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Early Subjective Response and Acquired Tolerance as Predictors of Alcohol Use and Related Problems in a Clinical Sample

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Abstract

Objective—Previous studies have demonstrated that a low subjective response to alcohol is a risk factor for Alcohol Use Disorders (AUDs), and a recent study suggests that acquired tolerance can be differentiated from initial subjective response and is also significantly associated with drinking problems. Because the prior study of subjective response and tolerance focused on a sample of moderate drinkers, the goal of the current study was to examine relations between early subjective response, acquired tolerance, alcohol use, and alcohol-related problems in a sample of young adults with clinically significant alcohol problems.

Method—The current study examined associations between early subjective response and acquired tolerance and both drinking behavior and alcohol-related problems within a sample of 113 heavy drinking young adults (66.1% male) volunteering for a clinical trial of naltrexone in combination with brief motivational counseling.

Results—Consistent with the one prior study examining simultaneous effects of early SR and tolerance, both early subjective response and acquired tolerance were positively associated with typical drinking behavior, though tolerance was a much stronger predictor within this clinical sample. In contrast to the prior study, early subjective response was inversely associated with risk for alcohol-related problems, and tolerance was not a significant predictor of problems.

Conclusions—The results suggested that, controlling for weekly drinking, a low early subjective response protected against acute negative consequences within a sample of heavy drinkers who had acquired significant tolerance to alcohol effects. It is possible that this protective

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effect may eventually shift to a risk factor by allowing individuals with a low subjective response to persist in a pattern of hazardous drinking.

The period between adolescence and adulthood, referred to as “emerging adulthood” (age 18–25; Arnett, 2005), is a time of increased alcohol consumption and problematic drinking patterns (Johnston et al., 2010). In addition to acute negative consequences (Hingson et al., 2005), emerging adults are at elevated risk for developing Alcohol Use Disorders (AUDs) (Knight et al., 2002; Slutske, 2005). Studies from nationally representative U.S. samples show peak onset of AUDs between the ages of 18 and 29. Although this pattern is evident for both alcohol abuse and dependence, risk is most pronounced for dependence, with rates more than double that of any other age group (Grant et al., 2004). As emerging adults move into young adulthood (late 20s and early 30s) and undergo major role changes including full-time employment, marriage, and parenthood, there is a tendency to “mature out” of heavy drinking patterns (Jochman and Fromme, 2010). New onset cases of alcohol use disorders also decrease following emerging adulthood (Vergés et al., 2012). Thus, identification of risk factors for heavy alcohol use and associated negative consequences during emerging adulthood is a major public health priority.

Genetic influences on the development of alcohol-related problems are now well established. Risk for developing an AUD is roughly four times greater among individuals with a family history of alcoholism (NIAAA, 2007), and twin studies have found that nearly 50% of the variance in AUD risk is attributed to genetic factors (Knopik et al., 2004; Liu et al., 2004). Although genetic factors play an important role, the mechanisms through which they operate are only beginning to be uncovered. One potential mechanism of genetic influence is subjective response (SR) to alcohol, with differential sensitivity to the pharmacological effects of alcohol associated with risk for alcohol-related problems. Previous studies suggest that SR may account for as much as 40–60% of the variance in AUD risk associated with genetics (Schuckit, 1999).

Most SR studies have used alcohol challenge paradigms to investigate individual differences in SR. Patterns of SR are then examined both as outcomes (e.g., differences in SR by family history status or heavy/light drinker status) and predictors of alcohol-related problems (See Morean and Corbin, 2010 and Quinn and Fromme, 2011 for recent reviews). Previous studies have identified both enhanced stimulation and reduced sedation/impairment in high-risk samples (Holdstock et al., 2000; King et al., 2002; 2011; Schuckit, 1980; 1984). Although a recent study also suggests that enhanced stimulant effects are associated with later risk for alcohol problems (King et al., 2011), evidence for the importance of SR as a predictor of later alcohol problems has been most consistently demonstrated for a low SR to sedation/impairment (Schuckit, 1994; Schuckit and Smith, 2000; Schuckit et al., 2004; Trim et al., 2009).

Conceptually, a low response to negatively experienced alcohol effects contributes to risk through a faulty feedback system in which individuals do not receive the signal to stop drinking despite high blood alcohol concentrations (BACs). Thus, individuals with a low SR may consume larger quantities of alcohol, leading to tolerance, which in turn confers risk for AUDs (Schuckit, 1994). Although it is presumed that a low SR reflects an innate difference in response to alcohol, alcohol challenge paradigms are not well suited to identifying innate (e.g., early) alcohol responses since participants must be 21 or over. Responses reported at age 21 may reflect either a low innate response to alcohol or differential development of tolerance.

It is important to differentiate early SR from tolerance given that tolerance is an alcohol dependence diagnostic criterion (APA, 2000). Unfortunately, there is limited human

research on individual differences in the development of tolerance. The most comprehensive study of chronic tolerance to date used a sample of non alcohol dependent young adult offspring from the Collaborative Study on the Genetics of Alcoholism (COGA), and found that greater tolerance was associated with heavier drinking and more alcohol-related problems (Schuckit et al., 2008). Moreover, the effects of tolerance remained when controlling for drinking behavior. There is also some evidence of important individual differences in tolerance from lab-based studies. For example, a series of studies by Newlin and Thomson (1991, 1999) demonstrated that individuals with a family history of alcoholism differed from those without a family history on both sensitization and tolerance to alcohol effects. In summary, research on the importance of individual differences in tolerance to alcohol as a predictor of alcohol-related problems warrants further attention.

Although alcohol challenge studies are generally unable to distinguish between the effects of early SR and tolerance, the Self-Rating of the Effects of Alcohol (SRE) measure (Schuckit et al., 1997) has the potential to disentangle these effects. The SRE asks individuals to report the number of drinks they need to consume to produce four separate effects (any effect, dizziness or slurred speech, stumbling gait, and passing out) during three different periods in their drinking history (first 5 drinking occasions, period of heaviest drinking, and most recent 3 months of regular drinking). Tolerance is conceptualized as an increase in the number of drinks needed to feel alcohol effects from early (first five) to later (most recent 3 months) drinking experiences.

Although the SRE has its own limitations (i.e. self-reports of drinking experiences that occurred many years prior), Schuckit et al. (2010) found that the SRE and an alcohol-challenge-based measure of SR performed similarly in structural equation models evaluating the relationship between SR and future heavy drinking. Further, using the SRE to assess acquired tolerance has potential advantages over single item measures. The SRE-based measure assesses multiple alcohol effects, and by evaluating drinking at two separate time points, tolerance scores calculated as the difference between the two time points may be less biased than simple self-reports of subjective changes in the experience of alcohol effects for a given number of drinks over time. Further, by providing a continuous tolerance score, the SRE based measure is not subject to individual differences in how individuals define the presence or absence of acquired tolerance (Schuckit et al., 2008). Supporting the potential of this approach, a recent study using the SRE to assess early SR and tolerance found that both were independent predictors of use and problems in a sample of undergraduate students (Morean and Corbin, 2008).

In the current study, we sought to replicate the Morean and Corbin (2008) study in a sample of heavy drinking young adults. Although research using the SRE has contributed to our understanding of early SR and tolerance, most studies have focused on light to moderate drinkers, and the few studies looking at heavier drinkers have used samples in their mid thirties and older. By that time, individuals are likely on an established trajectory of higher or lower-risk alcohol use. Further, the one study that differentiated early SR from acquired tolerance used a light to moderate drinking sample that reported relatively few alcohol-related problems. Thus, it is unclear to what extent an early SR and tolerance contribute to patterns of drinking behavior associated with more clinically significant problems. In the current study, we examined early SR and acquired tolerance as simultaneous predictors of both alcohol use and alcohol-related problems. With respect to alcohol use, we anticipated that the results would be similar to prior studies with a low early SR and greater acquired tolerance associated with heavier drinking. Our hypotheses regarding alcohol-related problems were more exploratory, as participants in the current sample were much heavier drinkers than in the Morean and Corbin (2008) study. Although this prior study found that a low early SR was associated with more alcohol-related problems, experienced heavy

drinkers may learn to more effectively avoid acute drinking consequences, and this may be more pronounced among individuals with a low innate response to alcohol and/or greater acquired tolerance.

Method

Participants

Participants (N = 113) were recruited for an ongoing, randomized, double-blind, placebo-controlled clinical trial of naltrexone in combination with brief motivational counseling for reduction of heavy drinking. All participants who met initial eligibility requirements and completed an intake assessment were included in the analyses, regardless of whether or not they enrolled in the clinical trial. The majority of participants (Mean age of 21.31, SD = 2.14) were male (66.4%), and Caucasian (78.1%). Other racial groups included African American (10.5%), multiracial (3.8%), Asian American (3.0%), and American Indian (1.0%), with another 1.9% from other racial/ethnic groups. A total of 4.8% of the sample reported Hispanic/Latino ethnicity. At intake, the average weekly consumption was 23.77 (SD = 16.60) standard drinks, and 75.6% of participants met criteria for an AUD (19.1% Alcohol Abuse only; 56.4% Alcohol Dependence).

Procedures

The Institutional Review Board of Yale University School of Medicine approved this study. All participants provided written informed consent prior to completing study procedures. Young adults ages 18–25 were recruited via flyers, television, newspaper and online advertisements. Compensation up to $500 was advertised and no explicit motivation to change drinking behavior was required. Individuals deemed preliminarily eligible based on pre-screening by phone or web questionnaire were invited to attend an intake appointment. At intake, following informed consent, participants underwent clinical interviews, including diagnostic evaluations for alcohol use disorders, drug use, and other psychiatric issues, as well as routine blood work, urine drug testing and pregnancy tests for women. It was also verified that participants met minimum levels of heavy drinking for inclusion in the trial (i.e., ≥5 standard drinks for men and ≥4 standard drinks for women on ≥4 days within the 28 days preceding intake). Participants then completed self-report web-based assessments at the research site or on their own. Individuals who could clearly be excluded at the initial intake appointment did not complete the self-report battery.

Measures

Demographics—Measures of interest to the current analyses included gender, age, and race/ethnicity. See all measure descriptives in Table 1.

Self-Rating of the Effects of Alcohol Form (SRE; Schuckit et al., 1997)—The SRE assessed both early SR and acquired tolerance. The form captures 4 effects of alcohol (feeling an effect, dizziness or slurred speech, stumbling gait, and passing out), with scores reflecting the number of drinks necessary to experience each effect. Each effect is measured at 3 time points; the first 5 drinking experiences (referred to as early SR in the remainder of the manuscript), the most recent 3 month period of regular drinking, and the 3 month period of heaviest drinking. Internal consistency reliability for the 4-item subscale was good for all 3 assessment periods (alphas ranged from .88 to .89). Since 97.4% of participants responded to at least 3 of the 4 items at each time point, we did not include the number of items answered as an additional predictor variable. Acquired tolerance was calculated by subtracting the score for early SR from the score for the most recent 3 month period of drinking. The difference reflects the change in response to alcohol over the course of the individual's drinking history, with higher scores reflecting greater acquired tolerance.

Eighty-two of the 103 participants (79.6%) showed an increase in the number of drinks needed to feel an effect of alcohol from early to more recent (past 3 month) drinking experiences. The computed measure of tolerance was correlated with the tolerance item on the YAACQ (described below) at .35 ($p < .001$), providing further evidence for the construct validity of this measure.

Daily Drinking Questionnaire (DDQ; Collins et al., 1985)—A revised version of the DDQ was used with separate questions assessing the frequency and quantity of alcohol use. Frequency comprised the number of drinking days during the past 3 months for each day of the week (e.g. number of Mondays on which alcohol was consumed). The values for each day of the week were summed and the total divided by 13 to yield the average number of drinking days per week. Quantity was based on participant's reports of the average number of drinks consumed on drinking days for each day of the week (e.g. average number of drinks on Saturdays on which alcohol was consumed). The values for each day of the week were summed and divided by 7 to yield a measure of average drinks per drinking day. In the current study, we created a composite of the frequency and quantity measures to yield an overall index of weekly consumption.

Young Adult Alcohol Consequences Questionnaire (YAACQ; Read et al., 2006)—The YAACQ is a 48-item measure assessing 8 categories of alcohol related consequences in the past year using a dichotomous yes/no self-report. Internal consistency reliability for the full scale was excellent (alpha = .91), and most subscales demonstrated good reliability (alphas between .70 and .80). However, internal consistency reliability of the academic subscale was marginal (alpha = .67) and the physical dependence subscale demonstrated poor reliability (alpha = .39). All participants completed at least 90% of the 48 items.

Data Analytic Plan

Prior to conducting the primary analyses, distributions of all variables were examined for outliers and normality assumptions. Although no outliers were identified, early SR and weekly consumption were positively skewed. Log transformation resulted in distributions that approached normality, with skewness statistics of −.19 and −2.47, respectively. Although the skewness statistic for acquired tolerance suggested some non-normality (skewness statistic = 3.18), we retained the raw scores as a histogram suggested a reasonably normal distribution, and transformation resulted in even greater skew. After addressing variable distributions, we examined zero order correlations (Table 2) to determine whether the associations among the variables were consistent with study hypotheses. We also examined partial correlations (See Table 3) between early SR, tolerance, and each of the YAACQ subscales (controlling for gender and race/ethnicity to be consistent with the later regression models). Next, simultaneous entry multiple regression analyses tested the primary hypotheses of interest. Separate models were tested for weekly consumption and alcohol-related problems, with gender, ethnicity, early SR, and tolerance entered as simultaneous predictors of the outcome of interest. The model predicting alcohol-related problems included weekly drinking as an additional predictor. In this model, we also examined potential indirect effects of early SR and tolerance on alcohol-related problems operating through weekly drinking using the product of coefficients method (PRODCLIN; MacKinnon et al., 2007). This approach uses asymmetric confidence intervals that are more appropriate for distributions of products (MacKinnon et al., 2004). If the confidence interval for the product of the *a* (e.g. early SR on weekly drinking) and *b* (e.g. weekly drinking on alcohol-related problems) paths does not contain the value of zero, the indirect (mediated) effect is statistically significant at the designated alpha level ($p = .05$ in our models).

Standardized regression coefficients are reported in the text with both unstandardized (and corresponding standard errors) and standardized coefficients reported in Table 4.

Handling of Missing Data

Data on gender was available for all participants (N = 113) with the number of valid responses for the other measures of interest ranging from n = 103 to n = 105. Given that most participants who were missing data on any single measure were also missing data for most other measures (including the outcome measures), we elected to use listwise deletion rather than trying to impute values for individuals with missing data. Thus, all correlation and regression models are based on a sample size of 102.

Results

Bivariate and Partial Correlations

Bivariate correlations (See Table 2) indicated that acquired tolerance was significantly and positively correlated with both weekly alcohol use and alcohol-related problems. In contrast, early SR was not significantly associated with weekly drinking, and was inversely associated with alcohol-related problems. Partial correlations (controlling for gender and race/ethnicity) indicated that early SR was inversely associated with all 8 YAACQ subscales, though not all reached statistical significance (See Table 3). This suggests that a low early SR was broadly protective, rather than specific to particular types of problems. It is also important to note that there was a significant inverse correlation between early response and acquired tolerance, such that needing more drinks to feel effects during early drinking experiences (i.e. low response) was associated with less tolerance.

Regression Model for Weekly Drinking

In the regression model for weekly drinking, indices of multicollinearity were examined against conventional cutoffs (tolerance < .10 and VIF > 10). All tolerance values were greater than .789 and all VIF values were less than 1.267, suggesting that multicollinearity was not a significant concern. The predictor variables collectively accounted for significant variance in the outcome (Adjusted $r^2 = .36$). Both early SR, $\beta = .37$, $p < .001$, and acquired tolerance, $\beta = .65$, $p < .001$, emerged as unique predictors in the multiple regression model. Consistent with prior research in lighter drinking samples, lower levels of early SR and greater acquired tolerance were associated with heavier weekly consumption (See Table 4). Gender and ethnicity were not significant predictors of weekly drinking (p's >.10).

Regression Model for Alcohol-related Problems

In the model for alcohol-related problems, indices of multicollinearity were again within normal limits, and the predictor variables accounted for significant variance in the outcome (Adjusted $r^2 = .19$). Ethnicity was a significant predictor of problems, $\beta = -.19$, $p < .05$, with minority participants reporting fewer problems than Caucasian participants. As anticipated, heavier weekly drinking was associated with more alcohol-related problems, $\beta = .29$, $p = .02$. Neither gender nor acquired tolerance was significantly associated with alcohol-related problems (p's > .10). Although early SR was a significant predictor of problems, the effect was in the opposite direction relative to the model for weekly drinking, $\beta = -.24$, $p = .03$, (See Table 4). Thus, a lower initial response to alcohol, as evidenced by needing more drinks to feel effects, was associated with *decreased* risk for alcohol-related problems.

We also tested for indirect effects of early SR and tolerance on problems operating through weekly drinking. For both early SR and tolerance, the confidence intervals for the products of the *a* and *b* paths (early SR/tolerance to weekly drinking and weekly drinking to alcohol-related problems, respectively) did not contain the value of zero (CI = 1.166, 12.969 for

early SR; CI = .140, 1.289 for tolerance), indicating that the indirect effects were statistically significant at the $p = .05$ level. A low early SR and greater acquired tolerance were both associated with heavier weekly drinking which, in turn, was associated with more alcohol-related problems. This indirect effect of a low SR which conferred increased risk for alcohol-related problems was in the opposite direction of the direct protective effect of a low early SR on problems.

Post Hoc Models Utilizing the Tolerance Item from the YAACQ

Given that the direct effect of early SR on alcohol-related problems was in the opposite direction of effects identified in previous studies, we conducted post-hoc analyses replacing the tolerance measure based on the SRE with the single tolerance item from the YAACQ. The tolerance item was removed from the YAACQ score used as the outcome variable. Results of this model were largely consistent with the model using the SRE derived measure of tolerance. Most importantly, the direct inverse relation between early SR and alcohol-related problems was replicated in this model, $\beta = -.24$, $p = .01$, with a lower early SR associated with reduced risk for alcohol-related problems.

Discussion

Prior research has demonstrated that a low level of sedation/impairment following alcohol consumption confers risk for AUDs, presumably due to lack of feedback regarding negative alcohol effects, which contributes to higher levels of consumption. Over time, higher levels of consumption contribute to acquired tolerance, further increasing risk for excessive drinking and subsequent development of alcohol dependence (Schuckit, 1994; Schuckit and Smith, 2000). In addition, one prior study demonstrated that acquired tolerance is independently predictive of use and problems and accounts for a level of variance that is similar to a low SR (Morean and Corbin, 2008). Although SR has been used to predict later risk for AUDs, initial assessments of SR have typically been with moderate social drinkers. The current study sought to address a gap in the literature by examining the importance of both SR and acquired tolerance as predictors of alcohol consumption and related problems in a sample of heavy drinking young adults.

In contrast to prior studies and study hypotheses, bivariate correlations between early SR and weekly alcohol consumption were not statistically significant. However, in a regression model that controlled for the effects of acquired tolerance, individuals who needed more drinks to feel an effect during early drinking experiences reported heavier weekly drinking. Nonetheless, even in the model that simultaneously examined early SR and acquired tolerance, the magnitude of the relation between acquired tolerance and weekly drinking was large ($\beta = .65$) relative to the magnitude of the relation between early SR and weekly drinking ($\beta = .37$). Collectively, these results suggest that the degree of acquired tolerance experienced by frequent heavy drinkers is strongly related to their current behavior, and that failure to account for the effects of acquired tolerance may result in biased estimates of the true relationship between early response and current drinking. Similarly, failure to account for the effects of early SR may obscure the true effects of tolerance on drinking outcomes. For example, a prior study of adolescents found that tolerance was a weak predictor of alcohol problems, and the authors speculated that this may have been due to the substantial variability in initial levels of consumption (Chung et al., 2002). Controlling for these differences in initial levels of consumption may allow effects of tolerance to more clearly emerge.

It may be particularly important to simultaneously examine initial SR and acquired tolerance as predictors of drinking outcomes within heavy drinking samples for whom it may take a large number of drinks to feel effects, even during early drinking experiences. Perhaps as a

consequence of this characteristic, the current study found a significant inverse association between initial SR and acquired tolerance. Those who needed more drinks to feel the effects of alcohol during early drinking experiences showed less habituation to alcohol with drinking experience. A ceiling effect may help explain this inverse association, as the current sample reported needing more drinks on average (6.03 drinks) to feel early alcohol effects compared to a mean of 3.90 in the Morean and Corbin (2008) sample. Thus, the lower levels of initial response to alcohol in this heavy drinking sample may have resulted in less room for the acquisition of tolerance and consequent differences in the univariate correlations and multivariate regression coefficients across studies. Alternatively, individuals with a lower initial response to alcohol may simply develop tolerance more slowly, such that greater tolerance would be observed in these individuals later in adulthood. Future studies examining relations among early SR, tolerance and drinking behavior in older adulthood are needed to address this possibility.

The results of the current study also diverged from those of previous studies with respect to the relation between early SR and alcohol-related problems. Accounting for the effects of tolerance and weekly drinking, those who initially needed more drinks to feel alcohol effects reported *fewer* alcohol-related problems. Thus, the effect of early SR in the current study was directly opposite that observed in the Morean and Corbin (2008) study, despite the fact that both studies relied on cross-sectional data and used the SRE and DDQ to assess early SR, tolerance, and weekly drinking. It is important to note that the current study utilized a different analytic approach by including weekly drinking as a predictor (mediator) in the model for alcohol-related problems. When we did not include weekly drinking in the model, the direct effect of early SR on alcohol-related problems was in the same direction but was not significant ($\beta = -.14$, $p = .19$). Although our analytic approach of controlling for weekly drinking allowed the inverse association between early SR and problems to emerge in this heavy drinking sample, the difference in approach does not fully explain the different findings across studies. Re-analysis of the data from the Morean and Corbin (2008) study showed that, even when the effects of weekly drinking were accounted for, there was no indication of a protective effect of a low early SR on problems in this lighter drinking sample. Given that the discrepant findings across studies cannot be attributed to differences in measures or methodology, it seems likely that the differences are related to the very different populations under study (heavy versus light drinkers). Thus, the discrepant results may reflect important differences in the effects of SR and acquired tolerance across populations at varying levels of risk.

Although the inclusion/exclusion of weekly drinking in the model for problems did not explain differences across studies, there was evidence that weekly drinking was important in understanding relations between early SR and alcohol-related problems. Although there was a direct effect with *decreased* risk for problems among those with a low early SR, there was also an indirect effect with low early SR associated with *increased* risk for alcohol-related problems through heavier weekly drinking. Thus, the direct and indirect effects of a low level of initial response to alcohol served to offset one another. As a consequence, those with a low early SR may not experience fewer *overall* problems but they do appear to experience fewer problems *relative to the amount consumed*. This may promote continued drinking at higher levels relative to those who initially experience alcohol effects more strongly.

Given the unexpected finding that a low early response to alcohol was associated with decreased risk for alcohol-related problems, we conducted post-hoc analyses using the single YAACQ tolerance item in place of the SRE based measure. The results of these analyses and the model using the SRE-based tolerance measure were largely consistent. Most importantly, needing more drinks to feel the effects of alcohol during early drinking

experiences was significantly associated with lower risk for alcohol-related problems across both models. This provides greater confidence in the veracity of the observed relations between early SR and alcohol-related problems.

Individuals with a low early SR may experience fewer alcohol-related problems at similar levels of consumption because of their ability to regulate their behavior even at high blood alcohol levels. Although such an explanation seems plausible, it is unclear why acquired tolerance did not show a similar inverse association with alcohol problems. One possible explanation is that acquired tolerance confers both risk and protection that serve to offset one another. On the one hand, those who acquire a high tolerance to alcohol should be less impaired than those with less tolerance at similar BACs. On the other hand, the development of tolerance may reflect neuroadaptation that results from heavy drinking (Heinz et al., 2003; Koob and Le Moal, 2008), which may facilitate the development of craving, loss of control, and other indicators of increasing alcohol problems.

In summary, although the current study replicated previous findings that a low initial response to alcohol and greater development of tolerance are associated with heavier drinking, in this clinical sample, a low early response was associated with lower levels of alcohol-related problems, controlling for weekly drinking. One possible explanation is that, as individuals escalate to a pattern of consistent heavy drinking and develop significant tolerance, a low early SR may protect them from acute negative consequences. Although protective in the short term, the absence of acute consequences may lead to continued escalation in drinking that ultimately leads to physical dependence and loss of control over drinking behavior. Future longitudinal studies examining changes in the relations between early SR and alcohol-related problems are needed to fully test this preliminary model and to further clarify discrepancies between the results of this study and previous studies.

This leads us to one of the limitations of the current study. Longitudinal studies are better suited to demonstrate the trajectory in which a low early response to alcohol contributes to initial protection, but long-term risk, for alcohol-related problems. Such studies are also critical as aspects of the environment surrounding the developmental period of emerging adulthood may contribute to this phenomenon. The environment of young adults may be more conducive to heavy drinking and protective against negative consequences, which may exacerbate risk for continued heavy drinking among individuals with a low early response to alcohol. Our study also used a retrospective report of early SR, which might be influenced by current levels of SR. A lab based SR measure would be less biased and perhaps more informative regarding the intricacies of the relation between SR and acquired tolerance. However, our statistical differentiation of early SR and tolerance does help to better isolate their potential unique influences.

The study sample was primarily Caucasian, male, and drank heavily at a frequency required for entry into a RCT to reduce heavy drinking thereby limiting the generalizability of the results. Moreover, although analyses accounted for gender, future studies with larger samples are important to establish that the pattern of results is similar for men and women. A final limitation is inherent to our use of the SRE, which focuses exclusively on effects of alcohol that can be considered sedating or impairing. As a consequence, we were unable to examine early positive effects and tolerance to these effects. Given that greater rewarding effects of alcohol, not just lower sedative effects, predict the frequency of binge drinking and risk for developing AUDs, (King et al., 2011), future research should consider adapting the SRE to include questions related to positive alcohol effects.

Despite the aforementioned limitations, this study is the first to differentiate early SR and acquired tolerance and investigate their association with alcohol consumption and problems

in a clinical young adult sample. The finding that early response to alcohol and the development of tolerance to alcohol effects over time were differentially related to the report of alcohol-related negative consequences is important and may contribute to a more complete understanding of the mechanisms through which a low SR contributes to risk for the development of alcohol-related problems.

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Table 1

Measure Descriptives

Measure	Mean	Standard Deviation
Early SR	6.03	2.81
DDQ-R Weekly Consumption	23.78	16.80
Acquired Tolerance	2.31	2.62
YAACQ Problems	20.71	9.66

Note. Early SR = Self-rating of Alcohol Effects first five drinking experiences; DDQ-R = Revised Daily Drinking Questionnaire; Acquired Tolerance = SRE Most Recent 3 months – Early SR: YAACQ Problems = Young Adult Alcohol Consequences Questionnaire.

Table 2

Intercorrelations for Acquired Tolerance, Early SR, Problems, Weekly Consumption, Ethnicity, and Gender

Variable	1 AT	2 SRE	3 YAACQ	4 DDQ-R	5 Gender
1. Acquired Tolerance (AT)	--				
2. Early SR	−0.360**	--			
3. YAACQ Problems (Total)	0.346**	−0.277**	--		
4. DDQ-R Weekly Consumption	0.529**	0.110	0.313**	--	
5. Gender	0.021	0.250*	−0.069	0.043	--
6. Ethnicity	−0.260**	0.189	−0.284**	−0.131	−0.081

Note. Sample size = 102; Gender was coded as female = 0 and male = 1; Ethnicity was coded as 0 = non-hispanic caucasian, 1 = other race/ethnicity; Acquired Tolerance = SRE most recent three month total - Early SR; Early SR = Self-rating of Alcohol Effects first five drinking experiences; YAACQ Problems = Young Adult Alcohol Consequences Questionnaire; DDQ-R = Revised Daily Drinking Questionnaire Log Transformed.

* $p < .05$,

** $p < .01$.

Table 3

Partial Correlations among Early SR, Tolerance, Weekly Drinking and YAACQ Subscales

	Tolerance	Weekly Drinking	YAACQ SOC	YAACQ IMPCNT	YAACQ SP	YAACQ SC	YAACQ RSK	YAACQ AC	YAACQ PD	YAACQ BLK	YAACQ TOT
Early SR	−.340	.134	−.105	−.065	−.167	−.289**	−.014	−.170	−.122	−.201*	−.220*
Tolerance		.517**	.254*	.238*	−.005	.132	.248*	.292**	.415**	.177	.296**
Weekly Drinking			.211*	.412**	.067	.165	.248*	.210*	.400**	.042	.295**

Note.

* p < .05;

** p <.01;

Sample Size = 98; Early SR= SRE score for subjective response during first 5 drinking occasions; Tolerance = SRE for the most recent 3-month period minus Early SR; Weekly Drinking = Typical Weekly Consumption from the Daily Drinking Questionnaire Revised (DDQ-R); YAACQ SOC = Young Adult Alcohol Consequences Questionnaire Social/Interpersonal Consequences, YAACQ IMPCNT = Impaired Control; YAACQ SP = Diminished Self-Perception; YAACQ SC = Poor Self-Care; YAACQ RSK = Risky Behavior; YAACQ AC = Academic/Occupational Consequences; YAACQ PD = Physiological Dependence; YAACQ BLK = Blackout Drinking; YAACQ Tot = Total problem score for all items on the YAACQ.

Table 4

Regression Analyses for Typical Weekly Drinking and Alcohol-related Problems

	DDQ-R Weekly Consumption *n* = 102				YAACQ Problems *n* = 102			
Predictor	**ΔR^2**	**B**	**SE**	**β**	**ΔR^2**	**B**	**SE**	**β**
	.362 **				.193 **			
Gender		−.041	.053	−.065		−.771	1.916	−.038
Ethnicity		−.025	.058	−.036		−4.197	2.097	−.188 *
Early SR (Log)		.692	.168	.368 **		−14.539	6.592	−.240 *
Acquired Tolerance		.075	.010	.653 **		.228	.456	.062
DDQ-R Weekly Consumption						9.117	3.669	.284 *

Note. Gender was coded as female = 0 and male = 1; Ethnicity was coded as 0 = non-hispanic caucasian, 1 = other race/ethnicity; Acquired Tolerance = Most recent three month total - Early SR; Early SR = Self-rating of Alcohol Effects first five drinking experiences; DDQ-R = Revised Daily Drinking Questionnaire Log Transformed; YAACQ Problems = Young Adult Alcohol Consequences Questionnaire.

* $p < .05$;

** $p < .01$

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