Published in final edited form as:

Alcohol Clin Exp Res. 2020 May ; 44(5): 1123–1131. doi:10.1111/acer.14322.

Relations Between Acute Effects of Alcohol on Response Inhibition, Impaired Control over Alcohol Use, and Alcohol-Related Problems

William R. Corbin, **Benjamin L. Berey**, **Jack T. Waddell**, **Robert F. Leeman**

Arizona State University (WRC, JTW), Tempe, Arizona; University of Florida (BLB, RFL), Gainesville, Florida; and Yale School of Medicine (RFL), New Haven, Connecticut.

Abstract

Background: Alcohol consistently impairs response inhibition in the laboratory, and alcohol impairment of response inhibition may lead to excess consumption or increases in intoxicated risk behavior, both of which contribute to risk for alcohol-related problems. To our knowledge, no prior studies have examined relations between alcohol impairment of response inhibition and either impaired control over alcohol (i.e., inability to adhere to predetermined drinking limits) or real-world alcohol-related problems. The current study addressed this gap in the literature.

Methods: Young adult social drinkers (N = 215, 76% male) participated in a between-subjects, placebo-controlled alcohol challenge study and completed self-reports approximately 2 weeks later. Multilevel models were used to examine the hypothesis that alcohol impairment of response inhibition would indirectly lead to alcohol-related problems through impaired control over alcohol use.

Results: Greater alcohol-induced impairment of response inhibition and impaired control over alcohol use were both significant predictors of alcohol-related problems. However, greater alcohol-induced response inhibition was not a significant predictor of impaired control over alcohol use.

Conclusions: To our knowledge, this is the first study demonstrating relationships between alcohol impairment of response inhibition and real-world alcohol-related problems and the first to address relationships between alcohol impairment of response inhibition and impaired control over alcohol use. These results suggest that impaired control over alcohol use may result from deficits in the trait ability to control behavior rather than deficits in alcohol-induced response inhibition. Regardless, results suggest that alcohol impairment of response inhibition and impaired control over alcohol are both worth-while intervention targets.

Keywords

Response Inhibition; Impaired Control Over Alcohol Use; Alcohol-Related Problems; Alcohol Consumption; Cued Go/No-Go

Reprint requests: William R. Corbin, PhD, Department of Psychology, Arizona State University, 900 S McAllister Ave, Tempe, AZ 85281; Tel.: 480-766-1846; Fax: 480-965-8544; wcorbin@asu.edu.

CONFLICT OF INTEREST

None of the authors have a conflict of interest.

Heavy drinking is prevalent among young adults (Grant et al., 2015) and is associated with myriad negative consequences, such as drinking and driving (Baker, Braver, Chen, Li, and Williams, 2002; Duncan, 1997), sexual assault (Abbey, 2002), injury, and death (Hingson et al., 2009). This is partly attributable to alcohol's negative impact on the ability to regulate behavior (Mulvihill et al., 1997; Weafer and Fillmore, 2008). Accordingly, individuals who are more susceptible to such impairment should presumably be at greater risk for alcohol-related problems. Thus, identifying individual differences in the extent to which alcohol produces impulsive/disinhibited behavior and the relation to alcohol-related problems has theoretical, clinical, and public health implications.

Impulsivity, or the proclivity toward swift action with suboptimal regard for future consequences (Brewer and Potenza, 2008; Moeller et al., 2001), is an established risk factor for heavy drinking and alcohol-related negative outcomes (Dick et al., 2010; Lejuez et al., 2010). Importantly, extensive empirical evidence suggests that impulsivity is a heterogeneous construct incorporating aspects of behavior and cognition (Caswell, Bond, Duka, and Morgan, 2015; King et al., 2014; MacKillop et al., 2016). One particular aspect of impulsive behavior that is sensitive to the acute effects of alcohol is behavioral response impulsivity (e.g., Bartholow et al., 2018; Fillmore, 2003; Fillmore and Weafer, 2012; Roberts, Monem, and Fillmore, 2016). Behavioral response impulsivity assesses motoric response inhibition and is commonly measured using computerized tasks (Hamilton et al., 2015; Jentsch et al., 2014). For example, the cued go/no-go task (CGNG; Fillmore and Weafer, 2004) operationalizes response inhibition as the ability to respond accurately to go targets and refrain from responding to no-go targets (i.e., avoiding inhibition errors). Greater impairment of response inhibition has been related to alcohol use in both human (Henges and Marczinski, 2012) and animal models (Wilhelm, Reeves, Phillips, and Mitchell, 2007). Further, several studies have shown that impairment of response inhibition increases following small-to-moderate doses of alcohol (for a review, see Weafer and Fillmore, 2016).

During a recent intravenous alcohol challenge study in which a blood alcohol level (BAL) of 0.8 g/kg was held constant for 80 minutes, Hendershot and colleagues (2015) examined response inhibition among primarily underage social drinkers. Results indicated that impairment of response inhibition increased on the CGNG task as BALs were rising and showed increased impairment, while BALs were held constant. Further, Miller and Fillmore (2014) used the CGNG task to evaluate response inhibition among social drinkers following a counterbalanced dose of oral alcohol(0.65g/kg) or placebo (0.0g/kg). Results indicated that impairment of response inhibition was significantly greater in the alcohol condition and that these effects persisted even 5 hours after drinking. In sum, alcohol affects response inhibition at a range of BALs (including moderate BALs), and impairment persists on the descending limb of the blood alcohol curve.

Although impairment of response inhibition under alcohol is presumed to lead to alcohol-related problems, surprisingly little research has addressed this possibility. We are not aware of any prior studies examining relations between impaired response inhibition under alcohol and real-world alcohol problems, but impaired response inhibition under alcohol is associated with subsequent ad libitum alcohol consumption (Weafer and Fillmore, 2008) and

increased alcohol craving (Papachristou et al., 2013). Impairment of response inhibition under alcohol has also been linked to willingness to drive after drinking (Weafer and Fillmore, 2012), and behavioral willingness correlates significantly with engagement in risky behavior (Pomery et al., 2009).

Like alcohol-impaired response inhibition, impaired control pertains directly to alcohol use. Impaired control over alcohol is defined as difficulty adhering to predetermined limits on drinking with regard to the amount one drinks and/or the amount of time spent drinking (Heather et al., 1993; Leeman et al., 2014; Leeman et al., 2012). Pertinent to the present study, impaired control over alcohol is potentially related to behavioral response impulsivity. That is, impaired control over alcohol may characterize a broad failure to control one's behavior in alcohol-specific contexts (Patock-Peckham et al., 2001). Impaired control over alcohol is often endorsed by young adult drinkers without an extensive history of heavy drinking (Beseler, Taylor, and Leeman, 2010), and by younger drinkers transitioning from social to problematic drinking (Buu et al., 2012). Further, impaired control over alcohol was one of the symptoms adult males in alcohol treatment recalled occurring the earliest in their drinking histories (Chick and Duffy, 1979). Thus, evidence indicates that impaired control over alcohol precipitates more problematic levels of alcohol use (Heather et al., 1993; Leeman et al., 2014; Leeman et al., 2012). Indeed, previous cross-sectional research has found that greater impaired control over alcohol relates to greater alcohol-related problems among college students (Leeman et al., 2007; Leeman et al., 2009; Nagoshi, 1999; Patock-Peckham and Morgan-Lopez, 2006) and young adults (Wardell et al., 2016). Prospectively, greater impaired control over alcohol predicted risk for alcohol dependence among adolescents and young adults from a community sample (Behrendt et al., 2008) and among college students (Leeman et al., 2009). Thus, efforts to understand links among impaired control over alcohol use, impaired response inhibition under alcohol, and alcohol-related problems are warranted. Evidence for such links would have important implications for interventions targeting "in-the-moment" impairment of behavioral control to reduce alcohol-related harms.

Prior studies have also failed to address underlying mechanisms linking impairment of response inhibition under alcohol to alcohol-related problems. One potential mechanism of influence is the ability (or inability) to adhere to self-imposed limits on alcohol use (i.e., impaired control; Heather et al., 1993). Given that behavioral response impulsivity (i.e., response inhibition) entails difficulty withholding responses to compelling stimuli, and young adults who drink frequently are likely to perceive alcohol as a compelling stimulus, those with impaired response inhibition may have difficulties adhering to predetermined limits on alcohol use (i.e., impaired control over alcohol). Although prior studies have not specifically examined relations between alcohol impairment of response inhibition and impaired control over alcohol use, laboratory-based studies have shown that alcohol impairment of response inhibition is related to greater overall ad libitum consumption (Gan et al, 2014; Weafer and Fillmore, 2008). Moreover, small-to-moderate doses of alcohol can impair response inhibition (Weafer & Fillmore, 2016), whereas higher quantities of alcohol are typically required to impair behavioral activation (de Wit, Crean, & Richards, 2000; Miller and Fillmore, 2014). Accordingly, one may still be capable of seeking alcohol, but the capacity to impede this impulse and adhere to self-imposed limits on alcohol (i.e., impaired

control) may be compromised. Thus, impaired response inhibition may contribute to impaired control over drinking within a session, and may exacerbate disinhibited behavior, leading to alcohol-related problems.

Accordingly, using data from a large alcohol challenge study (Corbin et al., 2015a, Corbin et al., 2015b), the aims of the current study were to examine direct effects of response inhibition following alcohol consumption on impaired control over alcohol use and alcohol-related problems, and the extent to which impaired control over alcohol mediates the relation between impairment of response inhibition and alcohol-related problems (See Fig. 1 for a graphic depiction of the theoretical model). We hypothesized that greater impairment of response inhibition would be associated with heightened impaired control over alcohol use and alcohol-related problems. Further, we hypothesized that response inhibition from alcohol would be indirectly related to alcohol problems via impaired control over alcohol use.

MATERIALS AND METHODS

Participants

Individuals between the ages of 21 and 30 (N = 215) were recruited from 2 college campuses, 1 in the northeast and 1 in the southwest region of the United States, and their surrounding communities. Participants were predominately male (N = 163), and 75% were Caucasian, with the remaining identifying as African American (2.3%), Asian (5.6%), American Indian/Alaskan Native (1%), or other (14%). Twenty-six percent of participants identified as Hispanic, and most were college students (72%). Because the parent study aimed to address relations between alcohol and gambling, eligible participants must have reported (i) that poker was among their top 3 preferred forms of gambling, (ii) playing poker at least once in the past year, and (iii) having consumed 3 or more drinks at least once per week, on average, over the past 3 months. To minimize potential risk associated with alcohol administration, participants were excluded if they reported (i) a flushing response to alcohol, (ii) current or past medical conditions that would contraindicate alcohol consumption, (iii) medications that would contraindicate alcohol consumption, or (iv) being pregnant. Individuals with a history of attendance in abstinence-oriented programs for alcohol or gambling were also excluded. All study procedures and protocols were approved by the Institutional Review Boards at both universities.

Procedure

Data collection involved 2 sessions, including a beverage administration session and a follow-up session for collection of survey and interview data. At the outset, all participants provided written informed consent. Next, female participants were required to take a pregnancy test, and all participants had to verify they were 21 years of age or older and provide a breath sample to verify a 0.00 g% blood alcohol concentration (BAC). Participants also completed a baseline cued go/no-go task to assess response inhibition at baseline.

Participants were randomly assigned, between-subjects to a beverage condition (target BAC = 0.08 g% or 0.00 g%) in groups of 2 to 4 participants. Group composition with regard to

sex and age varied, and efforts were made to ensure that participants did not know each other before the session. All participants within a group received the same beverage (113 placebo, 102 alcohol) and were brought into a simulated bar, with alcohol cues such as a front/back bar with barstools, a backlit wall with alcohol bottles, and neon liquor–related signs. Group beverage administration was used to increase the external validity of the drinking context (Baer, 2002; Gupta, and Derevensky, 1997). Although research supervisors were aware of the participant's beverage condition, study staff who served the beverages and administered all study measures (other than BAC measurements) were blind to study condition.

Participants in the alcohol condition were given a dose of alcohol that was precalculated based on their weight and sex to target a BAC of 0.08 g% (Curtin and Fairchild, 2003). Drinks consisted of 3 parts mixer (i.e., diet 7-up, cranberry juice, lime juice) and 1 part 80-proof vodka. Participants in the placebo condition consumed the same mixer, but were given flattened tonic water instead of alcohol with the same 3:1 ratio. The total beverage volume was administered in 3 equally sized beverages, and participants had 10 minutes to consume each beverage. Following the last beverage, participants underwent a 15-minute absorption period followed by a breath alcohol reading using a handheld breathalyzer. Breath alcohol readings were hidden from the view of research assistants and participants by the research supervisor. Following beverage administration, participants completed the first assessment of subjective response (SR) to alcohol and were allowed to play a simulated video poker game in the simulated bar laboratory (see Corbin and Cronce, 2017 for details). Results regarding video poker play and subjective response have been reported previously (Corbin and Cronce, 2017) and are outside the scope of the present study. As blood alcohol levels were descending, participants completed the cued go/no-go Task (CGNG; Fillmore and Weafer, 2004) in a separate area of the laboratory adjacent to the simulated bar to assess impairment of response inhibition relative to baseline performance. In accordance with NIAAA (2005) guidelines, participants who received alcohol were required to stay in the laboratory until their BAC was ≤0.02 g%.

Approximately 1 week after the first session, participants returned to the laboratory to complete both computer-based and interview-based assessments. This session lasted roughly 1 hour. Participants reported on a range of alcohol and gambling-related behaviors/cognitions (e.g., alcohol consumption and problems, impulsivity, impaired control over alcohol use). Participants were then debriefed and compensated.

Measures

Demographics.—Variables included biological sex, race, ethnicity, and college student status.

Alcohol Consumption.—Past 30-day alcohol use was assessed via the Timeline Followback (TLFB; Sobell and Sobell, 1992). Participants reported the frequency (number of episodes), quantity (number of standard drinks for each episode), and time of consumption (number of hours for each episode) for each drinking day for the 30 days prior to the first laboratory session. A standard drink conversion chart was used to ensure that

participants reported consumption in standard drink units (e.g., 12 oz beer, 1.5 oz hard liquor, 5 oz wine). The TLFB shows strong reliability across young adults (r = 0.86 to 0.97) and psychiatric patients (r = 0.73 to 1.0) and is positively associated with other measures of drinking frequency and quantity (Carey et al., 2004; Sobell and Sobell, 1992). Total consumption during the past 30 days was used as a covariate in analyses.

Manipulation Check.—To assess the effectiveness of the placebo manipulation, concurrent with the first BAC assessment after beverage administration, participants were asked to estimate their current BAC and the number of standard alcohol drinks they thought they had consumed.

Response Inhibition.—The cued go/no-go task (CGNG; Fillmore and Weafer, 2004) measures response inhibition as the ability to inhibit instigated "prepotent" responses. This task consists of 250 trials during which participants are asked to respond to "go" targets and inhibit responses to "no-go" targets, while responding as quickly as possible. Each trial consists of a fixation point (+) for 800 milliseconds, a 500-millisecond break, a cue (i.e., a vertical or horizontal box) followed by a variable delay (100, 200, 300, 400, or 500 milliseconds), and a target stimulus (i.e., the color green or blue). Participants were instructed to press the forward slash key (/) if the target stimulus was green, and to inhibit a response if the target stimulus was blue. The cues (vertical and horizontal boxes) signal the likelihood that the target stimulus will be green/blue as 80% of vertical boxes are green and 80% of horizontal boxes are blue. This creates a prepotent response to respond to vertical boxes, increasing the difficulty of inhibiting a response. The CGNG was assessed at baseline and again on the descending limb of the blood alcohol curve. The mean BAC immediately following the CGNG task was0.067 g%. The number of times a participant failed to inhibit a response was used as an index of difficulty with response inhibition.

Alcohol Problems.—Alcohol problems were assessed using the Rutgers Alcohol Problem Index (RAPI; White and Labouvie, 1989). This 23-item measure assessed problems associated with alcohol use (e.g., getting into fights, going to school/work drunk) during the past 3 months. Similar to prior studies (Leeman et al., 2007, 2009; Wardell et al., 2016), we removed 3 items related to impaired control over alcohol use to ensure that relations between impaired control over alcohol use and alcohol-related problems were not a function of overlapping items. The 20-item scale showed good internal consistency reliability in our sample (α = 0.84).

Impaired Control Over Alcohol Use.—The Impaired Control Scale (ICS; Heather et al., 1993; Heather et al., 1998) includes 10 items (rated on a 1 to 5 scale) assessing the degree to which participants (a) have difficulty reducing or stopping drinking, and (b) tend to drink more intensely/for longer than planned. Sample items include "I have found it difficult to limit the amount I drank," and "even when I intended having only 1 or 2 drinks, I have ended up having many more." Higher scores indicate greater difficulty limiting alcohol consumption. Participants were asked to respond to each question with respect to their behavior over the past 3 months. The ICS demonstrated good internal consistency reliability in our sample (α = 0.84).

Data Analytic Plan

Prior to conducting the primary analyses, all variables were examined for assumptions of normality and variables were transformed as necessary. We also removed participants in the alcohol condition who did not reach a BAC of 0.06 g% and participants in the placebo condition who did not believe they had consumed alcohol.

The primary analyses were conducted using multilevel models in Mplus 7.4 (Muthen and Muthen, 2015), given that participants were randomized to the alcohol and placebo conditions in groups of 2 to 4 and completed all study tasks within their assigned groups (individual participants nested within groups). Unconditional models were initially tested to determine the degree of variability in the outcomes that was attributable to the group in which each participant completed study procedures using the intraclass correlation (ICC). In the conditional models, group-level effects (beverage condition) were modeled at level 2, whereas individual-level covariates including biological sex (female = 0; male = 1), college status (0 = non-student; 1 = student), number of drinks consumed in the past 30 days from the TLFB, and baseline (sober) CGNG performance were included at level 1.

Consistent with recommendation by Enders and Tofighi (2007), all tests of level 1 covariate effects used group mean centering to identify their effects at the individual level, independent of group-level effects. In contrast, when level 2 variables (beverage condition) were added to the models, the level 1 variables were grand mean–centered to appropriately account for their effects. Tests of cross-level interactions employed group-mean centering of the relevant leve1 1 variable (e.g., CGNG performance following beverage consumption).

We first examined the main effect of beverage condition on CGNG performance, controlling for effects of the level 1 covariates, including baseline CGNG performance. Next, to evaluate relations between CGNG performance under alcohol (relative to placebo) and impaired control over alcohol use and alcohol-related problems, we examined beverage by CGNG interactions for these 2 outcomes. Cross-level interactions between beverage condition and CGNG performance were tested by specifying a random slope for the effect of CGNG performance on the relevant outcome (impaired control over alcohol use or alcohol-related problems) and including beverage condition as a predictor of the random slope at level 2. Significant interactions were decomposed using model constraints to examine simple main effects of CGNG performance on the outcomes by beverage condition. Interactions were also plotted using model constraints and loop plots within Mplus. A third model included both impaired control over alcohol use and alcohol-related problems as outcomes with cross-level interactions between beverage condition and CGNG performance following drink administration predicting both outcomes. This model also specified a direct effect of impaired control over alcohol use on alcohol-related problems. Tests of moderated indirect effects of CGNG impairment on alcohol-related problems through impaired control over alcohol use were planned if the interaction between beverage condition and CGNG performance was significant for impaired control over alcohol use, and impaired control over alcohol use was a significant predictor of alcohol-related problems.

RESULTS

Preliminary Analyses

Examination of the distributions of the variables identified significant positive skew for CGNG inhibition failures (baseline and postbeverage), typical monthly drinking, and alcohol-related problems. However, examination of residual plots suggested only minor deviations from normality, and robust maximum-likelihood estimation (MLR) is robust in the context of such minimal departures for normality. Further, leaving the variables in their original forms facilitates interpretation of the findings. Thus, analyses utilized the raw variables and MLR estimation.

Examination of BACs (in the alcohol condition) and estimated BAC and number of drinks consumed (in the placebo condition) identified 14 participants in the alcohol condition who did not reach a BAC of 0.06 g%, and 7 participants in the placebo condition who did not believe that they had consumed any alcohol ($n = 7$), resulting in a final sample size of 215 for the primary analyses. Sample descriptive statistics by beverage condition and bivariate correlations among study variables are provided in Tables 1 and 2, respectively.

Missing data were minimal (less than 5%) for all variables. A total of 12 participants did not have CGNG scores postbeverage administration, one participant was missing TLFB drinking data, and 5 participants were missing alcohol problems and impaired control data. There were no significant mean differences in drinking data between those who did and did not have valid postadministration CGNG data, and no significant mean differences in baseline or intoxicated CGNG performance between those who did and did not have valid drinking data. As such, it was appropriate to use FIML to estimate missing data.

Primary Analyses

In the unconditional model for CGNG performance, the ICC was 0.13, suggesting substantial group-level variability in CGNG performance. In the model for CGNG performance, the variances for the random slopes were not significant for any of the level 1 covariates (p values > 0.46), so the model was reestimated without random slopes and including FIML estimation of missing data. In this model, all exogenous variables were initially allowed to correlated and then the model was reestimated with the inclusion only significant correlations among the exogenous variables. Significant correlations were observed between past month drinking and both sex ($p < 0.001$) and student status ($p = 0.01$), with heavier drinking among men and college students. The only *significant* level 1 covariate predictor of postbeverage CGNG performance was baseline CGNG performance ($b = 1.02$, SE = 0.12, $p < 0.001$), with better baseline performance associated with better performance following drink administration. When beverage condition was added to the model at level 2, there was a significant effect of beverage condition, with more inhibition failures among participants in the alcohol condition, relative to the placebo condition ($b = 2.23$, SE = 0.73, $p = 0.002$).

In the unconditional model for impaired control over alcohol use, the ICC was 0.14, again suggesting substantial group-level variability in the outcome variable. In the initial model examining covariate effects with random slopes, the model would not converge and separate

models with one random effect per model showed that the model with a random effect of baseline response inhibition on impaired control was the source of the model nonconvergence. The model converged with the removal of this random effect, and none of the remaining random slopes for the level 1 covariates of impaired control over alcohol were significant (all p values > 0.50), so the model was reestimated without random slopes. Significant correlations among exogenous variables from the prior model were retained, and the correlation between baseline CGNG performance and postbeverage consumption was included given that baseline CGNG performance was a significant predictor of postbeverage CGNG performance in the prior model. In this model, the only significant level 1 covariate was past month alcohol use (b = 0.02, SE = 0.01, p = 0.002), with heavier drinking associated with greater impaired control over alcohol use. When the beverage condition by CGNG interaction was added to the model, the effect was in the expected direction but did not reach statistical significance (b = 0.02, SE = 0.02, p = 0.32).

In the unconditional model for alcohol-related problems, the ICC was 0.004 suggesting very little group-level variability in alcohol-related problems. To be consistent across analyses, we retained the multilevel framework for this analysis despite the very small ICC. In the initial covariate model without estimation of missing data, none of the random slopes for the level 1 covariates were significant (all p values > 0.26), so the model was reestimated without random slopes and missing data were estimated using FIML. The same correlations among exogenous variables from the model for impaired control over alcohol were retained. In this model, significant covariate effects were identified for student status (b = 3.09, SE = 1.11, p = 0.006), and past month alcohol use (b = 0.22, SE = 0.08, p = 0.003), with college students and heavier drinkers self-reporting more alcohol-related problems. When added to the model, the beverage condition by CGNG interaction was statistically significant (b = 0.62, SE = 0.26, p = 0.02). To decompose the interaction, separate models were examined by beverage condition, with CGNG performance after drink administration as a predictor of alcohol-related problems. Within the placebo condition, postbeverage CGNG performance was not significantly associated with alcohol-related problems (b = −0.18, SE = 0.26, p = 0.49). In contrast, postbeverage CGNG performance was a significant predictor of alcohol-related problems among participants who received alcohol (b = 0.44, SE = 0.22, p = 0.03). See Fig. 2 for a graphic depiction of the interaction.

In the final model testing the full moderated mediation model, cross-level interactions were simultaneously modeled for impaired control over alcohol use and alcohol-related problems, and alcohol-related problems were directly predicted by impaired control over alcohol. Impaired control over alcohol use and alcohol-related problems was also allowed to freely covary at level 2 of the model. Given that none of the random slopes for the level 1 covariates were significant for either impaired control over alcohol use or alcohol-related problems in prior models, we proceeded directly to testing a model with random slopes only for the effects of CGNG performance on the outcomes to allow for tests of cross-level interactions. FIML estimation of missing data was used in the model. Because there was little variability in alcohol problems at level 2 of the model (ICC = 0.004), the analysis failed to converge when estimating a correlation between impaired control over alcohol and alcohol-related problems. When this correlation was fixed to zero, the model converged but reached a saddle point, suggesting that the standard errors may not be trustworthy. Thus, we

also ran the model with MLF estimation which converged without problems. In the model with MLR estimation, the beverage condition by CGNG interaction was significant for alcohol-related problems ($b = 0.42$, SE = 0.17, $p = 0.01$), but not for impaired control over alcohol use ($b = 0.02$, SE = 0.03, $p = 0.59$). As hypothesized, impaired control over alcohol use was a robust predictor of alcohol-related problems ($b = 6.16$, SE = 0.80, $p < 0.001$). In the model with MLF estimation, the interaction for alcohol-related problems was no longer significant ($b = 0.42$, SE = 0.28, $p = 0.13$), and the interaction for impaired control remained nonsignificant ($b = 0.02$, SE = 0.03, $p = 0.58$). The direct effect of impaired control on alcohol-related problems remained strongly significant ($b = 6.16$, SE = 1.04, $p < 0.001$). Given the lack of a significant interaction between beverage condition and CGNG performance in the prediction of impaired control over alcohol, moderated indirect effects were not tested.

DISCUSSION

As alcohol use and related problems remain prevalent among young adults, it is vital to examine constructs related to risk for alcohol-related problems. Clinically, young adults are an important population given high rates of AUD (Grant et al., 2015). Although facets of impulsivity are established risk factors for AUD (Verdejo-García et al., 2008), less is known regarding underlying mechanisms linking these 2 constructs (Dalley et al., 2011). Results from this study extend the literature relating a behavioral facet of impulsivity and impaired control to alcohol-related problems. Consistent with prior research, alcohol consumption was associated with impaired response inhibition relative to placebo (Fillmore et al., 2005). Further, dampened response inhibition in the alcohol condition, but not in the placebo condition, was significantly associated with alcohol-related problems. The current study also replicated prior results linking impaired control over alcohol to alcohol-related problems (Behrendt et al., 2008; Leeman et al., 2009). Contrary to study hypotheses, alcohol impairment of response inhibition was not significantly related to impaired control. To our knowledge, there have been no prior published studies relating impaired control over alcohol use to impairment of response inhibition under alcohol.

It is possible that impaired control over alcohol use is more a result of deficits in the trait ability to control behavior than alcohol impairment of response inhibition. Indeed, results of cross-sectional studies suggest that negative urgency (i.e., impulsive behavior in response to intense negative affect) is moderately associated with impaired control over alcohol among young adults (Patock-Peckham et al., 2011). More recently, a laboratory-based alcohol administration study demonstrated that impaired control over alcohol use mediated the relation between positive urgency and peak BAC following ad libitum access to intravenous alcohol in a nonclinical sample (Vaughan et al., 2019). If impaired control over alcohol use is more closely related to trait impulsivity than impairment of behavioral control under alcohol, the finding of independent effects of impaired response inhibition under alcohol and impaired control over alcohol use in the current study is not surprising.

Although the current study provides novel information to refine our understanding of relations among alcohol impairment of response inhibition, impaired control over alcohol use, and alcohol-related problems, the findings should be considered in light of several

limitations. For example, the sample had a restricted range of drinking as very light drinkers and those who had been in treatment for alcohol-related problems were excluded. Although this restriction of range may limit the ability to generalize the findings to lighter or heavier drinking populations, it is an inherent problem in an alcohol administration study as it would not be ethical to administer alcohol to alcohol-naïve individuals or those in recovery. The current sample also was selected on the basis of previous gambling behavior, particularly poker, and thus could have higher levels of general impulsivity and lower levels of executive cognition functioning. However, when comparing levels of impulsive traits, behavioral impulsivity, and impaired control over alcohol use in the current study to other related studies, overall means tended to be similar (e.g., Berey et al., 2019; Hartman et al., 2015; Marczinski and Fillmore, 2003; Naidu et al., 2019). The use of a primarily Caucasian male sample also decreases generalizability.

Another limitation is that the data were essentially cross-sectional, as impaired control over alcohol use and alcohol-related problems were assessed roughly 2 weeks after the alcohol challenge, and participants reported alcohol-related problems over the past 3 months. Thus, we could not demonstrate temporal precedence of the relation between impaired control over alcohol and alcohol-related problems. Third, true to virtually all experimental studies, there was a departure from ecological validity. However, the current study mitigated this concern by having participants drink in a simulated bar laboratory that included alcohol-related cues (e.g., alcohol brand signage, alcohol glassware). Further, participants consumed alcohol in a group setting thus providing a social context, which is an important, yet often overlooked, aspect when conducting alcohol challenge studies (de Wit and Sayette, 2018). Although the group design adds a potential source of variability related to differences in composition (i.e., group size, gender composition), ICCs for group-level effects were small indicating that the particular group in which participants completed the study accounted for limited variance (2% or less) in the outcomes.

Despite these limitations, the current study addressed an important a gap in the literature by examining relations among alcohol impairment of response inhibition, impaired control over alcohol use, and alcohol-related problems. The current study replicates and extends prior research indicating that impaired response inhibition under alcohol and impaired control over alcohol use act as risk factors for alcohol-related problems. Moving forward, research should integrate multiple facets of impulsivity (both trait and state) to elucidate which facets of impulsivity are related to impaired control over alcohol use. Prospective studies are also needed to examine additional mechanisms through which alcohol impairment of response inhibition may contribute to future alcohol-related problems. These studies would benefit from inclusion of more diverse samples with respect to both race/ethnicity and alcohol-related risk.

ACKNOWLEDGMENTS

This project was supported by NIH Grants R01AA021148 (Corbin), T32AA025877 (Berey), R21AA023368 and UH2 AA026214 (Leeman), and the Mary F. Lane Endowed Professorship (Leeman). The content is solely the responsibility of the authors and does not necessarily represent the official views of National Institute on Alcohol Abuse and Alcoholism or National Institutes of Health. The sponsors had no role in the design or conduct of the study; collection, management, analysis, or interpretation of the data; or preparation, review, or approval of the manuscript.

REFERENCES

Abbey A (2002) Alcohol-related sexual assault: a common problem among college students. J Stud Alcohol Suppl 14:118–128.

Baer JS (2002) Student factors: understanding individual variation in college drinking. J Stud Alcohol 14:40–53.

Baker SP, Braver ER, Chen LH, Li G, Williams AF (2002) Drinking histories of fatally injured drivers. Injury Prev 8:221–226.

Bartholow BD, Fleming KA, Wood PK, Cowan N, Saults JS, Altamirano L, Miyake A, Martins J, Sher KJ (2018) Alcohol effects on response inhibition: variability across tasks and individuals. Exp Clin Psychopharmacol 26:251–267. [PubMed: 29863383]

Behrendt S, Wittchen HU, Höfler M, Lieb R, Low NCP, Rehm J, Beesdo K (2008) Risk and speed of transitions to first alcohol dependence symptoms in adolescents: a 10-year longitudinal community study in Germany. Addiction 103:1638–1647. [PubMed: 18821874]

Berey BL, Leeman RF, Pittman B, Franco N, Krishnan-Sarin S (2019) Does self-reported or behavioral impulsivity predict subjective response to low-dose alcohol? Alcohol Alcohol 54:180–187. [PubMed: 30649160]

Beseler CL, Taylor LA, Leeman RF (2010) An item-response theory analysis of DSM-IV alcohol-use disorder criteria and “binge” drinking in undergraduates. J Stud Alcohol Drugs 71:418–423. [PubMed: 20409436]

Brewer JA, Potenza MN (2008) The neurobiology and genetics of impulse control disorders: relationships to drug addictions. Biochem Pharmacol 75:63–75. [PubMed: 17719013]

Buu A, Wang W, Schroder SA, Kalaida NL, Puttler LI, Zucker RA (2012) Developmental emergence of alcohol use disorder symptoms and their potential as early indicators for progression to alcohol dependence in a high-risk sample: a longitudinal study from childhood to early adulthood. J Abnorm Psychol 121:897–908. [PubMed: 21842966]

Carey KB, Carey MP, Maisto SA, Henson JM (2004) Temporal stability of the Timeline Followback interview for alcohol and drug use with psychiatric outpatients. J Stud Alcohol Drugs 65:774–781.

Caswell AJ, Bond R, Duka T, Morgan M (2015) Further evidence of the heterogeneous nature of impulsivity. Pers Indiv Differ 76:68–74.

Chick J, Duffy JC (1979) Application to the alcohol dependence syndrome of a method of determining the sequential development of symptoms. Psychol Med 9:313–319. [PubMed: 472077]

Corbin WR, Cronce JM (2017) Effects of alcohol, initial gambling outcomes, impulsivity, and gambling cognitions on gambling behavior using a video poker task. Exp Clin Psychopharmacol 25:175–185. [PubMed: 28493742]

Corbin WR, Papova A, Morean ME, O’Malley SS, Krishnan-Sarin S, Abi-Dargham A, Anticevic A, Pearlson G, Petrakis I, Pittman BP, Krystal JH (2015) Integrating acquired preparedness and dual process models of risk for heavy drinking and related problems. Psych Addict Behav 29:864–874.

Corbin WR, Scott C, Boyd SJ, Menary KR, Enders CK (2015) Contextual influences on subjective and behavioral responses to alcohol. Exp Clin Psychopharmacol 23:59–70. [PubMed: 25643028]

Curtin JJ, Fairchild BA (2003) Alcohol and cognitive control: Implications for regulation of behavior during response conflict. J Abnorm Psych 112:424–436.

Dalley JW, Everitt BJ, Robbins TW (2011) Impulsivity, compulsivity, and top-down cognitive control. Neuron 69:680–694. [PubMed: 21338879]

de Wit H, Crean J, Richards JB (2000) Effects of d-amphetamine and ethanol on a measure of behavioral inhibition in humans. Behav Neurosci 114(4):830. [PubMed: 10959541]

de Wit H, Sayette M (2018) Considering the context: social factors in responses to drugs in humans. Psychopharmacology 235:935–945. [PubMed: 29470605]

Dick DM, Smith G, Olausson P, Mitchell SH, Leeman RF, O’Malley SS, Sher KJ (2010) Understanding the construct of impulsivity and its relationship to alcohol use disorders. Addict Biol 15:217–226. [PubMed: 20148781]

Duncan DF (1997) Chronic drinking, binge drinking and drunk driving. Psychol Rep 80:681–682. [PubMed: 9129384]

Enders CK, Tofighi D (2007) Centering predictor variables in cross-sectional multilevel models: a new look at an old issue. Psych Methods 12:121–138.

Fillmore MT (2003) Drug abuse as a problem of impaired control: current approaches and findings. Behav Cog Neurosci Rev 2:179–197.

Fillmore MT, Marczinski CA, Bowman AM (2005) Acute tolerance to alcohol effects on inhibitory and activational mechanisms of behavioral control. J Stud Alcohol 66:663–672. [PubMed: 16331852]

Fillmore MT, Weafer J (2004) Alcohol impairment of behavior in men and women. Addiction 99:1237–1246. [PubMed: 15369556]

Fillmore MT, Weafer J (2012) Acute tolerance to alcohol in at-risk binge drinkers. Psych Addict Behav 26:693–702.

Gan G, Guevara A, Marxen M, Neumann M, Junger E, Kobiella A, Mennigen E, Pilhatsch M, Schwarz D, Zimmermann US, Smolka MN (2014) Alcohol-induced impairment of inhibitory control is linked to attenuated brain responses in right fronto-temporal cortex. Biol Psychiat 76:698–707. [PubMed: 24560581]

Grant BF, Goldstein RB, Saha TD, Chou SP, Jung J, Zhang J, Pickering RP, Ruan WJ, Smith SM, Hunag B, Hasin DB (2015) Epidemiology of DSM-5 alcohol use disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions III. JAMA Psychiat 72:757–766.

Gupta R, Derevensky J (1997) Familial and social influences on juvenile gambling behavior. J Gambl Stud 13:179–192. [PubMed: 12913385]

Hamilton KR, Littlefield AK, Anastasio NC, Cunningham KA, Fink LH, Wing VC, Mathias CW, Lane SD, Schutz CG, Swann AC, Lejuez CW, Clark L, Moeller FG, Potenza MN (2015) Rapid-response impulsivity: definitions, measurement issues, and clinical implications. Personal Disord 6:168–181. [PubMed: 25867840]

Hartman JD, Patock-Peckham JA, Corbin WR, Gates JR, Leeman RF, Luk JW, King KM (2015) Direct and indirect links between parenting styles, self-concealment (secrets), impaired control over drinking and alcohol-related outcomes. Addict Behav 40:102–108. [PubMed: 25241309]

Heather N, Booth P, Luce A (1998) Impaired Control Scale: cross validation and relationships with treatment outcome. Addiction 93:761–771. [PubMed: 9692275]

Heather N, Tebbutt JS, Mattick RP, Zamir R (1993) Development of a scale for measuring impaired control over alcohol consumption: a preliminary report. J Stud Alcohol Drugs 54:700–709.

Hendershot CS, Wardell JD, Strang NM, Markovich MS, Claus ED, Ramchandani VA (2015) Application of an alcohol clamp paradigm to examine inhibitory control, subjective responses, and acute tolerance in late adolescence. Exp Clin Psychopharmacol 23:147–158. [PubMed: 26053322]

Henges AL, Marczinski CA (2012) Impulsivity and alcohol consumption in young social drinkers. Addict Behav 37:217–220. [PubMed: 21981824]

Hingson RW, Zha W, Weitzman ER (2009) Magnitude of and trends in alcohol-related mortality and morbidity among US college students ages 18–24, 1998–2005. J Stud Alcohol Drugs Suppl 16:12–20.

Jentsch JD, Ashenhurst JR, Cervantes MC, Groman SM, James AS, Pennington ZT (2014) Dissecting impulsivity and its relationships to drug addictions. Ann NY Acad Sci 1327:1–26. [PubMed: 24654857]

King KM, Patock-Peckham JA, Dager AD, Thimm K, Gates JR (2014) On the mismeasurement of impulsivity: trait, behavioral, and neural models in alcohol research among adolescents and young adults. Curr Addict Rep 1:19–32.

Leeman RF, Beseler CL, Helms CM, Patock-Peckham JA, Wakeling VA, Kahler CW (2014) A brief, critical review of research on impaired control over alcohol use and suggestions for future studies. Alcohol Clin Exp Res 38:301–308. [PubMed: 24117468]

Leeman RF, Fenton M, Volpicelli JR (2007) Impaired control and undergraduate problem drinking. Alcohol Alcohol 42:42–48. [PubMed: 17142826]

Leeman RF, Patock-Peckham JA, Potenza MN (2012) Impaired control over alcohol use: an under-addressed risk factor for problem drinking in young adults? Exp Clin Psychopharmacol 20:92–106. [PubMed: 22182417]

Leeman RF, Toll BA, Taylor LA, Volpicelli JR (2009) Alcohol-induced disinhibition expectancies and impaired control as prospective predictors of problem drinking in undergraduates. Psychol Addict Behav 23:553–563. [PubMed: 20025361]

Lejuez CW, Magidson JF, Mitchell SH, Sinha R, Stevens MC, De Wit H (2010) Behavioral and biological indicators of impulsivity in the development of alcohol use, problems, and disorders. Alcohol Clin Exp Res 34:1334–1345. [PubMed: 20491733]

MacKillop J, Weafer J, Gray JC, Oshri A, Palmer A, de Wit H (2016) The latent structure of impulsivity: impulsive choice, impulsive action, and impulsive personality traits. Psychopharmacology 233:3361–3370. [PubMed: 27449350]

Marczinski CA, Fillmore MT (2003) Preresponse cues reduce the impairing effects of alcohol on the execution and suppression of responses. Exp Clin Psychopharmacol 11:110–117. [PubMed: 12622349]

Miller MA, Fillmore MT (2014) Protracted impairment of impulse control under an acute dose of alcohol: a time-course analysis. Addict Behav 39:1589–1596. [PubMed: 24286706]

Moeller FG, Barratt ES, Dougherty DM, Schmitz JM, Swann AC (2001) Psychiatric aspects of impulsivity. Am J Psychiatry 158:1783–1793. [PubMed: 11691682]

Mulvihill LE, Skilling TA, Vogel-Sprott M (1997) Alcohol and the ability to inhibit behavior in men and women. J Stud Alcohol 58:600–605. [PubMed: 9391919]

Muthen LK, Muthen BO (1998–2015) Mplus User's Guide, 7th edn. Muthen & Muthen, Los Angeles, CA.

Nagoshi CT (1999) Perceived control of drinking and other predictors of alcohol use and problems in a college student sample. Addict Res 7:291–306.

Naidu ES, Patock-Peckham JA, Ruof A, Bauman DC, Banovich P, Frohe T, Leeman RF (2019) Narcissism and devaluing others: an exploration of impaired control over drinking as a mediating mechanism of alcohol-related problems. Pers Indiv Differ 139:39–45.

National Advisory Council on Alcohol Abuse and Alcoholism (2005) Recommended council guidelines on ethyl alcohol administration in human experimentation. Available from: http://www.niaaa.nih.gov/Resources/ResearchResources/job22.htm. Accessed January 10, 2019.

Papachristou H, Nederkoorn C, Havermans R, Bongers P, Beunen S, Jansen A (2013) Higher levels of trait impulsiveness and a less effective response inhibition are linked to more intense cue-elicited craving for alcohol in alcohol-dependent patients. Psychopharmacology 228:641–649. [PubMed: 23508556]

Patock-Peckham JA, Cheong J, Balhorn ME, Nagoshi CT (2001) A social learning perspective: a model of parenting styles, self-regulation, perceived drinking control, and alcohol use and problems. Alcohol Clin Exp Res 25:1284–1292. [PubMed: 11584147]

Patock-Peckham JA, King KM, Morgan-Lopez AA, Ulloa EC, Filson-Moses JM (2011) The gender specific mediational links between parenting styles, parental monitoring, impulsiveness, drinking control, and alcohol-related problems. J Stud Alcohol Drugs 72:247–258. [PubMed: 21388598]

Patock-Peckham JA, Morgan-Lopez AA (2006) College drinking behaviors: mediational links between parenting styles, impulse control, and alcohol-related outcomes. Psychol Addict Behav 20:117–125. [PubMed: 16784353]

Pomery EA, Gibbons FX, Reis-Bergan M, Gerrard M (2009) From willingness to intention: experience moderates the shift from reactive to reasoned behavior. Pers Soc Psychol B 35:894–908.

Roberts W, Monem RG, Fillmore MT (2016) Multisensory stop signals can reduce the disinhibiting effects of alcohol in adults. Alcohol Clin Exp Res 40:591–598. [PubMed: 26853439]

Sobell LC, Sobell MB (1992) Timeline follow-back, in Measuring Alcohol Consumption, pp 41–72. Humana Press, Totowa, NJ.

Vaughan CL, Stangl BL, Schwandt ML, Corey KM, Hendershot CS, Ramchandani VA (2019) The relationship between impaired control, impulsivity, and alcohol self-administration in nondependent drinkers. Exp Clin Psychopharmacol 27:236–246. [PubMed: 30688502]

Verdejo-García A, Lawrence AJ, Clark L (2008) Impulsivity as a vulnerability marker for substance-use disorders: review of findings from high-risk research, problem gamblers and genetic association studies. Neurosci Biobehav R 32:777–810.

Wardell JD, Quilty LC, Hendershot CS (2016) Impulsivity, working memory, and impaired control over alcohol: a latent variable analysis. Psychol Addict Behav 30:544–554. [PubMed: 27269291]

Weafer J, Fillmore MT (2008) Individual differences in acute alcohol impairment of inhibitory control predict ad libitum alcohol consumption. Psychopharmacology 201:315–324. [PubMed: 18758758]

Weafer J, Fillmore MT (2012) Acute tolerance to alcohol impairment of behavioral and cognitive mechanisms related to driving: drinking and driving on the descending limb. Psychopharmacology 220:697–706. [PubMed: 21960182]

Weafer J, Fillmore MT (2016) Low-dose alcohol effects on measures of inhibitory control, delay discounting, and risk-taking. Curr Addict Rep 3 (1):75–84.

White HR, Labouvie EW (1989) Towards the assessment of adolescent problem drinking. J Stud Alcohol 50:30–37. [PubMed: 2927120]

Wilhelm CJ, Reeves JM, Phillips TJ, Mitchell SH (2007) Mouse lines selected for alcohol consumption differ on certain measures of impulsivity. Alcohol Clin Exp Res 31:1839–1845. [PubMed: 17850219]

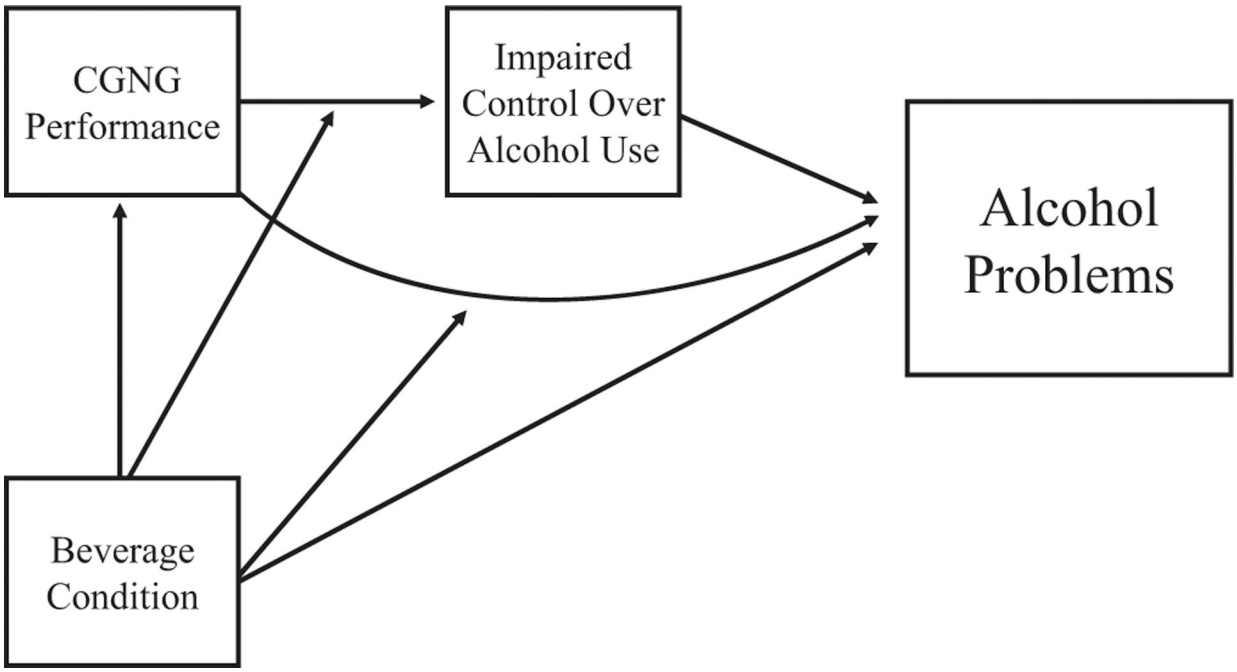

Fig. 1.

Hypothesized moderated mediation model predicting alcohol problems. Age, race, ethnicity, sex, college status, and baseline CGNG performance were included as covariates in the analysis.

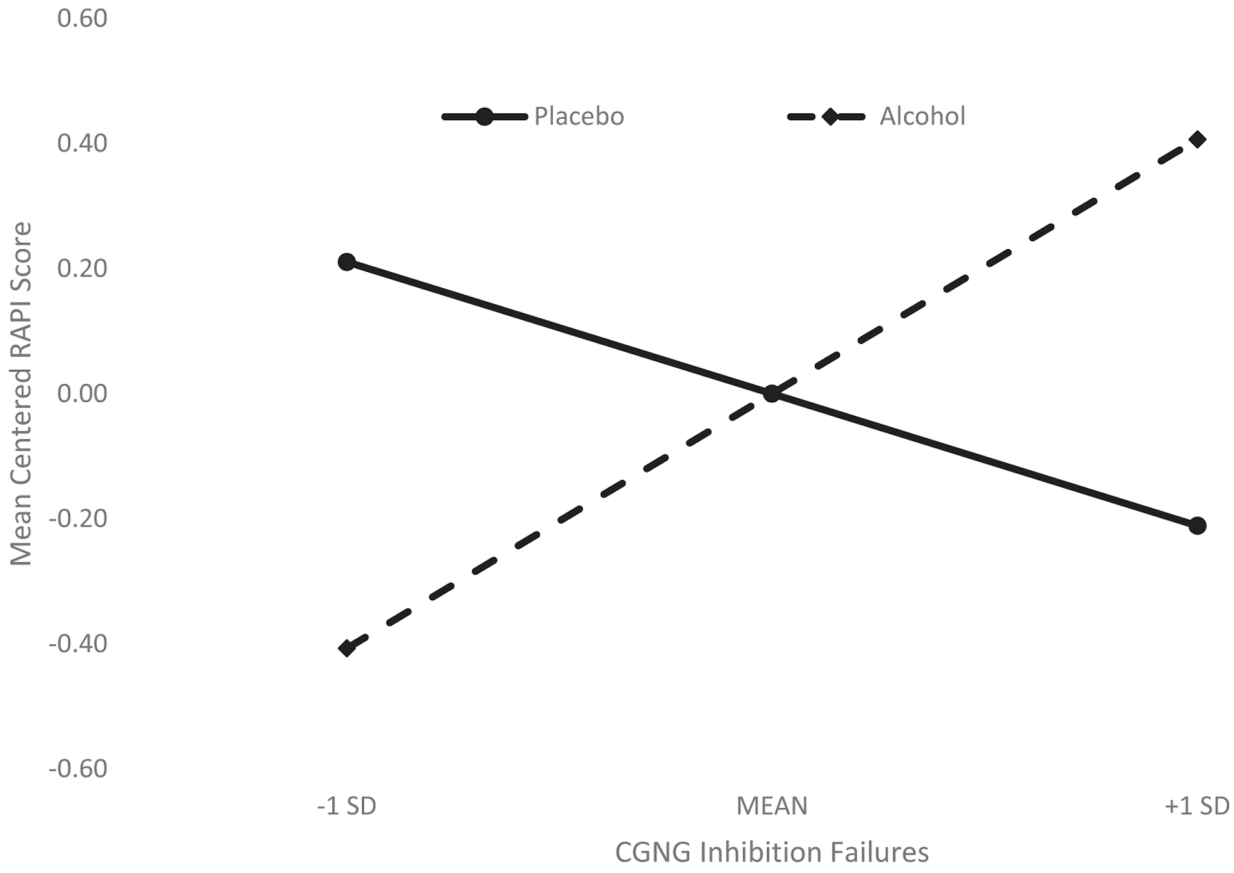

Fig. 2.
Beverage condition by CGNG interaction for alcohol problems.

Table 1.

Descriptive Statistics by Condition

Variable	Alcohol condition *N* = 102	Placebo condition *N* = 113
Age	22.81 (2.25)	22.86 (2.48)
Sex		
Male	77 (75.5%)	86 (76.1%)
Female	25 (24.5%)	27 (23.9%)
Race		
White/Caucasian	78 (76.5%)	84 (74.3%)
Black/African American	2 (2%)	3 (2.7%)
Asian	4 (3.9%)	8 (7.1%)
American Indian/Native	1 (1%)	–
Other	12 (11.8%)	17 (15%)
Missing	5 (4.9%)	1 (0.9%)
Ethnicity		
Hispanic/Latinx	18 (17.6%)	28 (24.8%)
Non-Hispanic/Latinx	78 (76.5%)	84 (74.3)
Missing	6 (5.9%)	1 (0.9%)
College status		
College Student	70 (68.6%)	84 (74.3%)
Nonstudent	28 (27.5%)	27 (29.3%)
Missing	4 (3.9%)	2 (1.8%)
Weekly drinking	13.30 (10.8)	14.50 (11.75)
CGNG (baseline)	3.53 (3.87)	4.18 (5.27)
CGNG (intoxicated)	6.58 (7.16)	5.08 (7.07)
Impaired control over alcohol use	2.00 (0.58)	2.13 (0.59)
Alcohol-related problems	8.05 (6.5)	9.16 (7.93)

Table 2.

Descriptive Statistics and Correlations Among Study Variables

Variable	Mean (SD)	4	5	6	7	8	9	10	11
1. Age	22.8 (2.4)								
2. Race	78% Caucasian								
3. Ethnicity	22% Hispanic								
4. Sex	76% Male	—							
5. College student status	74% Student	−0.17*	—						
6. Beverage condition	47% Alcohol	0.01	−0.05	—					
7. Weekly drinking	13.9 (11.3)	−0.31**	0.11	−0.05	—				
8. Sober CGNG	3.9 (4.7)	−0.10	0.16*	−0.04	−0.07	—			
9. Intoxicated CGNG	5.8 (7.1)	0.01	0.14	0.17*	−0.14*	0.69**	—		
10. Impaired control over alcohol use	2.1 (0.59)	0.002	−0.03	−0.11	0.34**	−0.03	−0.06	—	
11. Alcohol problems	8.6 (7.3)	0.04	0.12	−0.03	0.40**	−0.04	−0.02	0.60**	—

Nonnormally distributed variables were log-transformed for bivariate correlations, but raw means and standard deviations are presented for ease of interpretation. Age, race, and ethnicity were not included in correlational analyses due to lack of relations with most study variables.

*Significant at 0.05 level, and

**significant at 0.01 level.