & Ramchandani, 2013). This variability, coupled with the temporal lag between ingestion of alcohol and subsequent change in BAC, makes it difficult to link subjective responses and craving with immediate self-administration at various points during a given session. One novel approach is Computer-Assisted Self-Infusion of Ethanol (CASE; Zimmermann et al., 2008), which combines intravenous self-administration with a physiologically-based pharmacokinetic (PBPK) model of alcohol distribution and elimination (Plawecki, Han, Doerschuk, Ramchandani, & O'Connor, 2008; Ramchandani, Bolane, Li, & O'Connor, 1999). A key advantage of CASE is that intravenous alcohol self-administration can achieve rapid changes in arterial BAC (indexing brain alcohol exposure) that are virtually identical across participants. This paradigm provides a strong context for modeling within-session associations among subjective alcohol response, craving, and self-administration behavior, allowing greater precision than could be achieved in oral paradigms.

Moderation by Impaired Control over Alcohol

An important risk factor for AUD that is likely to play a role in behavioral responses to craving is trait impaired control over alcohol. Impaired control refers to difficulty limiting alcohol consumption as well as failed attempt to abstain from alcohol (Heather, Booth, & Luce, 1998). Although impaired control over alcohol is associated with heavy drinking and trait impulsivity, there is evidence that impaired control is a distinct construct (Leeman, Patock-Peckham, & Potenza, 2012). Importantly, impaired control may be a precursor to the development of AUD and alcohol-related problems (Langenbucher & Chung, 1995; Leeman et al., 2012; Nelson, Heath, & Kessler, 1998). Yet, research on the links between trait

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impaired control and proximal determinants of drinking behavior such as subjective responses to alcohol and craving has been limited. Historical accounts of “loss of control” drinking placed an emphasis on the role of craving (e.g., Jellinek, 1960; Marlatt, 1978), suggesting that impaired control may partially reflect an inability to control alcohol consumption in response to a strong desire to drink. Thus, trait impaired control over alcohol may be associated with stronger links between craving and alcohol use, thereby moderating this association. However, this moderation effect has not been empirically examined to our knowledge.

The Present Study

This study used the CASE paradigm to examine associations among subjective responses to alcohol, craving, and ongoing alcohol self-administration, as well as the moderating role of trait impaired control in these processes. We applied multilevel structural equation modeling (MSEM), which uses latent variable modeling to disaggregate within- and between-person sources of variance in mediation analysis (Preacher, Zyphur, & Zhang, 2010). Because subjective responses to alcohol and impaired control are likely to emerge early as risk factors for the progression of AUD, we also examined a sample of heavy drinkers in late adolescence, an age group that is relatively younger than most samples used in prior alcohol-administration research.

A conceptual diagram of the hypothesized MSEM model is shown in Figure 1. We forwarded the following hypotheses: (1) The associations among subjective responses to alcohol, craving, and alcohol-self administration will be evident at the within-person level of analysis when using a design and analysis strategy that appropriately isolates within-person from between-person variance; (2) There will be a positive within-person association between subjective stimulant response and craving, and a negative within-person association between subjective sedation and craving; (3) Craving will mediate within-person associations between subjective responses to alcohol and alcohol self-administration; (4) Higher trait impaired control over alcohol will be associated with a stronger within-person relationship between craving and alcohol self-administration; this moderation effect will be unique to impaired control, after controlling for typical quantity of alcohol consumption and trait impulsivity.

Method

Participants

Participants were heavy episodic drinkers (N=62; n=32 women)[1] with a mean age of 19.90 (SD=0.86) years. Participants selected one or more of the following categories to describe their ethnic/racial background: Caucasian (n=42; 68%), Hispanic/Latino (n=6; 10%), Asian (n=5; 8%), East Indian (n=5; 8%), Black/African American (n=3; 5%), and other (n=8; 13%). Participants reported drinking an average of 5.36 (SD=1.95) drinks per drinking day

[1] N=64 participants completed the alcohol infusion session. However, 2 participants were excluded because they had extreme outlying values with respect to BrAC curves, with evidence indicating that they did not comply with task instructions.

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on an average of 20.95 (*SD*=11.34) drinking days over the past 90 days, with a mean of 13.68 (*SD*=10.88) heavy drinking episodes (4+ drinks for women/5+ drinks for men).

Procedures

Participants were recruited via advertisements on public and local university websites that targeted social drinkers. Eligibility criteria, assessed via phone screen, included ages 19 (the legal drinking age in Ontario, Canada) to 21 years, at least one heavy drinking episode in the past month, no past alcohol treatment or current desire/attempts to reduce drinking, no current psychiatric medications or diagnoses requiring treatment, no recent illicit drug use except cannabis, no contraindications related to alcohol use or intravenous protocols, and no severe nicotine dependence (defined as a score of > 5 on the Fagerstrom Test for Nicotine Dependence).

Eligible participants completed an in-person assessment visit, which included informed consent, completion of self-report measures via computer (including measures of impulsivity and impaired control), and a Time Line Follow Back assessment of past 90-day alcohol use conducted by a trained interviewer (see Measures). A medical screening was conducted to confirm eligibility for the intravenous alcohol infusion, as verified by the study physician.

Participants proceeded to complete two laboratory sessions involving intravenous alcohol administration. In the first session, participants received a controlled infusion designed to maintain blood alcohol concentration (BAC) at 80mg% using a clamping paradigm (Ramchandani et al., 1999). Data from this session are reported separately (Hendershot et al., 2015). Participants who proceeded in the study then completed an ad libitum intravenous self-administration session using the CASE paradigm. Participants were instructed to refrain from eating for 4 hours and from consuming alcohol for 24 hours prior to the CASE session. Upon arrival, participants submitted a breath alcohol (BrAC) reading to confirm a BAC of zero, and consumed a standardized snack. Female participants also completed a pregnancy test.

The CASE session took place in a research hospital setting under medical supervision. Participants were seated in a recliner chair and a registered nurse placed an indwelling catheter. Next, participants completed baseline questionnaires (described below) and received instructions about the protocol. CASE sessions consisted of free-access intravenous self-administration of alcohol, previously described as *Freibier* (German for “free beer”; Zimmermann et al., 2009; Zimmermann et al., 2008). Participants self-administered an intravenous infusion consisting of 100 percent dehydrated ethanol diluted with saline to a concentration of 6.0 percent ethanol (v/v). Participants submitted ‘drink’ requests by pressing an electronic button. Each button press triggered an infusion from a dual-channel infusion pump at an individually-tailored infusion rate, estimated with the PBPK model (Plawecki et al., 2008), to yield an incremental BAC increase of 7.5 mg% over 2.5 minutes. During each infusion the electronic button deactivated and additional drink requests could not be made. When infusions were not already in progress, the CASE software specified a descending BAC slope rate of −1 mg% per minute. A safety ceiling of 100 mg% was

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programed such that the drink button was temporarily deactivated when a subsequent drink request was projected to raise BAC above this safety ceiling.

Participants were instructed to self-administer alcohol to achieve a level of intoxication that was pleasurable, but to avoid experiencing unpleasant effects. The session began with a priming phase, during which participants self-administered four successive requests, yielding a target BAC of 30 mg% over the first 10 minutes. Upon completion of the priming phase a 5-minute waiting period ensued, and then the ad libitum phase began and lasted for the remainder of the session (120 minutes total). In-session BrAC readings were entered into the software, permitting real-time adjustment of model-projected BAC profiles over the session. Participants completed questionnaires at several points during the session (following the priming phase at approximately 15 minutes, and then during the ad libitum phase at approximately 30, 60, and 90 minutes).[2] The catheter was removed after the session and participants remained in the laboratory until BAC fell below 30mg%. Other papers report further details on the development of the CASE/*Freibier* paradigm (Zimmermann et al., 2009; Zimmermann et al., 2008; Zimmermann et al., 2013) and its use in this sample (Hendershot, Claus, & Ramchandani, 2014). Associations between Session 1 (clamp session) variables and Session 2 (CASE session) self-administration behavior are reported in a separate manuscript (Hendershot, Wardell, McPhee, & Ramchandani, under review).

Measures

Impaired Control Scale (ICS; Heather et al., 1993)—The ICS served as a trait measure of impaired control. We used Part 3 of the ICS, which assesses beliefs regarding impaired control over drinking behavior (10 items; e.g., “Even if I intended having only one or two drinks, I would end up having more”). This subscale is useful for assessing impaired control in young heavy drinkers, who may be unlikely to report a history of attempts to restrict drinking (see Heather et al., 1993). Items are rated on a 5 point scale ranging from 1=*strongly disagree* to 5= *strongly agree*. The ICS has good psychometric properties (Heather et al., 1998) and Cronbach’s α in this sample was .90.

Impulsivity—Impulsivity was measured with 8 items comprising the impulsivity subscale of the Impulsive Sensation Seeking Scale (ImpSS), a widely used measure of impulsivity that is part of the Zuckerman-Kuhlman Personality Questionnaire (Zuckerman, Kuhlman, Joireman, Teta, & Kraft, 1993). We included this measure in our analysis to isolate the moderating role of impaired control over alcohol from trait impulsivity. The impulsivity subscale of the ImpSS contains items reflecting lack of planning/forethought, which is more central to the concept of impaired control than is sensation seeking. Moreover, research has shown that sensation seeking is less predictive of alcohol-related problems (Cyders, Flory, Rainer, & Smith, 2009; Smith et al., 2007). Thus, we isolated the impulsivity items of the

[2]The subjective questionnaires were administered at two additional time points: at baseline (before the standardized priming phase) and at the very end of the self-administration session. These time points could not be modeled in the current analysis because they were not immediately followed by ad libitum self-administration. Moreover, although between-person individual differences in baseline ratings of stimulation and sedation were substantially correlated with mean post-alcohol ratings (r=.61 for stimulation; r=.33 for stimulation), we did not adjust post-alcohol ratings for baseline ratings (for example, by calculating residualized change scores) because this would complicate interpretation of the results of the MSEM. Given that the purpose of this analysis was to disaggregate between-person from within-person associations with subjective responses during self-administration, the analysis did not lend itself to examining changes from baseline levels of subjective stimulation and sedation.

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ImpSS, consistent with some previous research using this measure (Breen & Zuckerman, 1999; McDaniel & Zuckerman, 2003). For each item, participants indicated whether the statement was true or false. These items were summed to produce the impulsivity scale score (Cronbach's alpha = .79).

Timeline Followback (TLFB)—Alcohol use was assessed with the TLFB (Sobell & Sobell, 1992), a structured calendar assessment of drinking behavior. The TLFB was used to estimate past 90-day drinking frequency, average number of drinks per drinking day, and heavy episodic drinking frequency (4 or more drinks for women or 5 or more drinks for men).

Biphasic Alcohol Effects Scale (BAES)—Subjective response to alcohol was measured using the BAES (Martin, Earleywine, Musty, Perrine, & Swift, 1993), which contains 7 items assessing subjective stimulation (e.g., "energized," "high") and 7 items assessing subjective sedation (e.g., "drowsy," "tired"). Participants responded on a visual analogue scale (0–100) to indicate the extent to which they were currently experiencing each effect; participants were not asked to explicitly attribute their ratings to the effects of alcohol per se (Rueger, McNamara and King, 2009). Mean responses for each subscale at each of the 4 time points were used for analyses. Scores were transformed to a 0–10 scale (by dividing by 10) in order to aid model estimation. Cronbach's alphas ranged from .86 to .90 for stimulation and .78 to .88 for sedation across the 4 repeated assessments.

Craving—Craving was assessed at each time point with a single item that read, "How much do you want more of the infusion?" Participants responded on a 0–100 visual analogue scale, with values rescaled to a 0–10 scale. This approach to assessing craving is consistent with several alcohol administration studies (De Wit, 2000; Leeman, Corbin, & Fromme, 2009). The craving item was administered after the BAES at each time point.

Data Analysis Plan

One participant was excluded from analyses because of missing data on all subjective response variables. An additional participant was excluded due to extreme outlying values on all repeated measures variables (i.e., strings of 100 or 0 responses to items across all time points). Therefore, the final sample for the analysis was N=60. All variables in the model reasonably approximated univariate normal distributions (skewness<1.19; kurtosis<1.75). One extreme outlying value was observed on the impaired control variable (3.65 *SD* above the mean and clearly disconnected from the distribution), which was recoded to one unit greater than the next most extreme value to reduce its influence (Tabachnick & Fidell, 2007).

To test our hypotheses, we conducted multilevel structural equation modeling (MSEM) in Mplus version 7.3 (Muthén & Muthén, 2012) using the robust maximum likelihood estimator (MLR). We specified our MSEM consistent with the recommendations of Preacher et al. (2010) for modeling multilevel mediation when all variables contain both Level 1 (within-person) and Level 2 (between-person) variance (i.e., 1-1-1 mediation). When applied to repeated-measures data nested within individuals, this approach uses latent variable modeling to partition the variance into latent between-person components (latent estimates

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of person-level means across time points) and latent within-person components (latent estimates of within-person deviations from the person-level averages; Lüdtke et al., 2008; see also Simons, Wills, & Neal, 2014). This allows for an examination of within-person meditation without conflating the effects with between-person sources of variance (Preacher et al., 2010).

MSEM is analogous to more traditional techniques for disaggregating within- and between-person sources variance in a multilevel modeling (MLM) framework, which typically involve centering each observation of a predictor variable around the individual-level mean and including both this person-centered variable and the individual-level mean in the analysis (Raudenbush & Bryk, 2002). In contrast, MSEM uses latent variable modelling to partition the variance into the between- and within-person components, conferring a number of advantages such as reduced bias in the estimation of the between-person parameters and a more flexible framework for modeling multilevel mediation (Lüdtke et al., 2008; Preacher, Zhang, & Zyphur, 2011; Preacher et al., 2010). The results of MSEM can be interpreted in a similar fashion as results from the traditional MLM approach, in that the between-person level models associations between aggregate individual differences in the predictor variable and the outcome variable, whereas the within-person level models associations between state-like, time-varying changes in the predictor variable (i.e., within-person fluctuations over time relative to the person-level average) and the outcome variable (Preacher et al., 2010; see also Simons et al., 2014).

Data were structured such that there were 4 cases for each participant, corresponding to the 4 administrations of the subjective questionnaires (stimulation, sedation and craving) throughout the *ad lib* portion of the session. In addition, measured BrAC data for each participant were lagged such that subjective responses and craving assessed at a given time point were modeled as predictors of the BrAC reading taken approximately 15 minutes later. Given the rapidity with which self-administration during the CASE session is reflected in BrAC, this provided an index of alcohol self-administration in the period immediately following each subjective assessment.[3] Thus, within-person associations of subjective responses and craving with BrAC could be interpreted as associations of within-person ups and downs in subjective responses and craving during the session with immediately subsequent alcohol self-administration. Fifty-two participants had complete data on the repeated-measures variables at all four time points; eight participants had complete data at 3 of the 4 time points. Thus, the rate of missing data on the repeated-measures variables was low (8 time points out of a total of 240 possible time points; 3%). For any time point at which a participant did not have complete data on all of the repeated-measures variables, that entire time point was treated at missing and excluded from analyses. However, all 60 participants were retained as the analysis can accommodate differences across participants in the number of time points with Full Information Maximum Likelihood estimation (FIML).

[3]Although BrAC was measured every 15 minutes on average, for the present analysis we only included BrAC measurements taken approximately 15 minutes after the subjective questionnaires were administered. BrAC readings taken at 60, 90, and 120 min were not modeled in the present analysis as no subjective assessments were scheduled prior to these measurements.

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We examined hypothesized associations among subjective responses, craving, and BrAC, as well as the moderating role of impaired control, together in one MSEM model. Given that we hypothesized a relatively complex model, we applied a systematic model building approach. This approach involved adding hypothesized parameters to the model in a step-by-step fashion to evaluate the relative fit of each progressively more complex model (see Simons et al., 2014 for a similar approach). Our goal was to build the model according to our theoretically-based hypotheses while at the same time balancing model fit with parsimony. So, in addition to examining hypothesized parameters, certain parameters that were not hypothesized to be significant (e.g., direct paths from subjective response to BrAC) were examined during the model building phase to establish the relative fit of the hypothesized model against alternative plausible models. We planned to retain associations in the final model if they improved model fit, as determined by statistically significant likelihood ratio tests (calculated using formulas specific for MLR; Muthen & Muthen, n.d.). All paths in the model were estimated simultaneously at both levels 1 and 2 in order to permit disaggregation of within-person and between-person variance.

After arriving at the best fitting model, the statistical significance of indirect associations from subjective responses to craving to BrAC were evaluated using the MODEL CONSTRAINT command in MPLUS to generate standard errors (SE) and 95% confidence intervals (CI) for the estimates of the within- and between-person indirect associations[4] (Preacher et al., 2010). The delta method was used for estimating SEs and CIs as bootstrapping is not currently available for MLM with random slopes in MPLUS. To investigate the moderating influence of impaired control, we examined the hypothesized path from impaired control to the random slope for the within-person association between craving and BrAC. We planned to follow up by examining the conditional indirect associations between subjective responses and BrAC via craving by conditioning the random slope on high (1SD above the mean), average (mean), and low (1SD below the mean) levels of impaired control (i.e., moderated mediation).

Results

Descriptive Analyses

Table 1 shows the observed means, standard deviations, and confidence intervals for the subjective response and craving variables at each assessment, as well as the BrAC readings taken approximately 15 minutes after each assessment. Inspection of the means for the subjective stimulation, craving, and BrAC variables suggested that these variables rose and then fell during the session, on average. In contrast subjective sedation showed a slight average increase throughout the session. Standard deviations suggested considerable variability across participants at each time point. Mean BrAC immediately following the standardized priming phase was 27.53 mg% (95% CI [26.55, 28.51]), with little variability (*SD*=3.87). Across all observed BrAC measurements (including those not modeled in the

[4]As detailed in Preacher et al., 2010, estimates of indirect associations were calculated as a function of the fixed and/or random slopes comprising the indirect association. When a random slope was estimated at level 1, the between-person association between the two variables was estimated by adding the mean of each random slope to its corresponding “contextual effect” (Preacher et al., 2010). The MODEL CONTRAINT command was used to estimate standard errors for these between-person associations.

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MSEM analyses), peak observed BrAC during self-administration averaged 82.08 mg% (*SD*=24.51, 95% CI [75.88, 88.29]).

Table 2 shows means, standard deviations, and bivariate associations among individual difference variables and repeated measures variables aggregated across the session. As suggested by the large standard deviation in BrAC, there was substantial between-person variability in self-administration (see Hendershot et al., 2014). There were no differences based on sex, age, or ethnicity with respect to impaired control, impulsivity or subjective responses. The only observed sex differences were that men reported more drinks per drinking day and greater average craving during the CASE session than women.

Intraclass correlation coefficients were .51 for stimulation, .61 for sedation, .56 for craving, and .55 for BrAC, indicating that the total variance in these variables was comprised of fairly equal components of within-person and between-person variance.

Summary of Model Building Process

Table 3 shows the results of the model building process including the likelihood ratio tests and model fit estimates for each of the models tested. We began with a base model (Model 1) that included the hypothesized indirect associations from subjective response variables to BrAC mediated via craving while disaggregating within-person and between-person variance. Covariance estimates between stimulation and sedation at both the within- and between-person levels also were included. This base model included random intercepts but no random slopes. Also, the base model included the covariance estimates among the between-person moderators (impaired control, drinks per drinking day, and impulsivity) as well as their covariances with stimulation and sedation at the between person-level; however, paths from the between-person moderators to the random intercepts for craving and BrAC were constrained to zero in the base model in order to examine the impact on model fit of including these associations at a later step.

The next step in our model building process involved testing the addition of the direct associations from stimulation and sedation to BrAC (Model 2), which was necessary to determine whether the hypothesized indirect associations between subjective responses and BrAC were fully or partially mediated by craving. As shown, model fit estimates suggested that these direct paths should be retained. Also, because we hypothesized that the within-person association between craving and BrAC would vary among participants (as a function of individual differences in impaired control), we next examined the fit of a model that included a random slope for this within-person association, along with the covariances among this random slope, the random intercepts, and between-person subjective response variables (Model 3). Again, model fit indices supported the addition of these parameters to the model, and so they were retained (see Table 3). Next, we performed a data-driven step of examining the relative fit of models that included random slopes for the other within-person pathways (including all covariances among random slopes, intercepts, and between-person subjective response; Models 4a–d); this was necessary to determine the appropriate random effects structure in order to achieve proper model specification. Estimating the random slope for the within-person association between stimulation and craving further improved model

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fit; however, the inclusion of other random slope factors did not, and so these random slopes were not retained in the final model.

We next tested the hypothesis that the strength of the within-person association between craving and BrAC would depend on levels of impaired control, and that this moderating effect of impaired control would not be accounted for by alcohol use or trait impulsivity. To do so, we added the paths from impaired control, drinks per drinking day, and impulsivity to the random intercepts for craving and BrAC (to control for main effects) along with the paths from these variables to the random slope for the association between craving and impaired control (to test for moderation). Inclusion of these paths led to significant improvement in model fit according to the likelihood ratio test; however, the AIC and BIC values increased slightly, suggesting that this model may include unnecessary parameters. Indeed, of the 9 paths added at this step, only two were statistically significant (the paths from impaired control to the random slope factor and the random intercept for craving). Thus, we removed the nonsignificant paths from drinks per drinking day and impulsivity to the random intercepts and slope to obtain a more parsimonious model. Trimming these parameters did not result in significant decrements in model fit and resulted in a more parsimonious model as reflected in improved AIC and BIC values (Table 3).

Multilevel Mediation Model

The results of the final multilevel mediation model are presented in Figure 2. As hypothesized, there was a significant positive within-person association between stimulation and craving (as indicated by the statistically significant mean of the random slope; slope A). There was also a negative within-person association between sedation and craving (which was modeled as a fixed slope; see Figure 2). In turn, within-person variance in craving significantly predicted within-person variance in subsequent BrAC (at average levels of impaired control), as shown by the statistically significant intercept for the random slope (slope B) in Figure 2. Moreover, the direct within-person associations between both subjective response variables and BrAC were statistically significant and positive, indicating that both stimulation and sedation predicted unique variance in BrAC at the within-person level even after controlling for their indirect associations through craving (i.e., partial mediation).

At the between-person level, there were few significant associations among the variables (see Figure 2). One exception was a statistically significant negative between-person association between sedation and BrAC, indicating that individuals reporting lower sedation overall during the session had higher BrAC on average. Also as shown in Figure 2, individual differences in impaired control were significantly associated with variance in the random intercept for craving, indicating a between-person association between trait impaired control and average craving. Moreover, impaired control was significantly associated with variance in the slope for the within-person association between craving and BrAC, suggesting that participants who reported greater trait impaired control over alcohol showed stronger within-person associations between craving and subsequent BrAC during the self-administration session.

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Analysis of Indirect Associations

Given the significant association between impaired control and the random slope for the within-person association between craving and BrAC, we conditioned this slope on low, average, and high levels of impaired control in order to examine the conditional indirect associations from subjective responses to craving to BrAC. The within-person indirect association between stimulation and BrAC through craving was statistically significant and positive when conditioned on high (estimate=3.15, *SE*=1.26, *p*=.012, 95% CI [0.68, 5.63]) and average (estimate=2.10, *SE*=0.93, *p*=.023, 95% CI [0.28, 3.92]) levels of impaired control, but not on low levels of impaired control (estimate=1.05, *SE*=0.81, *p*=.195, 95% CI [−0.54, 2.63]). The within-person association between sedation and BrAC through craving was statistically significant and negative when conditioned on all three levels of impaired control: high (estimate=−1.80, *SE*=0.78, *p*=.021, 95% CI [−3.33, −0.27]), average (estimate=−1.29, *SE*=0.51, *p*=.012, 95% CI [−2.29, −0.28]), and low (estimate=−0.77, *SE*=0.34, *p*=.023, 95% CI [−1.43, −0.11]).

Discussion

Subjective responses to alcohol have received extensive empirical attention as risk factors for heavy drinking and AUD (Morean & Corbin, 2010; Quinn & Fromme, 2011). Some recent theoretical accounts of the role of subjective responses in drinking behavior have invoked within-person processes as mechanisms through which subjective responses relate to risk for AUD (e.g., state increases in subjective stimulation following alcohol consumption may be rewarding and lead to increased motivation to drink, thereby driving further alcohol consumption; King, de Wit, et al., 2011; King, Roche, et al., 2011; Ray et al., 2010). However, most research to date has focused exclusively on between-person associations among subjective responses and drinking behavior, with little empirical attention given to within-person associations over the course of a drinking episode. Through disaggregating within-person and between-person sources of variance, this study found evidence for the largely within-person nature of the associations among subjective responses, craving, and alcohol self-administration during a laboratory session.

In our MSEM model, we observed within-person associations between stimulation and craving (positive) and between sedation and craving (negative), which were not evident at the between-person level. These findings indicate that, irrespective of individual differences in average levels of subjective response and craving during the session, state fluctuations in stimulation and sedation within individuals over time were associated with corresponding state changes in craving. In turn, state changes in craving at a given time point proximally predicted alcohol self-administration, as indexed by BrAC measured 15 minutes later. Further, the hypothesized within-person indirect associations from subjective response variables to BrAC mediated via craving were statistically significant (when conditioned on average levels of impaired control). These findings advance the literature on subjective responses by providing novel empirical support for momentary within-person associations of subjective responses with alcohol consumption. Thus, the findings have implications for theoretical conceptualizations of the role of subjective responses in heavy drinking during a critical period of development (i.e., late adolescence).

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This study highlights the importance of disaggregating within-person and between-person sources of variance in subjective alcohol response research. For instance, consistent with prior between-person analyses (Ray et al, 2010; Rose et al., 2010), we did not observe a significant association between individual differences in average levels of sedative response to alcohol and craving. However, after extracting between-person variance from the repeated-measures data, a significant, negative association was evident at the within-person level. That is, regardless of average level of sedation, state increases in sedation were associated with corresponding declines in craving at a given point in time. Although differences in the observed associations between this and prior work could also be related to methodological differences (e.g., self-administration vs. standardized dosing paradigm), the current findings nonetheless contribute to a growing recognition of the importance of disentangling within-person and between-person processes in psychological research (Armeli, Todd, & Mohr, 2005; Curran & Bauer, 2011).

Our observation that most associations in our MSEM model were significant only at the within-person level may at first glance appear to be inconsistent with prior studies that have found associations among subjective responses and drinking behavior in between-person analyses. For example, studies have reported that individual differences in average subjective responses during a laboratory alcohol session, or subjective responses following a priming dose of alcohol, are associated with total alcohol consumption in an ad lib drinking session (e.g., Corbin et al., 2008; DeWit et al., 1989). However, one possible explanation for this apparent discrepancy is that these studies may have captured within-person associations between state fluctuations in subjective responses and alcohol consumption at the between-person level, with variability across individuals reflecting a “snap shot” of various points in the within-person process. Yet, it is important to acknowledge that prior studies may have indeed observed true between-person associations (i.e., trait-like individual differences in subjective response and overall self-administration) that were not detected in the present study for various other reasons (e.g., methodological differences, differences in sample composition). Further, we did observe a significant, negative association between individual differences in average sedation over the course of the session and average BrAC, a finding that is generally consistent with theoretical models of subjective responses to alcohol. Taken together, these findings suggest that the influence of sedation on alcohol-self administration may operate at both within-person and between-person levels, likely through different mechanisms. While this study provides an important first step toward disentangling within- and between-person sources of variance in these associations, further research is necessary to fully elucidate the mechanisms through which subjective response variables influence alcohol consumption at different levels of analysis.

Although the findings largely supported our hypotheses, we also observed some unanticipated results that serve to highlight the complexity in the links among subjective responses and alcohol self-administration. First, craving was only a partial mediator of the within-person associations of stimulation and sedation with BrAC, as we also observed direct within-person associations from stimulation and sedation to BrAC. Second, at the within-person level, sedation showed a negative indirect association with BrAC via craving, but also showed a positive direct association with BrAC. This pattern of findings has been termed *inconsistent mediation* (MacKinnon, Krull, & Lockwood, 2000), and may indicate

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that state changes in sedation could have opposing influences on self-administration behavior through different mechanisms, even at the within-person level. That is, the positive within-person association between sedation and BrAC could perhaps be explained by variables not included in this study that are positively correlated with both sedation and BrAC at the within-person level (e.g., positive perceptions of sedative effects of alcohol, negative reinforcement processes). Thus, more research is needed to further clarify these associations, including studies examining multiple mediators at both within-person and between-person levels.

Another important contribution of this study was the examination of the moderating role of trait impaired control over alcohol. Historically, impaired control over alcohol has held a central position in theoretical accounts of addiction (Jellinek, 1960), and contemporary research suggests an important role for impaired control in the development of AUD (Leeman et al., 2012). However, few studies to date have examined processes that may be related to impaired control in the context of alcohol self-administration. We found that individuals with relatively high levels of self-reported impaired control showed stronger within-person associations between craving and subsequent self-administration during the session, resulting in stronger within-person indirect associations between subjective response and self-administration mediated via craving. We also controlled for impulsivity and drinks per drinking day to help establish the specificity of impaired control in these associations. Further, while the negative within-person indirect association between sedation and BrAC mediated via craving was statistically significant at both relatively high and low values of impaired control, the positive within-person indirect association between stimulation and BrAC via craving was only statistically significant for participants reporting relatively greater impaired control. This finding suggests that impaired control may be especially important as a moderator of the link between stimulation, craving, and ongoing alcohol-self administration. Future research should extend the current findings by manipulating self-control processes, perhaps by providing an incentive to encourage participants to limit self-administration (Leeman et al., 2013; Muraven, Collins, & Neinhaus, 2002). This will allow for a direct examination of within-person subjective response processes linked to the acute experience of impaired control, and would provide an experimental paradigm that could be used to examine the efficacy of interventions that target impaired control processes.

This study supports the utility of CASE for examining theorized within-person associations between subjective responses to alcohol and ongoing self-administration. By combining the intravenous route of administration with a PBPK model, the CASE paradigm enables assessment of relatively rapid BrAC changes as a function of self-administration in the period immediately following the subjective assessments, while holding incremental changes in BAC virtually constant across participants. This level of control is not possible with traditional oral alcohol administration procedures. Thus, applying CASE allowed us to gain new insights into the role of subjective responses and craving in ongoing alcohol self-administration over the course of an alcohol session.

Despite the novelty of the findings and the strength of the methods and analytic approach, there are some limitations to this study that must be considered. An important limitation of

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the CASE paradigm is that the increased experimental control of this method comes at a cost to external validity. In real world drinking contexts, a multitude of additional factors are known to influence alcohol consumption, including alcohol-related cues, social influences, and automatic processes. Several of these factors also likely play a role in subjective responses to alcohol. However, the goal of this study was to focus on the specific role of subjective responses to alcohol and craving in alcohol self-administration. In this context, we prioritized the advantages of the CASE paradigm, which does not intend to replicate a natural drinking scenario, but affords greater experimental precision in studying the observed associations. The next step will be to build upon this study by examining the influence of manipulating environmental cues that are present in real-world drinking contexts.

An additional limitation is that the absence of a placebo condition makes it impossible to attribute subjective responses solely to pharmacological effects. Contextual cues and expectancy processes undoubtedly influence subjective responses in naturalistic drinking contexts, with probable implications for craving, self-administration, and impaired control. The present design did not allow us to model these processes nor did it allow us to separate pharmacological from non-pharmacological effects. However, it should be noted that a placebo manipulation has not been validated for the current paradigm—perhaps reflecting the questionable likelihood of maintaining a placebo manipulation during an extended intravenous self-administration session.

Moreover, we cannot rule out the possibility that baseline levels of stimulation, sedation, and craving prior to alcohol administration may have influenced ratings of subjective responses to alcohol. While adjusting post-alcohol ratings for baseline ratings (e.g., by calculating residualized changed scores) may have helped to isolate variance attributable to individual differences in resting levels of stimulation and sedation from variance attributable to the effects of alcohol, this would have introduced complications to the interpretation of the MSEM results by impacting the nature of the within- and between-person sources of variance reflected in the distributions of subjective ratings at each time point. Still, it is important to interpret the findings in the context of the limitations of not controlling for baseline ratings. For example, within-person variance in stimulation and sedation could be limited by floor or ceiling effects as a result of relatively high or low resting levels of stimulation and sedation among some participants. In this case, differences in resting levels of stimulation and sedation, rather than subjective responses to alcohol per se, may be partially responsible for the differences observed in the between-person versus within-person components of the model. Further, it is also possible that the magnitude of initial changes from baseline levels of stimulation and sedation in response to alcohol may have implications for the degree to which alcohol is perceived as rewarding, which could have independent effects on craving and self-administration processes.

A related point is that the instructions given to participants at the outset of the session (i.e., to achieve a level of intoxication that was pleasurable, but to avoid experiencing unpleasant effects) could have influenced both level of alcohol self-administration and perceptions of alcohol's effects (e.g., through activating alcohol expectancies). However, given that the

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same instructions were given to all participants, it is not possible to determine what effect the instructions may have had on the findings.

While the present study provides an important step toward establishing temporal associations among state changes in subjective responses and ongoing alcohol self-administration within a single session, it is still important to note that these findings are correlational. Further, while we included a measure of impulsivity to examine the specificity of associations with impaired control over and above trait impulsivity, the measure we used assessed a relatively narrow component of impulsivity (i.e., lack of planning or forethought). Given that impulsivity is a multifaceted construct (Smith et al., 2007), future studies should include more comprehensive assessments of impulsivity. Finally, while our focus on young heavy drinkers is appropriate given the developmental course of AUD, further research is necessary to extend these analyses to other populations, as associations among subjective responses to alcohol and craving have been shown to vary across social drinkers and alcohol dependent samples (e.g., Bujarski & Ray, 2014).

In summary, this study provides further insight into the role of subjective responses to alcohol and craving in alcohol self-administration among young heavy drinkers. The findings are consistent with theoretical conceptualizations that invoke reward-related, within-person processes, and also suggest that these processes may be moderated by individual differences in risk factors such as impaired control over alcohol. An important next step will be to evaluate the potential relevance of these findings for studying pharmacological (Miranda, Ray, et al., 2014) or psychoeducation (Schuckit et al., 2015) interventions that consider subjective responses to alcohol in the context of youth prevention efforts.

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General Scientific Summary

This study found that state changes in subjective stimulant and sedative effects of alcohol during an intravenous alcohol self-administration session were associated with craving for alcohol, which in turn predicted ongoing self-administration behavior. In addition, participants reporting greater trait impaired control over alcohol showed stronger associations between craving and alcohol self-administration.

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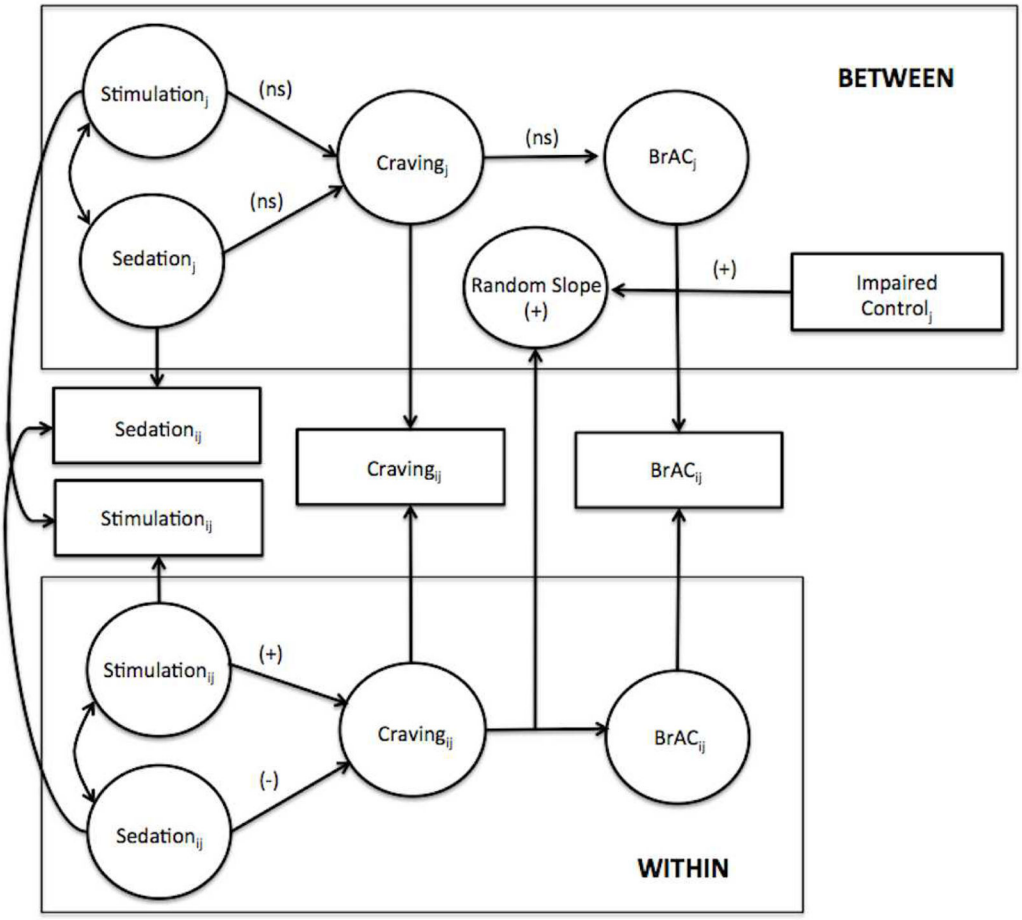

Figure 1.

Conceptual diagram of the multilevel structural equation model (MSEM) showing hypothesized associations at each level of analysis. The center panel represents the observed variables, with observations at each of the four time points (*i*) for every participant (*j*). Each (*i*) measurement of BrAC is lagged approximately 15 minutes from the corresponding measurement of subjective response and craving. The top panel shows the between-person component of the model and the bottom panel shows the within-person component. Symbols in parentheses above path arrows denote whether the path is hypothesized to be positive (+), negative (−), or non significant (ns). As shown, we hypothesized that the associations among stimulation, sedation, craving and BrAC would be significant at the within-person level but not at the between person level. Random intercepts for all within-person associations are estimated but are not depicted in the figure for simplicity. A random slopes for the within-person association between craving and BrAC was estimated, as variance in this slope was hypothesized to be associated with individual differences in impaired control over alcohol (i.e., moderated by impaired control). This random slope factor is shown on the between-person level as the value of the slope varies across participants. BrAC= Breath alcohol content.

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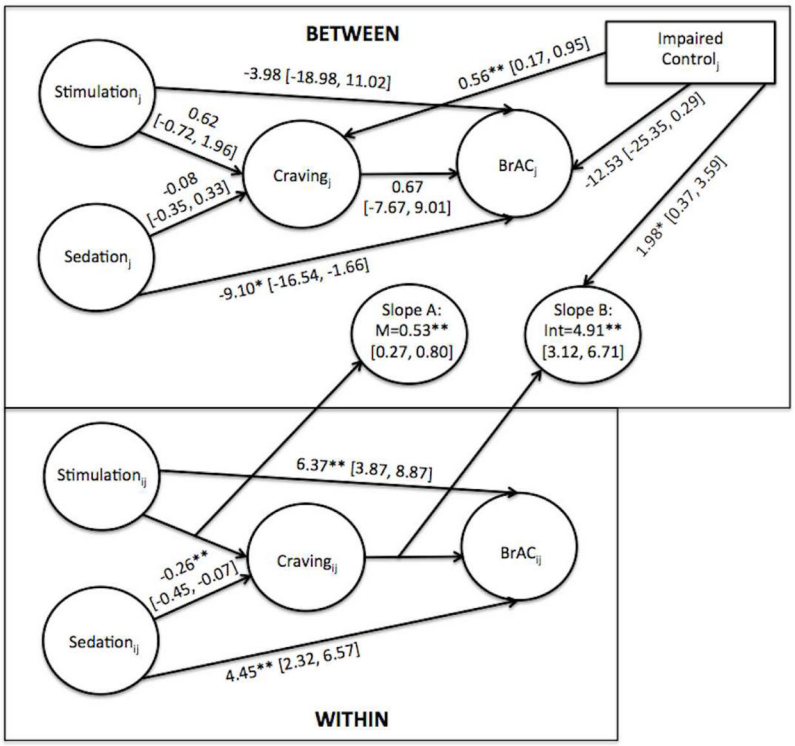

Figure 2.

Final multilevel structural equation model (MSEM) of the associations among subjective response, craving, BrAC, and impaired control. Unstandardized coefficients are shown with 95% confidence intervals in square brackets. In this figure, the observed variables are omitted, but estimation of latent between and within components was done as depicted in Figure 1. The top panel shows the between-person component of the model and the bottom panel shows the within-person component. Random intercepts for all within-person associations were estimated but are not depicted in the figure for simplicity. Random slopes for the within-person associations between stimulation and craving (Slope A) and between craving and BrAC (Slope B) were estimated; random slopes freely covaried with one another and all random intercepts, but these covariances are omitted from the figure for simplicity. The random intercepts and random slope B were regressed on impaired control; the intercepts (int) of the random slopes represent the predicted value of the slope at average levels of impaired control. Although not shown in the figure, impulsivity and drinks per drinking day were also included in the model, but only the covariances among these variables and impaired control were retained in the final model (i.e., paths to the random intercepts and slope factors were not retained). BrAC= Breath alcohol content. *p<.05, **p<.01.

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Table 1

Observed means, standard deviations, and time of assessment for repeated measures of subjective variables (stimulation, sedation and craving) as well as measured BrAC at each time point used in the analysis.

Timepoint		**1**	**2**	**3**	**4**
Time of subjective assessment (min)		15	30	60	90
Subjective variables					
Stimulation	*M*	48.75	54.41	55.84	53.37
	SD	14.22	12.73	13.84	14.55
	95% CI	[45.12, 52.37]	[51.18, 57.63]	[52.31, 59.37]	[49.59, 57.14]
Sedation	*M*	28.66	33.50	37.73	39.73
	SD	15.40	15.40	15.40	15.40
	95% CI	[24.73, 32.59]	[29.81, 37.20]	[33.35, 42.12]	[35.25, 44.22]
Craving	*M*	53.75	55.93	58.19	50.39
	SD	19.14	16.44	18.30	25.53
	95% CI	[48.86, 58.63]	[51.77, 60.09]	[53.52, 62.86]	[43.76, 57.01]
Time of BrAC assessment (min)		30	45	75	105
Observed BrAC	*M*	48.48	63.60	70.71	67.39
	SD	11.83	21.67	27.51	27.16
	95% CI	[45.49, 51.48]	[58.12, 69.08]	[63.69, 77.73]	[60.33, 74.44]

Note. Time in min refers to time since the start of the alcohol infusion (including the priming phase). The first subjective assessment followed the priming phase and preceded the start of the ad lib phase (which occurred at approximately 15 min). BrAC readings were lagged 15 minutes from the corresponding subjective assessments. In the present analysis, we only included BrAC measurements taken approximately 15 minutes after the subjective questionnaires were administered.

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Table 2

Means, standard deviations, and correlations among between person variables and person-level means of subjective response, craving, and BrAC during the CASE session.

	1	2	3	4	5	6	7	8	9	*M*	*SD*
1. Impaired Control	-									1.97	0.66
2. Impulsivity	.04	-								2.88	2.41
3. Avg Quantity	.32*	.19	-							5.28	1.94
4. Women	.08	−.05	−.35**	-						0.52	0.50
5. Age	.01	−.03	−.35**	.14	-					19.92	0.87
6. White	−.13	.03	−.08	.06	.31*	-				0.68	0.47
7. Mean stimulation	.07	.03	.17	−.12	−.06	.18	-			52.84	11.12
8. Mean sedation	−.14	−.20	−.19	.01	−.02	.04	−.04	-		34.63	14.27
9. Mean craving	.34**	.03	.28*	−.28*	−.18	.03	.47**	−.14	-	54.32	16.77
10. Mean BrAC	.00	.12	.22†	−.21	−.23†	.05	.15	−.36**	.49**	62.45	19.70

Note.

† p≤.10;

* p≤.05;

** p≤.01; *n*=60 for all variables.

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Table 3

Summary of model building process for multilevel mediation model.

Model	Hypothesis/Rationale for Step	Results	AIC	BIC	vs.	χ^2	df	*p*
1. Base model. Indirect associations from subjective response variables to BrAC mediated via craving at both within- and between-person levels. No direct paths from stimulation and sedation to BrAC. No random slopes.	At the within-person level, subjective responses will be associated with craving, and craving will be associated with BrAC.	Hypothesized associations observed.	4938.81	4948.52	-	-	-	-
2. Add direct paths from stimulation and sedation to BrAC at both levels.	No hypothesis; Data driven step of determining partial or full mediation.	Inclusion of direct paths significantly improved model fit.	4905.69	4916.50	1	46.22**	4	<.01
3. Add random slope for within-person association between craving and BrAC.	Random slope will have significant variance (which will then be predicted by impaired control in step 5).	Inclusion of random slope significantly improved model fit.	4905.30	4917.50	2	12.98*	5	.02
4. Add random slopes for other within-person associations:	No hypothesis; Data driven step of determining appropriate random effects structure.	Random slope for stimulation to craving should be included.						
a. stimulation to craving			4901.66	4915.52	3	14.13*	6	.03
b. sedation to craving			4907.62	4921.48	3	6.72	6	.35
c. stimulation to BrAC			4902.54	4916.41	3	8.73	6	.19
d. sedation to BrAC			4906.82	4920.69	3	0.74	6	.99
5. Add paths from impaired control, drinks per drinking day, and impulsivity to random intercepts and random slope for the within-person association between craving and BrAC.	Impaired control will be independently associated with the random slope (i.e., a significant moderator of the association) while controlling for alcohol use and trait impulsivity; paths to random intercepts are necessary to control for main effects before examining cross-level interaction.	Significant paths from impaired control to random slope observed; No paths from drinks per drinking day or trait impulsivity were significant.	4902.35	4918.71	4a	17.96*	9	.04
6. Trim nonsignificant paths from between-person covariates to random slope and intercepts.	No hypothesis; Data-driven step of trimming model of unnecessary parameters to achieve best-fitting model.	Model fit the data just as well as model 5 and is more parsimonious.	4894.13	4908.82	5	3.61	6	.73

Note. Model 6 represents the final model. AIC= Akaikeinformation criterion; BIC = Bayesian information criterion (sample size adjusted); vs. = comparison model for likelihood ratio test; χ^2 value is the test statistic for the likelihood ratio test.

*p≤.05;

**p≤.01.