ORIGINAL ARTICLE

Alcohol-related blackouts among college students: impact of low level of response to alcohol, ethnicity, sex, and environmental characteristics

Priscila D. Gonçalves,^{1,2,3} Tom L. Smith,¹ Robert M. Anthenelli,¹ George Danko,¹ Marc A. Schuckit¹

¹Department of Psychiatry, University of California, San Diego, CA, USA. ²Instituto de Psiquiatria, Serviço de Psicologia e Neuropsicologia, Universidade de São Paulo (USP), São Paulo, SP, Brazil. ³Instituto de Psiquiatria, Grupo Interdisciplinar de Estudos de Álcool e Drogas (GREA), USP, São Paulo, SP, Brazil.

Objective: To explore how a genetically-influenced characteristic (the level of response to alcohol [LR]), ethnicity, and sex relate to environmental and attitudinal characteristics (peer drinking [PEER], drinking to cope [COPE], and alcohol expectancies [EXPECT]) regarding future alcohol-related blackouts (ARBs). **Methods:** Structural equation models (SEMs) were used to evaluate how baseline variables related to ARB patterns in 462 college students over 55 weeks. Data were extracted from a longitudinal study of heavy drinking and its consequences at a U.S. university.

Results: In the SEM analysis, female sex and Asian ethnicity directly predicted future ARBs (beta weights 0.10 and -0.11, respectively), while all other variables had indirect impacts on ARBs through alcohol quantities (beta weights ~ 0.23 for European American ethnicity and low LR, 0.21 for cannabis use and COPE, and 0.44 for PEER). Alcohol quantities then related to ARBs with beta = 0.44. The SEM explained 23% of the variance.

Conclusion: These data may be useful in identifying college students who are more likely to experience future ARBs over a 1-year period. They enhance our understanding of whether the relationships of predictors to ARBs are direct or mediated through baseline drinking patterns, information that may be useful in prevention strategies for ARBs.

Keywords: Alcohol; blackout; college students; peer drinking; drinking to cope; drinking behavior; alcohol drinking in college; binge drinking

Introduction

Alcohol-related blackouts (ARBs) are impairments in the ability to encode memories for partial (fragmentary) or entire (en-bloc) events during drinking, and are most likely to develop at blood alcohol concentrations (BACs) \ge 0.20 mg/dL.^{1,2} In the U.S., about 50% of college students who drink experience ARBs during their college years.^{3,4} These ARBs are related to additional alcohol-related adverse consequences, such as unwanted sex, emergency room visits, and early death.⁵⁻⁷ The heavy drinking patterns associated with ARBs could also indicate a vulnerability for developing an alcohol use disorder (AUD).^{4,8} The risk for ARBs is higher among individuals of European American (EA) descent than in those with Asian backgrounds,^{3,4,9} a finding that could reflect, in part, the protective effect of alcohol-related skin flushing and the related greater sensitivity to alcohol in almost half of Japanese, Chinese, and Korean drinkers. Several recent investigations have also noted an equal or higher prevalence of alcohol-related memory lapses among females as compared to males,^{4,10,11} and another reported a higher

likelihood that a heavy drinking episode is more likely to be followed with additional drinking the next day in females, a phenomenon that could contribute to additional ARBs.¹²

The risk for ARBs also relates to many additional characteristics, including a low level of response to alcohol (LR).^{11,13} A lower LR reflects the need for higher BACs to produce effects, and increases the risk of excessive alcohol use by encouraging association with heavy drinkers and contributing to attitudes that such drinking is common and desirable.^{11,14,15} Alcohol-related memory lapses are also affected by attitudinal and environmental characteristics. For example, in college students, higher rates of heavy drinking and alcohol-related problems (including ARBs) correlate with heavy peer drinking,^{15,16} greater levels of drinking to cope with stress,¹⁷⁻¹⁹ and more positive expectancies regarding positive aspects of using alcohol.²⁰ ARBs are also more likely in individuals who use marijuana.²¹

Our research group has an interest in how the characteristics listed above relate to each other and to patterns of ARBs over time.^{11,21} These studies, and others in the literature, have primarily used correlations and regression analyses, but few have used structural equation models (SEM). In the current study, we applied SEM to data gathered during the freshman and sophomore college years, a period likely to be associated with heavy drinking,^{1,22} to investigate the relationships of lower LR,

Correspondence: Marc Alan Schuckit, 8950 Villa La Jolla Drive, B-218, 92037, La Jolla, CA, USA.

E-mail: mschuckit@ucsd.edu

Submitted Nov 16 2016, accepted Apr 07 2017, Epub Aug 31 2017.

personal and peer drinking, drinking to cope with stress, alcohol expectancies, demographic characteristics (sex and ethnicity), and marijuana use to ARBs. Using data extracted from a larger protocol focused on preventing heavy drinking,17 we hypothesized that: 1) ARBs would be common and persist over time in this sample; 2) ARBs would correlate positively with diverse characteristics, including demographic variables (being female and of EA ancestry), higher baseline drinking and its correlates (e.g., lower LR, heavy-drinking peers, using alcohol to cope with stress, and higher alcohol expectancies), and marijuana use; and 3) these variables would relate directly to the occurrence of ARBs over time, including higher ARB rates for females, who, compared to men, need fewer drinks to increase the BAC to levels likely to produce ARBs.²³ We also hypothesized a direct negative relationship of Asian ethnicity to ARB risk, whereby the high doses required to produce ARBs in individuals of Asian descent are less likely to occur, as a consequence of the different patterns of alcohol-metabolizing enzymes in that group and the subsequent negative effects of alcohol consumption at even relatively lower BACs.24 At the same time, we expected that other predictors of ARBs that are more closely linked to consuming higher quantities of alcohol (e.g., LR, peer drinking, and drinking to cope with stress) would also have an impact on ARBs through mediation by alcohol quantities themselves.

Methods

Participants

After approval from the University of California, San Diego (UCSD) Human Protections Committee and using informed consent, the current data were generated from 500 freshmen students who agreed to participate in a larger protocol focused on preventing heavy drinking.¹⁷ Study recruitment began with a questionnaire (described below) that was distributed to a sample of entering freshmen at UCSD. To be eligible for the study, participants had to have consumed alcohol in the previous 6 months, never met the DSM-IV²⁵ criteria for alcohol or other substance dependence, not currently meet criteria for a major psychiatric disorder (e.g., major depressive, bipolar, or schizophrenic disorders), and deny a severe flushing response to one or two drinks, thus excluding individuals who could potentially carry the ALDH2*2 allele.9 For the larger study, students were randomly assigned to interventions or control groups, with the former receiving two different forms of alcohol education.17

Measures

Initially, students from a list supplied by the UCSD Registrar of first-time freshmen were invited to fill out an online screening instrument based on the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA) interview²⁶ and the Self-Report of the Effects of Alcohol questionnaire (SRE).^{13,17,21} The SRE measures LR by determining the average number of standard drinks (containing 10-12 g of ethanol) required to experience up to

four possible alcohol-related effects (feeling the initial effects, slurring one's speech, walking in an uncoordinated manner, and passing out) during the first five times of drinking.²⁷ The average number of drinks needed to produce up to four effects actually experienced usually ranges from about three to four drinks in non-AUD populations.^{11,21} Using the inclusion and exclusion criteria described above, 500 individuals, representing > 90% of UCSD students who were invited to participate, entered the study in a sample chosen to include similar numbers who were above and below the median of LR.

All baseline and follow-up data were gathered online using Survey Monkey, with each relevant questionnaire available 24 hours a day for a 7-day period. Baseline assessments began in January 2014 and included demographic characteristics, the LR to alcohol based on the SRE (SRE [LR]), patterns of alcohol use (usual and maximum drinking quantities: frequency of consuming four or more drinks in a single occasion), and marijuana use in the prior month. Data were also gathered regarding environmental and attitudinal variables, including perceived drinking among the four closest peers as measured on the Important People and Activities (IPA) scale.²⁸ drinking to cope with stress (Drinking to Cope Scale, or DTC),²⁹ and alcohol expectancies (EXPECT) using a short form of the Alcohol Expectancy Questionnaire (AEQ).^{11,30} Drinking patterns, attitudes and environmental characteristics, and marijuana use all referred to the prior month. Historically in our work with non-AUD adolescents and young adults, average scores on the DTC are about 9.6 based on the six possible items, each of which is scored on a scale of almost never (1) to almost always (4).³¹ The DTC included using alcohol to forget worries, relax, cheer up, lessen depression or anxiety, boost self-confidence, and to fill in when feeling there is nothing better to do. The short version of the AEQ true/false items used in this study were extracted from the AEQ subscales of expectations of alcohol's effects on sexual enhancement, social behavior, improved cognitive and motor abilities, and increased arousal, with scores in non-AUD adolescents usually in the range of 2.0, 2.1, 0.2, and 2.2 across these four scales. Examples of specific items in the version of the AEQ used herein include "a person can talk with people of the opposite sex better after a few drinks"; "people feel more caring and giving after a few drinks of alcohol"; "a person can do things better after a few drinks of alcohol"; and "alcohol helps people stand up to others."

Participants were followed over 55 weeks, with followup assessments occurring at seven time points (4, 8, 16, 20, 29, 42, and 55 weeks) after baseline.¹⁷ The present analyses were limited to the 462 students (92.4%) who completed at least seven of the eight assessments. At each time point, participants were asked about the occurrence of alcohol-related memory impairments in the prior month (Question: "Have you had blackouts [could not remember later what you have done] while drinking alcohol?"). ARB patterns were calculated as the number of follow-up assessment(s) in which students reported alcohol-related memory lapses during the 55-week followup period.

Statistical analysis plan

Data with skewed distributions received square-root. logarithmic, or inverse-reflected transformations before further analyses, and missing data were handled through a maximum likelihood procedure. Subsequently, the hypothesized model in Figure 1 was developed and evaluated using AMOS software³² incorporating maximum likelihood estimations. The SEM³³ steps included an assessment of the measurement model, a confirmatory factor analysis examining correlations among latent variables (Figure 2). and incorporation of the measurement model within the final full SEM after dropping components that were not significant within the model (Figure 3). Goodness-of-fit criteria for models in these analyses included: 1) ratio of χ^2 to degrees of freedom (CMIN/DF) \leq 3: 2) comparative fit index (CFI) \geq 0.90; 3) non-normal fit index (NNFI) close to 1.0; 4) root mean square error of approximation (RMSEA) ≤ 0.05 ; and 5) root mean squared residual (SRMR) $\leq 0.08.^{34}$

Development of a hypothesized model

The hypothesized model shown in Figure 1 was designed after considering the relevant variables shown to relate to ARBs as presented in the Introduction, including ethnicity, sex, marijuana use, SRE (LR), peer drinking, drinking to cope, alcohol expectancies, and alcohol use patterns, in predicting the occurrence of ARBs. In Asian individuals, taking into account the prominent effect that alcoholrelated flushing has on how a person reacts to alcohol even after drinking small quantities and the cultural differences which discourage alcohol consumption among women,^{9,24} we emphasized the hypothesis that ethnicity and sex would have both direct effects on the ARB risk and operate indirectly on said risk. For the remaining baseline variables, we also proposed both direct and mediated effects on ARBs through drinking quantities. To optimize the use of SEM, latent variables were used whenever possible, as shown in Figure 2.

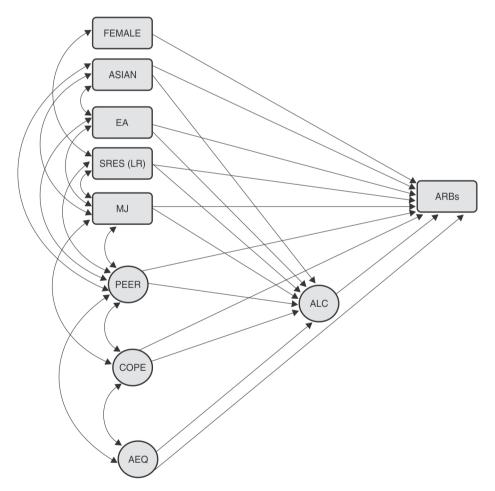


Figure 1 Hypothesized model of relationships of predictive variables to alcohol-related blackouts (ARBs). The initial structural equation model was created to evaluate whether and how female sex, Asian or European American (EA) ethnicity, Self-Report of the Effects of Alcohol level of response (SRE [LR]), marijuana use (MJ), peer drinking (PEER), drinking to cope (COPE), and alcohol expectancies (EXPECT) contribute directly and/or indirectly to the number of follow-up assessments in which participants reported ARBs. Alcohol-drinking quantity (ALC) was predicted to contribute directly to the outcome as well as to mediate other baseline variables. ARBs are a manifest variable of the number of follow-up assessments in which at least one ARB was reported.

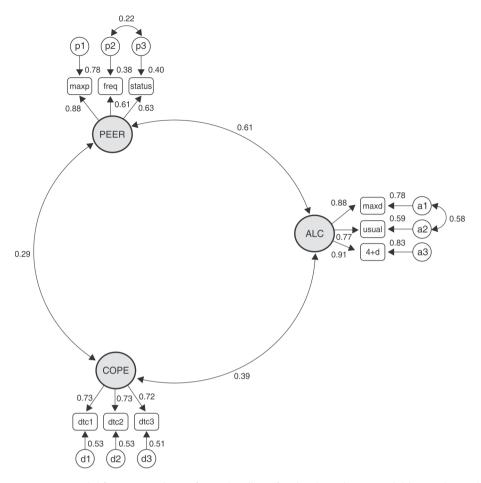


Figure 2 Final measurement model for 462 students: factor loadings for the three latent variables and correlations among the three. The measurement model of the structural equation models (SEM) is the part that relates actually measured variables to their assumed latent (not directly measured) variables and evaluates the relationships (correlations) among the latent variables. Here, all measured variables had significant loadings on their latent variables, and all three latent variables were significantly correlated with each other. PEER (the latent variable "peer drinking") was generated from the Important People and Activities Scale²⁸ using averages for four peers for three perceived peer drinking items: maximum quantity (maxp) on a 0-to-10 drink scale, frequency (freq) of days per month from zero (0) to daily (30), and peer drinking status (status) as average number of four peers who drank, scored dichotomously as abstainer/light drinker (0) vs. heavier drinker (1); COPE (the "drinking to cope" variable) was created by grouping six questions with responses ranging from almost never (1) to almost always (4) into three variable parcels, each combining two items from the DTC scale²⁹ (dtc1 using items = forget worries and depression/anxiety, dtc2 using items = relax and more self-confident, and dtc3 using items = cheer up and nothing better to do); ALC (the "alcohol-drinking quantity" variable) is composed of three indicators assessing variables for the prior month: maximum drinking quantity (maxd), usual drinking quantity (usual), and number of times subject consumed four or more drinks per occasion (4 + d).

Defining latent variables

For the present analyses, four latent variables were used within the Pearson product-moment correlations and the SEM:

- The latent variable PEER was composed of three perceived peer drinking items obtained from questions based on the IPA²⁸ scale: a) maximum quantity (from 0 to 10 drinks); b) frequency (days per month, from none [0] to daily [30]); and c) peer status (abstainer/light drinker [0] vs. heavier drinker [1]) The averages among the four closest peers were used for each of the three peer variables.
- The variable COPE was generated from the coping subscale of the COPE scale²⁹ regarding the frequency with which alcohol was used to cope in the month prior to

baseline (answers ranged from almost never [1 point] to almost always [4 points]). The six questions were grouped into three parcel variables with two items in each.

- 3) The latent variable EXPECT, for alcohol expectancies, was composed of endorsement of true/false items from four subscales of the AEQ regarding believing alcohol enhances sexual activities, social behavior, cognitive/ motor abilities, and arousal (e.g., alcohol makes people feel stronger and more powerful).^{30,31}
- 4) The latent variable ALC was established to capture alcohol use patterns at baseline. It comprised three baseline drinking variables obtained from a questionnaire based on the SSAGA²⁶ that included usual and maximum drinking quantities and frequency of four or more drinks per occasion.

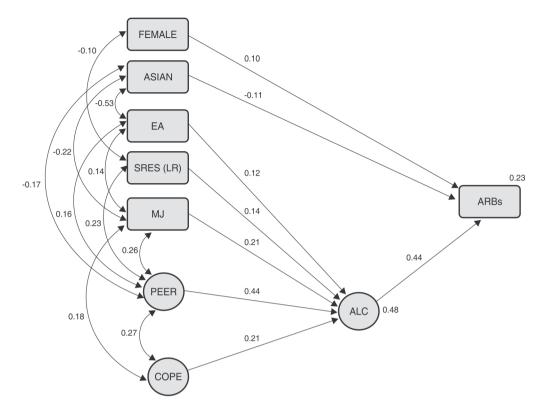


Figure 3 Full structural equation model evaluating whether and how specifically hypothesized variables predict alcohol-related blackouts (ARBs). The specifically hypothesized predicting variables contributing directly and/or indirectly (i.e., through mediation) to the predicted outcome were as follows: EA = European American vs. Asian; SRE (LR) = level of response to alcohol, measured by the Self Report of the Effects of Alcohol questionnaire for determining the average number of standard drinks (containing 10-12 g of ethanol) required to experience up to four possible alcohol-related effects (feeling the initial effects, slurring one's speech, walking in an uncoordinated manner, and passing out) during the first five times of drinking²⁷; MJ = any marijuana use; PEER = peer drinking, using averages across four close peers (taken from the Important People and Activities Scale²⁸) for maximum quantity = 0 to 10, status = abstainer/light drinker (0) vs. heavier drinker (1), and peer drinking frequency = number of days per month from zero (0) to daily (30); COPE = drinking to cope, created by grouping six drinking to cope questions with responses ranging from almost never (1) to almost always (4) into three parcel variables, each combining two items from the DTC scale²⁹ (parcel 1 = forget worries and depression/anxiety, parcel 2 = relax and more self-confident, parcel 3 = cheer up and nothing better to do); ALC = alcohol-drinking quantity, composed of three indicators assessing variables for the prior month: maximum drinking quantity, usual drinking quantity, and number of times subject consumed four or more drinks per occasion. The predicted outcome was ARBs as the number of follow-up assessments in which at least one such blackout was reported (range, none to seven). All correlations and paths presented here were significant.

Use of SEM to determine mediation effects

Analyses of direct associations and indirect statistical mediation within the model were conducted within Mplus Version 7.³³ Here, a bootstrapping approach with 1,000 resamples was used to mitigate effects of any deviation from normality. Results are displayed as 95% confidence intervals (2.5th and 97.5th percentiles), where a mediation relationship is operating if the intervals do not contain zeroes.

Results

Table 1 presents the baseline characteristics for the 462 students who completed the protocol, along with whether subjects received educational videos or were controls in the larger study. To help evaluate whether females and males differed significantly on most baseline

Rev Bras Psiquiatr. 2018;40(2)

characteristics or if the sexes could be pooled for analyses, the table lists data for the two sexes separately. Significant sex differences were only observed for two variables, including the expected SRE-based LR, in which males reported needing more alcohol to produce effects compared to females. A significant sex difference was also noted for the social behavior subscale scores of the AEQ, but this difference was small. Mean participant age was 18 years, 63% were female, and most selfreported ethnicity as Asian (Japanese, Chinese, or Korean identities) or EA. Regarding LR, subjects reported needing an average of about four drinks to experience alcohol-related effects on the SRE questionnaire. In the prior month they had consumed a mean of four drinks on a usual occasion with, six as their maximum, and reported two occasions on which they consumed four or more drinks, with 42% having used marijuana at least once in the previous month. Most (86%) participated in an

Baseline variables	Females n=290	Males n=172	
Demographic			
Age	18.1 (0.46)	18.1 (0.43)	
Ethnicity (%)			
European American	35.5	32.6	
Asian	32.4	40.1	
Hispanic	17.6	14.5	
Other	14.5	12.8	
Alcohol			
SRE (LR)	4.0 (1.84)	4.5 (5.52)*	
Usual quantity/occasion [†]	4.1 (2.37)	4.4 (3.61)	
Maximum quantity/occasion [†]	6.3 (3.91)	6.7 (5.56)	
Times consumed 4+ drinks/occasion [†]	2.4 (2.61)	2.5 (2.96)	
Alcohol-related blackout (%) †	24.8	18.6	
Other substances			
Used marijuana (%)	42.1	42.4	
Attitudinal and environmental characteristics			
Peer drinking [†]			
Maximum quantity	5.1 (2.07)	5.0 (2.50)	
Status	0.5 (0.27)	0.5 (0.30)	
Frequency	4.61 (3.51)	4.8 (4.00)	
Drinking to cope [†]	9.2 (3.40)	8.7 (2.84)	
Alcohol expectancies $(AEQ)^{\dagger}$			
Sexual enhancement	2.1 (0.88)	2.0 (0.95)	
Social behavior	2.1 (0.88)	2.2 (0.93) [‡]	
Improvement of cognitive/motor abilities	0.1 (0.40)	0.2 (0.59)	
Arousal	2.0 (1.01)	1.9 (1.00)	
Active education group participation (%)	84.5	87.2	

Data presented as mean (standard deviation) or %.

SRE (LR) = Level of Response to Alcohol (LR) as measured by the SRE,²⁷ which is the average number of standard drinks (containing 10-12 g of ethanol) required to experience up to four possible alcohol-related effects (feeling the initial effects, slurring one's speech, walking in an uncoordinated manner, and passing out) during the first five times of drinking; PEER = peer drinking taken from the Important People and Activities Scale²⁶ using averages across four close peers for maximum quantity = from 0 to 10, status = abstainer/light drinker (0) vs. heavier drinker (1), and peer drinking frequency = number of days per month from zero (0) to daily (30); COPE = drinking to cope, i.e., the six-item coping subscale of the DTC scale²⁹ regarding the frequency with which alcohol was used to cope with stress (item responses ranged from almost never [1] to almost always [4]); AEQ = shortened version of the Alcohol Expectancies Questionnaire, containing three true (0)/false (1) items in each of its four subscales (with a subscale score range of 0 to 3).³¹

education group in the larger study. About 20% of these subjects reported an ARB in the month prior to entering the study. While not shown in the table, 39.4% of participants reported experiencing an ARB over the 55-week follow-up period; of these, 16.0% reported an ARB in one of the seven time points of assessment, 6.9% in two assessments, 4.3% in three assessments, 4.8% in four assessments, and 7.3% in five or more assessments.

Table 2 presents the product-moment correlations among the nine baseline variables of interest, as well as how each correlated with the number of assessments in which one or more ARBs were reported. The number of follow-up periods in which ARBs were reported correlated significantly with all baseline items. Educational group assignment (not displayed in the table) was not related to the number of follow-up assessments in which ARBs were reported. For demographic variables, being female or of EA descent was related to a higher prevalence of ARBs, while an Asian ancestry related to fewer assessment periods with ARBs. Positive correlations with ARBs were noted for the SRE-based LR score (indicating that more drinks were required for effects, i.e., a lower LR per drink), the baseline drinking latent variable, and baseline marijuana use. Among the latent variables for baseline attitudinal and environmental characteristics, positive correlations with ARBs were observed for higher perceived peer drinking, drinking to cope, and positive expectations of the effects of alcohol. Baseline drinking correlated negatively with Asian ethnicity and positively with EA ethnicity, SRE-based LR, peer drinking, drinking to cope, and alcohol expectancies

Figure 1 depicts the hypothesized model with manifest variables represented by squares (female sex, Asian ethnicity, EA ethnicity, SRE [LR], marijuana use, and outcome [number of follow-up assessments in which ARBs were reported]), and latent variables shown in circles (PEER, COPE, EXPECT, and ALC). The model was structured to evaluate whether drinking quantities (ALC) might have partially mediated the relationships of the other baseline variables to the number of assessments in which ARBs were reported. We also hypothesized that

^{*} p < 0.01 for t and χ^2 tests.

[†]During month prior to baseline.

[‡]p < 0.05.

 Table 2
 Product-moment correlations among baseline variables that correlated with the number of follow-up assessments in which ARBs were reported

	ARBs	Female sex	Asian	EA	SRE (LR)	Marijuana*	ALC*	PEER*	COPE*
Female sex Asian ethnicity EA ethnicity SRE (LR) Marijuana use [§] ALC [§] PEER [§] CODE [§]	0.12^{*} - 0.19^{\dagger} 0.20^{\dagger} 0.15^{\ddagger} 0.23^{\dagger} 0.42^{\dagger} 0.29^{\dagger}	-0.08 0.03 -0.10* -0.01 0.01 0.03	-0.54 [†] -0.01 -0.22 [†] -0.15 [‡] -15 [‡]	$\begin{array}{c} 0.01 \\ 0.15^{\ddagger} \\ 0.22^{\dagger} \\ -0.15^{\ddagger} \end{array}$	0.10 [‡] 0.29 [†] 0.22 [†]	0.34 [†] 0.27 [†]	0.47 [†]	0.00 [†]	
COPE [§] EXPECT [§]	0.16 [‡] 0.13 [‡]	0.09 0.00	0.03 0.04	0.07 -0.03	0.08 0.07	0.16 [‡] 0.04	0.32 [†] 0.11*	0.23 [†] 0.11*	0.30^{\dagger}

ARBs = number of follow-up assessments in which at least one alcohol-related blackout was reported (range, 0 to 7); EA = European American; SRE (LR) = level of response to alcohol as measured by the SRE,²⁷ i.e., the average number of standard drinks (containing 10-12 g of ethanol) required to experience up to four possible alcohol-related effects (feeling the initial effects, slurring one's speech, walking in an uncoordinated manner, and passing out) during the first five times of drinking; ALC = alcohol-drinking quantity, a latent variable composed of usual and maximum drinking quantity/occasion and number of times in which four or more drinks were consumed in a single occasion; PEER = a latent variable created using variables taken from the Important People and Activities Scale²⁸ using averages across four close peers for maximum quantity = from 0 to 10, status = abstainer/light drinker (0) vs. heavier drinker (1), and peer drinking frequency = number of days per month, from zero (0) to daily (30); COPE = a latent variable created by grouping six items from the Drinking to Cope (DTC) scale²⁹ into three variable parcels, each combining two items (first parcel, forget worries and depression/anxiety; second parcel, relax and more self-confident; third parcel, cheer up and nothing better to do); EXPECT = a latent variable composed of the four subscales extracted from the Alcohol Expectancies Questionnaire (AEQ) about expected effects of alcohol (enhancing sexual activities, social behavior, cognitive/motor abilities, and arousal).³¹

* p < 0.05; ^{'†} p < 0.001; [‡] p < 0.01.

[§] During month prior to baseline.

baseline variables would have direct relationships with the ARB outcome, especially for female sex and Asian heritage.

Figure 2 presents the measurement model regarding the performance of the items included in each latent variable. This model demonstrated good fit, with CMIN/ DF = 2.08; CFI = 0.99; NNFI = 0.98; RMSEA = 0.048 (0.028-0.068); and SRMR = 0.038. It is important to note that, in an initial run of the full model shown in Figure 3, EXPECT was included, did not add significantly, and was dropped from the analyses, but was included in the measurement model in Figure 2.

The final SEM (Figure 3) was composed of three latent variables (ALC, COPE, and PEER) and six manifest variables (female sex, Asian ethnicity, EA ethnicity, SRE [LR], marijuana use, and the ARB outcome, i.e., the number of follow-up assessments in which ARBs were reported). Only significant correlations and paths with significant beta weights (p < 0.05) are included in Figure 3. In this SEM, female sex, Asian heritage and ALC related directly to the ARB outcome. The remaining baseline variables (EA, SRE [LR], marijuana use, PEER, and COPE) added significantly to the model, but the associations with the ARB outcome were indirect. An analysis of mediation demonstrated that for these five variables (EA, SRE [LR], marijuana use, PEER, and COPE), the baseline latent variable of alcohol-drinking quantities (ALC) mediated their associations with the ARB outcome. The observed indirect pathways included: EA-ALC-ARBs (0.016, 0.079), SRE (LR)-ALC-ARBs (0.040, 0.123), marijuana use-ALC-ARBs (0.034, 0.109), PEER-ALC-ARBs (0.101, 0.216) and COPE-ALC-ARBs (0.036, 0.130). The final SEM in Figure 3 had good fit indices, with CMIN/DF = 1.71; CFI = 0.97; NNFI = 0.98; RMSEA = 0.039 (0.027-0.51): and SRMR = 0.044. This model explained 23% of the variance for the ARB outcome.

Discussion

This paper examined the relationships of the pattern of ARBs over time to demographic characteristics (sex and ethnicity), LR to alcohol, drinking quantities, marijuana use, and attitudinal and environmental characteristics associated with drinking among college freshmen. The final SEM revealed that only female sex and Asian descent were directly linked to ARB outcomes, with the remaining variables only relating to the ARB outcome through the latent variable for baseline drinking patterns (ALC).

Consistent with the high rates of ARBs predicted in Hypothesis 1 and with several recent papers,^{3,4} 40% of these university freshmen reported an ARB in at least one follow-up assessment over the 55-week study period, including 23% who reported ARBs at more than one assessment. A prior paper in this series reported large increases in drinking as students returned to school for their sophomore year,¹⁷ indicating that the heavy episodic drinking required to produce ARBs is likely to continue well into the college years.⁴

Regarding the second hypothesis, univariate analyses (Table 2) positively linked the majority of relevant baseline characteristics with the number of follow-up assessments in which an ARB was reported, and revealed a negative association with Asian ethnicities. As for Hypothesis 3, direct pathways to the pattern of ARBs were seen only for females and for Asian individuals, with the remainder of predictors operating only indirectly through alcohol quantities. This finding has not been reported before, may offer clues regarding the most efficient ways of working to prevent ARBs at universities (where, for example, female students might benefit from learning their risk is especially high), and was strong enough to not be as sensitive to higher numbers of drinks, as is true for males.

The possible reasons for the unique direct associations of ARB patterns with female sex and Asian ethnicities in Figure 3 require further speculation. About 40% of Asian individuals experience skin flushing when they consume alcohol, including about 10% who develop severe nausea with as little as half a standard drink.9,24 Studies have consistently reported that the flushing phenomenon is related to higher rates of abstinence, lower drinking frequencies, and lower usual and maximum quantities of drinking - results that are likely to reflect cultural as well as biological differences from those with EA backgrounds.9,24 Thus, it is not surprising that Asian students would be less likely to be heavy drinkers and less likely to develop ARBs. The relative protection from ARBs conferred by the flushing mechanism in Asians could be powerful enough to discourage heavy drinking and decrease ARB risk even without considering usual alcohol guantities and frequencies. Additional research is needed regarding this possibility.

The direct positive relationship of the ARB outcome with female sex is also interesting, especially in light of the higher rate of ARBs in females as compared to males in some recent studies.^{4,10,11} One possible contributor to this finding may be the higher BAC per drink seen in women.²³ Thus, there is less likelihood that the latent ALC variable created while considering both males and females, and which includes maximum drinks and times per month the respondent consumed four or more drinks in a single occasion, would have the same ability to mediate the effect of sex on the pattern of ARBs over time. Or, perhaps the direct link of female sex to ARB patterns may reflect sex-related differences in hormones, or social and cultural issues that impact the sexes differentially but that were not directly measured in our protocol. Regardless of the biological and/or culturallyrelated mechanisms involved, women who drink binge amounts on any occasion are almost six times more likely to drink heavier amounts on future occasions in levels likely to be associated with experiencing ARBs.¹²

It is also worth noting that the sex differences in ARBs occurred despite no significant differences between males and females on usual and maximum drinks per occasion (Table 1). This finding is consistent with data that women have a higher BAC per drink, in that higher BACs are related to a greater probability of experiencing an ARB. The similarity in drinking quantities between the sexes is also consistent with the manner in which drinking practices in the two sexes have become more similar in recent years.³⁵

However, regarding the current findings, it is important to note that the original study from which these data were extracted used the same cutoff for heavy drinking (i.e., four or more drinks on a single occasion) for men and women, a step that was inconsistent with the prevailing approach in the alcohol field of using a cutoff of five or more drinks for men and four or more drinks for women. Further work will be needed to determine if the same conclusions would be drawn if these sex-specific cutoff points for binge-like drinking had been used in the analyses. More work is also needed to better understand possible mechanisms that contribute to sex differences in ARB rates.

The SEM also demonstrated that drinking quantities mediated the relationships of LR. marijuana use, drinking among peers, and drinking to cope to ARBs, although alcohol expectancies did not contribute directly or indirectly to the model. Several of these mediation effects have been observed before (e.g., LR operating through drinking quantities to impact alcohol-related problems, and low LR as a predictor of ARB patterns).^{11,14} Additionally, baseline drinking patterns mediated the relationships of peer drinking and drinking to cope with ARB outcomes, an effect consistent with several prior reports.^{16,19} Finally, marijuana use also operated though drinking patterns to impact ARB patterns; this is in line with several other studies among college students which have found similar relationships among marijuana use, drinking quantities, and ARBs.^{21,36} It is noteworthy that, although no direct links were seen between marijuana use in the prior month and future ARBs within the model, there was a significant zero-order correlation between marijuana use in the prior month and ARBs (Table 2).

The relatively weak performance of alcohol expectancies in the SEM despite the significant zero-order correlation in Table 2 is also worthy of note. Due to restrictions on the amount of time students would be willing to devote to the eight assessments (including baseline), and as in another prospective study conducted in the UK, the protocol used a brief version of the AEQ,³⁷ which may not have been sensitive enough to identify an effect in the present study.

Recent studies have shown that LR, peer drinking, and drinking to cope with stress may offer opportunities for identifying young drinkers at high risk for adverse alcohol consequences and enrolling them in an appropriate prevention program.¹⁷ Thus, efforts to diminish heavy drinking could be enhanced by focusing on a college student's LR, marijuana use, peer drinking, and drinking to cope, and are likely to have the additional benefits of decreasing the prevalence of ARBs as well.

It is important to remember that our data were extracted from a larger study focusing on the effectiveness of different programs to prevent heavy drinking. In the current analyses, the prevention groups of the study were pooled, and there was no significant relationship between group assignment (educational vs. control group) and the ARB outcome. Still, it will be important to carry out additional studies in the absence of other interventional protocols.

There are additional caveats to consider when viewing these results. First, the number of ARBs might have been higher if participants were not enrolled in a prevention study. Second, no distinction was made between fragmentary and en-bloc ARBs, so we cannot distinguish specific predictors between those two subgroups. Third, because of unanticipated funding delays, data collection for the larger study that was slated to coincide with the start of a new school year was delayed until January 2014; thus, baseline assessment of drinking patterns included Christmas and the New Year's holiday, both of which are typically associated with heavier drinking. Fourth, the data used here were limited to those available from the original study; thus, there were no measures of academic performance or culturally-related beliefs of different ethnic groups, heavy drinking (binge) periods were defined with the same maximum drinks per occasion for males and females, and all information related to drinking was obtained by self-report, without corroborating informants. Fifth, the data presented here were obtained from a single university in Southern California that has a high proportion of Asian and Hispanic students. Further research should investigate ARB prevalence and patterns at other universities to determine the generalizability of the current data. It is also important to remember that SEM tests a specific model of the relationships among predictors and an outcome, but does not evaluate whether that model is superior to other models that might be proposed.

In conclusion, these analyses demonstrated a high rate of ARBs in college students. While the study from which the data were extracted was conducted at a California university, rates of heavy drinking and ARBs in youth have been demonstrated to be high in Brazil as well.¹² Evidence from additional analyses at UCSD indicate that identifying individuals at high risk for AUDs and directly addressing their avenue of predisposition (e.g., a low LR to alcohol) can significantly decrease their heavy drinking and associated problems over the subsequent 55 weeks.¹⁷ A similar program might be considered in Brazil. Based on the data reported herein, thought should be given to whether a modified prevention approach might be useful for women and Asian individuals, in light of their potential differential vulnerability to ARBs, which operates relatively independently of the alcohol quantities consumed.

Acknowledgements

This work was supported by the National Institutes of Health/National Institute on Alcohol Abuse and Alcoholism (NIH/NIAAA; 1 R01 AA021162 and 5 U10 AA08401) and by Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq; 203313/2014-3). PDG received a postdoctoral fellowship from CNPq to work at MAS's research laboratory, and was a scholar in the Alcohol Medical Scholars Program during 2015/2016. MAS received a grant from The Foundation for Alcohol Research (ABMRF) in 1988.

Disclosure

MAS gave a presentation on the genetics of alcoholrelated disorders to Anheuser-Busch InBev executives at Yale University in 2013, for which he received travel costs and an honorarium. The other authors report no conflicts of interest.

References

- White A, Hingson R. The burden of alcohol use: excessive alcohol consumption and related consequences among college students. Alcohol Res. 2013;35:201-18.
- 2 Perry PJ, Argo TR, Barnett MJ, Liesveld JL, Liskow B, Hernan JM, et al. The association of alcohol-induced blackouts and grayouts to blood alcohol concentrations. J Forensic Sci. 2006;51:896-9.
- 3 Barnett NP, Clerkin EM, Wood M, Monti PM, O'Leary Tevyaw T, Corriveau D, et al. Description and predictors of positive and negative alcohol-related consequences in the first year of college. J Stud Alcohol Drugs. 2014;75:103-14.

- 5 Eshelman LR, Messman-Moore TL, Sheffer N. The importance of substance-related sexual victimization impact on substance use and risk perception in female college students. J Interpers Violence. 2015;30:2616-35.
- 6 Mundt MP, Zakletskaia LI. Prevention for college students who suffer alcohol-induced blackouts could deter high-cost emergency department visits. Health Aff (Millwood). 2012;31:863-70.
- 7 Sipilä P, Rose RJ, Kaprio J. Drinking and mortality: long-term followup of drinking-discordant twin pairs. Addiction. 2016;111:245-54.
- 8 Anthenelli RM, Klein JL, Tsuang JW, Smith TL, Schuckit MA. The prognostic importance of blackouts in young men. J Stud Alcohol. 1994;55:290-5.
- 9 Luczak SE, Shea SH, Hsueh AC, Chang J, Carr LG, Wall TL. ALDH2*2 is associated with a decreased likelihood of alcoholinduced blackouts in Asian American college students. J Stud Alcohol. 2006;67:349-53.
- 10 Hingson R, Zha W, Simons-Morton B, White A. Alcohol-induced blackouts as predictors of other drinking related harms among emerging young adults. Alcohol Clin Exp Res. 2016;40:776-84.
- 11 Schuckit MA, Smith TL, Heron J, Hickman M, Macleod J, Munafo MR, et al. Latent trajectory classes for alcohol-related blackouts from age 15 to 19 in ALSPAC. Alcohol Clin Exp Res. 2015;39:108-16.
- 12 Sanchez ZM, Ribeiro KJ, Wagner GA. Binge drinking associations with patrons' risk behaviors and alcohol effects after leaving a nightclub: sex differences in the "Balada com ciência" portal survey study in Brazil. PLoS One. 2015;10:e0133646.
- 13 Ray LA, Hart EJ, Chin PF. Self-rating of the effects of alcohol (SRE): predictive utility and reliability across interview and self-report administrations. Addict Behav. 2011;36:241-3.
- 14 Quinn PD, Fromme K. Subjective response to alcohol challenge: a quantitative review. Alcohol Clin Exp Res. 2011;35:1759-70.
- 15 Henry KL, Slater MD, Oetting ER. Alcohol use in early adolescence: the effect of changes in risk taking, perceived harm and friends' alcohol use. J Stud Alcohol. 2005;66:275-83.
- 16 Borsari B, Carey KB. Peer influences on college drinking: a review of the research. J Subst Abuse. 2001;13:391-424.
- 17 Schuckit MA, Smith TL, Clausen P, Fromme K, Skidmore J, Shafir A, et al. The low level of response to alcohol-based heavy drinking prevention program: one-year follow-up. J Stud Alcohol Drugs. 2016;77:25-37.
- 18 Corbin WR, Farmer NM, Nolen-Hoekesma S. Relations among stress, coping strategies, coping motives, alcohol consumption and related problems: a mediated moderation model. Addict Behav. 2013;38:1912-9.
- 19 Park CL, Levenson MR. Drinking to cope among college students: prevalence, problems and coping processes. J Stud Alcohol. 2002; 63:486-97.
- 20 Patrick ME, Wray-Lake L, Finlay AK, Maggs JL. The long arm of expectancies: adolescent alcohol expectancies predict adult alcohol use. Alcohol Alcohol. 2010;45:17-24.
- 21 Schuckit MA, Smith TL, Shafir A, Clausen P, Danko G, Goncalves PD, et al. Predictors of patterns of alcohol-related blackouts over time in youth from the collaborative study of the genetics of alcoholism: the roles of genetics and cannabis. J Stud Alcohol Drugs. 2017;78:39-48.
- 22 Fromme K, Corbin WR, Kruse MI. Behavioral risks during the transition from high school to college. Dev Psychol. 2008;44:1497-1504.
- 23 Baraona E, Abittan CS, Dohmen K, Moretti M, Pozzato G, Chayes ZW, et al. Gender differences in pharmacokinetics of alcohol. Alcohol Clin Exp Res. 2001;25:502-7.
- 24 Luczak SE, Yarnell LM, Prescott CA, Myers MG, Liang T, Wall TL. Effects of ALDH2*2 on alcohol problem trajectories of Asian American college students. J Abnorm Psychol. 2014;123:130-40.
- 25 American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV). Arlington: American Psychiatric Publishing; 1994.
- 26 Hesselbrock M, Easton C, Bucholz KK, Schuckit M, Hesselbrock V. A validity study of the SSAGA – a comparison with the SCAN. Addiction. 1999;94:1361-70.
- 27 Schuckit MA, Smith TL. Stability of scores and correlations with drinking behaviors over 15 years for the self-report of the effects of alcohol questionnaire. Drug Alcohol Depend. 2013;128:194-9.

- 28 National Institute on Alcohol Abuse and Alcoholism. Project MATCH Hypotheses: Results and Causal Chain Analyses. [cited 2017 May 03]. archive.org/stream/projectmatchhypo00long/projectmatch hypo00long_djvu.txt.
- 29 Cooper ML, Russell M, George WH. Coping, expectancies, and alcohol abuse: a test of social learning formulations. J Abnorm Psychol. 1988;97:218-30.
- 30 Brown SA, Christiansen BA, Goldman MS. The Alcohol Expectancy Questionnaire: an instrument for the assessment of adolescent and adult alcohol expectancies. J Stud Alcohol. 1987;48:483-91.
- 31 Schuckit MA, Smith TL, Heron J, Hickman M, Macleod J, Lewis G, et al. Testing a level of response to alcohol-based model of heavy drinking and alcohol problems in 1,905 17-year-olds. Alcohol Clin Exp Res. 2011;35:1897-904.
- 32 Arbuckle JL. Amos. Version 18.0. Chicago: IBM SPSS; 2014.

- 33 Muthén LK, Muthén BO. Mplus user's guide. 7th ed.Los Angeles: Muthén & Muthén; 2012.
- 34 Hu LT, Bentler PM. Fit indices in covariance structural analysis: sensitivity to under parameter-sized model misspecification. Psychol Methods. 1998;3:424-53.
- 35 White A, Castle IJ, Chen CM, Shirley M, Roach D, Hingson R. Converging patterns of alcohol use and related outcomes among females and males in the United States, 2002 to 2012. Alcohol Clin Exp Res.2015;39:1712-26.
- 36 Haas AL, Wickham R, Macia K, Shields M, Macher R, Schulte T. Identifying classes of conjoint alcohol and marijuana use in entering freshmen. Psychol Addict Behav. 2015;29:620-6.
- 37 Schuckit MA, Smith TL, Trim R, Heron J, Horwood J, Davis JM, et al. The performance of elements of a 'level of response to alcohol'-based model of drinking behaviors in 13-year-olds. Addiction. 2008;103:1786-92.