Published in final edited form as:

Am J Drug Alcohol Abuse. 2018 ; 44(3): 329–338. doi:10.1080/00952990.2017.1339054.

Interaction between the *ADH1B*3* allele and drinking motives on alcohol use among Black college students

Michelle J. Zaso, M.S.¹, Jessica M. Desalu, M.S.¹, Jueun Kim, M.S.¹, Kavita Suryadevara, B.S.¹, John M. Belote, Ph.D.², and Aesoon Park, Ph.D.¹

¹Syracuse University, Department of Psychology, Syracuse, NY, USA

²Syracuse University, Center for Reproductive Evolution/Department of Biology, Syracuse, NY, USA

Abstract

Background—Black young adults have lower rates of alcohol use than other racial groups. Genetic factors may protect against drinking; specifically, the *ADH1B*3* allele is present almost exclusively in Black populations and has been protective against alcohol use and alcohol use disorder. The protective effects of the *ADH1B*3* allele, however, may differ as a function of alcohol-promoting cognitions.

Objectives—The current study examined whether *ADH1B*3* moderated relations of drinking motives with alcohol consumption among Black college drinkers.

Methods—Participants were 241 undergraduate students of self-identified Black race (mean age = 20 years; 66% female) who reported consuming alcohol at least once in the past 30 days.

Results—*ADH1B*3* was not significantly associated with drinking motives or drinking behaviors. However, significant, albeit small, interaction effects of *ADH1B*3* with drinking motives on drinking behavior were found; presence of an *ADH1B*3* allele protected against greater drinking quantity among students with high social motives (incidence rate ratio [IRR] = 0.95, 95% CI [0.92, 0.99]) and against frequent drinking among students with low coping motives (IRR = 1.06, 95% CI [1.01, 1.11]).

Conclusion—Such findings represent a novel demonstration of genetic modulation of alcohol-related cognitions within Black college drinkers, although replication is needed. Results represent an initial step toward better characterizing individual differences in associations of drinking motives with drinking behavior, with potential implications for interventions aimed at motivational processes in alcohol use.

Keywords

alcohol dehydrogenase; Black students; drinking motives

Address correspondence to: Aesoon Park, Ph.D., Department of Psychology, Syracuse University, 430 Huntington Hall, Syracuse NY 13244; aepark@syr.edu; Phone: 315-443-2391; Fax: 315-443-4085.

Financial Disclosures: The authors report no relevant financial conflicts.

Black adolescents and young adults are more likely to abstain from alcohol use than other racial groups^{1,2} and, when drinking, are less likely to drink heavily and get drunk than their White and Hispanic peers.^{1,3} Despite such lower rates of alcohol consumption, Black college students report similar levels of negative drinking consequences as their non-Black college peers.^{4,5} Further, Blacks' experience of negative drinking consequences rises rapidly across young adulthood such that Black adults report significantly more negative drinking consequences than White adults at equivalent levels of alcohol consumption.^{6,7} Such apparent racial differences suggest unique risk and protective factors for alcohol consumption within the Black population.

Genetic factors may protect Black young adults from alcohol use. Variations in alcohol metabolism genes (including alcohol dehydrogenase [ADH] and aldehyde dehydrogenase [ALDH]) have been found to influence drinking behavior.^{8–12} Specifically, variations in the alcohol dehydrogenase 1B (*ADH1B*) gene influence the activity of alcohol dehydrogenase, which is involved in the first step of alcohol metabolism by catalyzing the reaction converting alcohol to acetaldehyde.¹³ The rate that alcohol is metabolized into acetaldehyde differs based upon several variants, or alleles, of the *ADH1B* gene conferred by a single nucleotide polymorphism (SNP). The *ADH1B**3 allele, specifically, increases the reactivity of alcohol dehydrogenase, thus increasing metabolism of alcohol to acetaldehyde.¹⁴ Buildup of acetaldehyde can result in negative reactions, such as facial flushing, nausea, or increased pulse.¹⁵ Carriers of an *ADH1B**3 allele who experience these negative reactions may limit their subsequent alcohol consumption, rendering presence of an *ADH1B**3 allele protective against drinking. The *ADH1B**3 allele is observed almost exclusively in Blacks, present in almost 25% of Blacks,¹⁶ and has been shown to protect against hazardous drinking and alcohol use disorders in Blacks.^{17–19} Thus, presence of an *ADH1B**3 allele may be one factor protective against alcohol consumption unique to the Black population.

The *ADH1B**3 allele may be especially protective among Blacks who are at an increased risk for alcohol use based upon their drinking motives. Drinking motives represent the reasons individuals choose to drink, and drinking motives have been suggested to be the most proximal determinants of drinking behavior.²⁰ Individuals may be motivated to drink to experience certain outcomes – drinking to increase positive affect (i.e., enhancement motives), to improve social interactions (i.e., social motives), to reduce negative affect (i.e., coping motives), or to comply with perceived external pressures to drink (i.e., conformity motives).²¹ Each of these motives have been shown to have distinct associations with drinking behavior, although the majority of existing research is based upon primarily White samples. Social motives generally have been associated with alcohol consumption, enhancement motives with heavy drinking, and coping motives with alcohol-related problems among predominantly White samples.²¹ However, limited research of Black college students suggests different patterns of associations between drinking motives and drinking behavior among Black college students. Specifically, among Black college students, enhancement (but not social, coping, or conformity) motives have been uniquely associated with individual differences in drinking behavior (e.g., drinking quantity, weekly drinking, heavy episodic drinking), after controlling for other drinking motives;^{22,23} in contrast, social and coping motives were associated only with within-person variations in drinking across drinking episodes.²³ Finally, in contrast to relatively well-established

positive associations of enhancement, social, and coping motives with drinking behavior, research has demonstrated nonsignificant and sometimes positive associations of conformity motives with drinking behavior among general and high-risk^{24–26} college student samples. Thus, the current study explored associations of enhancement, social, and coping motives with drinking behavior in an exclusive Black college sample.

Research suggests associations of drinking motives with drinking behavior may differ as a function of alcohol metabolism genes. Previous research suggests presence of a protective *ALDH2*2* variant, another alcohol metabolism allele found almost exclusively in Asian populations, was associated with lower weekly drinking, number of heavy drinking episodes, and maximum lifetime alcohol use among Asian college students ($N = 69$) as implicit coping (but not enhancement) motives increased.²⁷ While this investigation yielded important insights into implicit drinking motives (i.e., primarily automatic processes, as assessed through implicit association tests), genetic modulation by alcohol metabolism genes in explicit motives (i.e., primarily conscious processes, as assessed through self-report) remain unexplored.

Further, *ALDH2* genotype has modulated another aspect of alcohol-related cognitions – drinking expectancies, or beliefs about the effects of alcohol consumption. Tension reduction and sexuality expectancies were more weakly associated with drinking quantity among female carriers of a protective *ALDH2*2* variant than noncarriers in an Asian college student sample ($N = 117$).²⁸ Presence of an *ADH1B*3* allele may have similar protective influences on drinking among Black college students as a function of drinking motives, although such genetic moderation has not yet been tested.

Study Aims and Hypotheses

The current study aimed to examine the relationship between the *ADH1B*3* allele and enhancement, social, and coping motives on alcohol consumption in a Black college drinking sample. Since existing (albeit limited) research has suggested associations of enhancement motives with individual differences in drinking behavior among Black college students,^{22,23} it was hypothesized that enhancement motives would be associated with alcohol consumption. Regarding genetic modulation in these associations, we did not formulate hypotheses regarding associations of specific drinking motives with drinking behavior given that this is a new investigation; it was hypothesized that the *ADH1B*3* allele would protect against drinking when students endorsed high levels of motivation to drink for enhancement, social, and/or coping reasons. Existing research has demonstrated genetic modulation (e.g., *CRHBP*, *DRD4*, 5-HTTLPR) of a parenting skills training program in a sample of Black adolescents^{29,30} and stressful life events in a sample of Black adolescents³¹ and a sample of Black college students.³² However, to date, no research has examined potential modulation of alcohol-promoting cognitions and the ethnically specific alcohol protective allele, *ADH1B*3*, within the Black population.

Materials and Methods

Participants and Procedure

Data were drawn from a cross-sectional study of 251 Black college students recruited from a private, predominantly White university in the northeastern United States [CITATION]. Eligible participants were current undergraduate students of self-identified Black race who were at least 18 years of age and reported alcohol use at least once in the past 30 days. Participants were recruited through the university's undergraduate research participation pool, email solicitations through electronic mailing lists to diverse student organizations, flyers, and respondent-driven sampling.

Upon arriving to the test site, participants were briefed on study procedures and provided written, informed consent. Participants completed a paper and pencil questionnaire that assessed demographic information, alcohol and substance use, and their correlates. Following completion of the questionnaires, participants provided a 2.0mL saliva sample for genotyping. Ten samples (4% of the original sample) could not be genotyped after multiple attempts and were dropped from analyses, resulting in a final sample of 241 college students. Students whose samples could not be genotyped did not differ significantly from students whose samples were genotyped on any study variables at $p > .05$. Participants were compensated with research credit (if recruited through the university's undergraduate research participation pool) or \$15 (if recruited through other means). Participants could receive up to an additional \$15 for referring future, eligible participants (\$5 per referral, up to 3 referrals permitted). All study procedures were approved by the university's institutional review board.

Measures

ADH1B*3—Genomic DNA for polymerase chain reaction (PCR) analysis was extracted from saliva samples using the Qiagen DNeasy Blood and Tissue Kit (Valencia, California) following manufacturer's instructions. Samples were checked by agarose gel electrophoresis to assess the quality of DNA extracts. The single nucleotide polymorphism (SNP) that defines *ADH1B*3* (i.e., rs2066702) was genotyped through PCR amplification of the region around exon 9 (Arg370Cys) and allele-specific fluorescence using the ThermoFisher TaqMan® SNP genotyping assay in an Applied Biosystems™ (ABI) 7500 real-time PCR instrument by Salimetrics, LLC (Carlsbad, California). Samples were genotyped twice to ensure concordance.

The observed prevalence of the *ADH1B*3* allele did not deviate significantly from Hardy-Weinberg equilibrium, $\chi^2(1, N = 241) = 0.90$; observed genotypes included *ADH1B*1/1* ($n = 158$), *ADH1B*1/3* ($n = 77$), and *ADH1B*3/3* ($n = 6$). Participants were dichotomized as carriers of at least one protective, low-risk allele (*ADH1B*3*) or non-carriers for main analyses, because modeling a cross-product gene-environment interaction using a three-category polymorphic genotype may increase false positive and false negative findings³³ and only a small number of participants in our sample (3%) carried two copies of the *ADH1B*3* allele, similar to previous studies.^{18,19} We note that ancillary analyses with a continuous genotype classification of the number (instead of presence) of *ADH1B*3* alleles yielded the

same pattern of significance of the interaction effects between *ADH1B* and drinking motives.

Drinking motives—Participants reported their motivations to consume alcohol through the Drinking Motives Questionnaire, Revised (DMQ-R).³⁴ Using a 1 (*almost never/never*) to 5 (*almost always/always*) Likert scale, participants reported their motivations to consume alcohol for social (“Because it improves parties and celebrations”), coping (e.g., “To forget your worries”), and enhancement (e.g., “Because it gives you a pleasant feeling”) reasons. While the DMQ-R also contains a subscale assessing conformity motives, the present study focused only on social, coping, and enhancement motives due to inconsistent findings on the impact of conformity motives on alcohol use^{24,26} and concern with increasing Type I error. Sum scores for the three subscales (Cronbach’s $\alpha = .84, .84$, and $.87$, respectively) were used in analyses. The DMQ-R has demonstrated good reliability and validity among racially diverse adolescent samples.³⁵

Drinking behavior—Participants reported their alcohol consumption on each of the past 30 days using the Timeline FollowBack calendars.³⁶ Participants were provided a calendar and instructed to record the total number of standard drinks they consumed on each day. The definition of a standard drink was given to participants as a 12-oz can or bottle of beer, 5-oz glass of wine, 8-oz glass of malt liquor, or 1.5-oz shot of liquor straight or in a mixed drink. Calendars included campus activities, national and local events, and holidays to help participants recall their alcohol use. Answers were recoded into three variables: frequency of any alcohol use, typical quantity of alcohol use in a drinking occasion, and frequency of binge drinking (defined as 4+ standard drinks for women and 5+ standard drinks for men in a single drinking day)³⁷ in the past 30 days.

Potential confounding variables—Two items were administered to assess sex (0 = *female* and 1 = *male*) and age, which were included as covariates in all analyses.

Data Analytic Strategies

All study analyses were conducted in SPSS, Version 23. There was missing data from two participants on age, and these cases were excluded from relevant analyses; there was no missing data in any drinking motives or alcohol consumption variables. Multivariate outlier analyses based on Mahalanobis distance using a χ^2 distribution did not identify any significant multivariate outliers (Mahalanobis $D^2 = 0.11 - 15.82$, $p > .001$).³⁸ Independent samples *t*-tests (for continuous variables; i.e., age, drinking motives, alcohol consumption) and a chi-square difference test (for the categorical variable; i.e., sex) were conducted to examine differences in study variables as a function of *ADH1B*3* presence. The effects of *ADH1B*3* and drinking motives on alcohol consumption were examined through generalized linear models, which allow the estimation of non-normally distributed error variance.³⁹ The negative binomial distribution was specified to accommodate over-dispersed count outcomes (i.e., variance > mean);⁴⁰ we modeled typical drinking quantity with a negative binomial distribution, because they were both count variables of a number of standard drinks and were characterized by a positively skewed non-negative distribution.³⁹ As a measure of effect sizes for individual predictors, incidence rate ratios (IRRs) were

estimated along with their 95% confidence intervals (CIs). Separate analyses were conducted for the three alcohol consumption variables; all drinking motives were included together in the same model to examine the unique associations of specific drinking motives on alcohol consumption over and above other motives. To control for potential confounding interaction effects of covariates with all predictors in the model,⁴¹ all models included two-way interaction terms of each covariate with both *ADH1B*3* presence and drinking motives (e.g., age $\times$ *ADH1B*3*). For significant interactions, we conducted simple effects analyses to examine the associations of drinking motives with alcohol consumption separately for *ADH1B*3* carriers and noncarriers.

In addition to main analyses that included all drinking motives subscales together in the same model, ancillary analyses were conducted with each subscale in a separate model to examine consistency of study findings. Additional ancillary analyses ($n = 182$) were conducted excluding participants at least 21 years of age (i.e., legal drinkers; $n = 57$) to explore whether the moderating effects of *ADH1B* on the relations between drinking motives and alcohol consumption varied as a function of legal drinking status.

Results

Descriptive Statistics

Descriptive statistics and bivariate correlation coefficients of all study variables are shown in Table 1. Participants were on average 20 years of age ($SD = 4.11$) and 66% female. All participants were full-time college students, with 38% freshmen, 29% sophomores, 18% juniors, and 15% seniors. Participants reported drinking alcohol on an average of over six of the past 30 days ($SD = 4.28$), consuming an average of four standard drinks on each drinking occasion ($SD = 2.48$), and engaging in binge drinking almost three times ($SD = 3.59$) in the past 30 days. Social, coping, and enhancement motives were significantly and positively associated with drinking frequency, drinking quantity, and binge drinking frequency, $r_s = .20$ – $.42$, $p_s < .01$, with the exception of a nonsignificant association between coping motives and drinking quantity, $r = .10$, $p = .11$. *ADH1B*3* presence was not significantly associated with any drinking motives or drinking behaviors, $r_s = -.03$ – $-.10$, $p_s = .13$ – $.68$. As shown in Supplementary Table 1, independent samples *t*-tests and a chi-square difference test indicated no significant differences in any study variables as a function of *ADH1B*3*.

Generalized Linear Models

Results from negative binomial generalized linear models are shown in Table 2. There were significant interaction effects of *ADH1B*3* with social motives on drinking quantity (IRR = 0.95, $p = .01$) as well as with coping motives on drinking frequency (IRR = 1.06, $p = .02$). There were no significant interaction effects of *ADH1B*3* with enhancement motives on any drinking behaviors. Further, there were no significant interaction effects of *ADH1B*3* with any drinking motives on binge drinking frequency.

Ancillary analyses dropping all nonsignificant covariates yielded the same pattern of significance for interactions of *ADH1B*3* with drinking motives as analyses that included all covariates; results available upon request. Ancillary analyses with each drinking motives

subscale in a separate model yielded the same significant interaction effects of *ADH1B*3* and drinking motives. Additional ancillary analyses of data from only non-legal drinkers ($n = 182$) yielded the same significant interaction effects of *ADH1B*3* and drinking motives as analyses with all participants.

To help illustrate the observed differences in alcohol use based upon *ADH1B*3* and drinking motives, mean levels (and standard error bars) of alcohol consumption as a function of presence of *ADH1B*3* and drinking motives are shown in Figure 1. Among students with high social motives (upper 50%), carriers of an *ADH1B*3* allele reported lower drinking quantity ($M = 3.75$; $SD = 1.92$) than noncarriers ($M = 5.00$; $SD = 2.52$). Presence of the *ADH1B*3* allele appeared to protect against greater drinking quantity among students with high social motives. Simple effects analyses corroborated this pattern such that greater social motives were associated with greater quantity of alcohol use among noncarriers ($IRR = 1.04$, $p < .001$) but not among carriers ($IRR = 0.75$, $p = .99$). In contrast, presence of an *ADH1B*3* allele protected against frequent drinking among students with low coping motives. Among students with low coping motives (lower 50%), *ADH1B*3* carriers reported lower drinking frequency ($M = 4.61$; $SD = 3.09$) than noncarriers ($M = 5.99$; $SD = 4.05$). Simple effects analyses corroborated this pattern such that greater coping motives were associated with greater frequency of alcohol use among carriers ($IRR = 1.05$, $p = .02$) but not among noncarriers ($IRR = 0.99$, $p = .56$).

Discussion

The present study examined the relationship between *ADH1B*3*, drinking motives, and drinking behavior among a sample of Black college students. It extends previous research by demonstrating that associations of drinking motives with drinking behavior differ across *ADH1B* genotype. Specifically, presence of an *ADH1B*3* allele protected against drinking quantity as social drinking motives increased and against frequent drinking as coping drinking motives decreased. Thus, *ADH1B*3* may mitigate the association of drinking motives with drinking behaviors; however, this genetic moderation may vary across different drinking motives. Although replication is needed, such findings represent a novel demonstration of an alcohol metabolism gene variant modulating the influences of alcohol-related cognitions on drinking behavior in the Black population.

When reporting high social drinking motives, carriers of an *ADH1B*3* allele consumed a lower quantity of alcohol than noncarriers, as hypothesized. Students endorsing high social motives may drink during social gatherings to improve their social interactions, and their drinking may be positively reinforced by contributing to favorable social outcomes. Once these students begin drinking, however, *ADH1B*3* carriers may slow their drinking to minimize the physiological consequences of alcohol consumption that could yield physical (e.g., nausea, increased pulse) and social (e.g., facial flushing) repercussions due to acetaldehyde buildup.¹⁵ Thus, *ADH1B*3* presence and its associated negative effects may reduce the reinforcement value of alcohol consumption, thereby protecting against increased drinking quantity when students drink to improve their social gatherings.

Unexpectedly, presence of an *ADH1B*3* allele protected against frequent drinking when students reported low (as opposed to high) coping drinking motives. When reporting high coping motives, carriers drank as frequently as noncarriers. When motivated to drink to deal with negative emotion, carriers appear to consume alcohol despite experiencing negative consequences such as the unpleasant effects of acetaldehyde accumulation afforded by the *ADH1B*3* allele. This finding is in line with previous findings that coping motives are more strongly associated with alcohol-related problems than other drinking motives.²¹ Drinking behavior by students endorsing high coping motives may be driven by negative reinforcement (i.e., reduction of negative emotions) and not necessarily deterred by negative physiological side effects from drinking associated with *ADH1B*3*.

The *ADH1B*3* allele modulated the influence of social and coping, but not enhancement, motives on drinking behavior. Existing research demonstrates that variation in another alcohol metabolism gene, *ALDH2*, modulated the influence of implicit coping, but not enhancement, motives on drinking among Asian students.²⁷ Alcohol metabolism gene variants may have less pronounced effects on drinking as a function of enhancement motives. Students with high enhancement motivation drink to increase positive affect (“Because it gives you a pleasant feeling”), and carriers of *ADH1B*3* may be less likely to endorse motivation to drink to experience positive reactions (i.e., for enhancement), given that their alcohol consumption is accompanied by concurrent negative physiological reactions afforded by the allele. Our sample consisted of current drinkers (excluding abstainers), and thus all carriers presumably had experiences with the negative physiological responses to alcohol afforded by the allele. Further, our findings suggest unique associations of enhancement motives with drinking over and above other motives, consistent with previous research among Black college students.^{22,23} Enhancement motives may have strong associations with Black college student drinking regardless of *ADH1B* genotype.

*ADH1B*3* modulated associations of drinking motives with drinking frequency and quantity but not frequency of binge drinking. Black students engaging in frequent binge drinking may normalize negative alcohol-related consequences (including negative physiological effects of acetaldehyde accumulation afforded by *ADH1B*3*) as part of the drinking experience, thus becoming less influenced by *ADH1B*3*-based protection in associations of drinking motives with drinking behavior. Alternatively, the infrequent binge drinking episodes reported by our sample of Black college drinkers may have been driven more by situational factors (e.g., special occasions, etc.) than drinking motives or genetics. Binge drinking occasions were relatively infrequent in the current sample of Black college drinkers, with over two-thirds of students reporting only one or two binge drinking episodes in the past 30 days, and these rates were slightly below national estimates among U.S. college students.⁴² However, these results may be due, in part, to the current study’s assessment of binge drinking episodes over the past 30 days, and drinking behavior over this relatively short time period may be more influenced by environmental factors than drinking over longer periods; given its novelty, our findings await replication within larger samples whose drinking behaviors are assessed over longer periods.

The current findings suggest that *ADH1B* genotype modulates the relationship between drinking motives and drinking behavior. However, previous studies also suggest that

drinking motives might mediate genetic effects on drinking behavior. Research suggests aggregated genetic contributions to drinking motives,⁴³ although not specific to *ADH1B*3*. Also, presence of a protective *ALDH2* alcohol metabolism gene variant was associated with lower social, enhancement, and coping motives, which in turn were associated with reduced risky drinking among Asian-American college students.⁴⁴ Similarly, genetic variation in the dopaminergic system (rs3779084) was associated with enhancement motives, which in turn was associated with alcohol consumption among European-American female smokers.⁴⁵ However, *ADH1B* genotype was not associated with drinking motives in the current sample ($r = -.03$ to $-.08$). Nonetheless, such associations may manifest in larger samples or when considering the cumulative effects of multiple risky alleles on drinking behavior. The negative side effects afforded by *ADH1B*3* also may not be as large as those for other candidate genes, including variants within alcohol metabolism genes; *ADH1B*3* was associated with lower ethanol-oxidizing activity and, thus, weaker protection against alcohol use disorders than *ADH1B*2*.⁴⁶ Further, additional research has suggested that genetic risks for drinking (i.e., familial risk for alcoholism) may be better conceptualized as having joint contributions to drinking motives and drinking behavior (i.e., correlated cause model) than having influences on drinking motives that in turn influence drinking behavior (i.e., mediated model).⁴⁷ Future research is needed to explore the possible ways through which alcohol metabolism gene variation and drinking motives interplay to influence drinking behavior.

Research into genetically based differences in associations of drinking motives with drinking behavior may have long-term implications for prevention or intervention efforts to address Black college student drinking. Despite lower rates of alcohol use among Black relative to non-Black students,¹⁻³ Black students experience comparable levels of negative drinking consequences^{4,5} and are at risk for escalations in consequences during the transition to adulthood.^{6,7} College drinking interventions have often targeted alcohol-related cognitions through personalized feedback on reasons for drinking⁴⁸ or positive/negative alcohol expectancies,^{49,50} exploration of expectancy effects on drinking,⁵¹ and alcohol expectancy challenges.^{52,53} Although a meta-analysis demonstrated overall support for feedback on expectancies and/or motives in college drinking interventions,⁵⁴ another meta-analysis demonstrated that college drinking interventions have reduced success among samples with a greater proportion of Black students.⁵⁵ Genetic factors, including *ADH1B*3*, may be important sources of individual differences in associations of drinking motives with drinking behavior. In line with the promise of personalized medicine that tailors treatment based upon genetic or other biomarkers to improve treatment effectiveness,^{56,57} genetically informed interventions tailored to students' genetic risks may be more effective (especially when culturally tailored) across racial groups than universal, exhaustive strategies.⁵⁸ The current findings represent an initial step in better understanding interplay between genetics and alcohol-related cognitions in drinking among Black students, although more research is needed to examine whether genetically based differences in associations of drinking motives with drinking behaviors may, in part, contribute to the limited efficacy of brief alcohol interventions for Black students and whether genetically informed interventions may hold promise for reducing Black college student drinking.

Findings should be interpreted with respect to several limitations and future directions. First, findings were based upon a sample of Black college student drinkers. Generalizability of study findings to other populations of different age and socioeconomic status is precluded. Further, study eligibility criteria required that all participants report alcohol consumption at least once in the past 30 days, thus the relationship between *ADHIB*3*, drinking motives, and alcohol use among occasional or non-drinkers remains unknown. Given that the *ADHIB*3* allele has been shown to protect against drinking among Blacks,^{18,19} study eligibility criteria may have excluded potential carriers who refrain from alcohol use due to negative reactions following drinking. However, this potential bias due to exclusion of abstainers may be negligible given that the prevalence of *ADHIB*3* was within Hardy-Weinberg equilibrium in our sample and matched those of other studies among Blacks (34 – 41%).^{18,19} Second, the current findings are based on cross-sectional, correlational data, and thus causal relationships cannot be assumed. *ADHIB*3* may influence drinking by altering the alcohol-related learning that contributes to drinking motives, or *ADHIB*3*-based protection against alcohol consumption may limit carriers' experience with alcohol and, thus, opportunities to learn about alcohol's effects. In addition to the interaction of *ADHIB* with drinking motives on alcohol consumption (as modeled in the current study), the interaction of *ADHIB* with drinking behavior may affect drinking motives. Ancillary analyses using our cross-sectional data suggested genetic moderation of the association of typical drinking quantity (but not drinking frequency or binge drinking frequency) with drinking motives, whereby *ADHIB*3* presence was more strongly associated with reduced social and enhancement drinking motives among students who reported higher levels of typical drinking quantity (IRR = 0.95, $p = .001$ and IRR = 0.95, $p = .01$, respectively). Longitudinal or experimental designs are needed to better resolve the moderating role of *ADHIB*3* in the associations of drinking motives and drinking behavior. Third, our sample of 250 students is considered to be small in size and thus the current genetic moderation findings require replication in larger, independent samples due to increased concern of potential false positive findings when investigating genetic moderation.⁵⁹ Large, population-based samples with increased power to detect genetic effects would be useful. While these findings await replication with larger samples, the current findings represent an important step toward understanding the relationships between alcohol metabolism genotypes, alcohol-related cognitions, and alcohol use behavior in the Black population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding: This work was supported by the NIH under Grant [NUMBER].

References

1. Johnston, LD., O'Malley, PM., Miech, RA., Bachman, JG., Schulenberg, JE. Demographic Subgroup Trends Among Adolescents in the Use of Various Licit and Illicit Drugs, 1975–2015. Institute for Social Research, The University of Michigan; Ann Arbor, MI: 2016. (Monitoring the Future Occasional Paper No. 86)

2. Substance Abuse and Mental Health Services Administration (SAMSHA). Results from the 2013 National Survey on Drug Use and Health: Summary of National Findings. U.S. Department of Health and Human Services; Rockville, MD: 2014. NSDUH Series H-48, HHS Publication No. (SMA) 14-4863
3. O'Malley PM, Johnston LD. Epidemiology of alcohol and other drug use among American college students. *J Stud Alcohol Suppl.* 2002; (s14):23–39. DOI: 10.15288/jsas.2002.s14.23 [PubMed: 12022728]
4. Clarke N, Kim S-Y, White HR, Jiao Y, Mun E-Y. Associations between alcohol use and alcohol-related negative consequences among Black and White college men and women. *J Stud Alcohol Drugs.* 2013; 74(4):521–531. DOI: 10.15288/jsad.2013.74.521 [PubMed: 23739015]
5. Barnett NP, Clerkin EM, Wood M, Monti PM, O'Leary Tevya 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(1):103–114. DOI: 10.15288/jsad.2014.75.103 [PubMed: 24411802]
6. Mulia N, Ye Y, Greenfield TK, Zemore SE. Disparities in alcohol-related problems among White, Black, and Hispanic Americans. *Alcohol Clin Exp Res.* 2009; 33(4):654–662. DOI: 10.1111/j.1530-0277.2008.00880.x [PubMed: 19183131]
7. Witbrodt J, Mulia N, Zemore SE, Kerr WC. Racial/ethnic disparities in alcohol-related problems: differences by gender and level of heavy drinking. *Alcohol Clin Exp Res.* 2014; 38(6):1662–1670. DOI: 10.1111/acer.12398 [PubMed: 24730475]
8. Li D, Zhao H, Gelernter J. Strong association of the alcohol dehydrogenase 1B gene (ADH1B) with alcohol dependence and alcohol-induced medical diseases. *Biol Psychiatry.* 2011; 70(6):504–512. DOI: 10.1016/j.biopsych.2011.02.024 [PubMed: 21497796]
9. Li D, Zhao H, Gelernter J. Further clarification of the contribution of the ADH1C gene to vulnerability of alcoholism and selected liver diseases. *Hum Genet.* 2012; 131(8):1361–1374. DOI: 10.1007/s00439-012-1163-5 [PubMed: 22476623]
10. Li D, Zhao H, Gelernter J. Strong protective effect of the aldehyde dehydrogenase gene (ALDH2) 504lys (*2) allele against alcoholism and alcohol-induced medical diseases in Asians. *Hum Genet.* 2012; 131(5):725–737. DOI: 10.1007/s00439-011-1116-4 [PubMed: 22102315]
11. Takeuchi F, Isono M, Nabika T, Katsuya T, Sugiyama T, Yamaguchi S, et al. Confirmation of ALDH2 as a major locus of drinking behavior and of its variants regulating multiple metabolic phenotypes in a Japanese population. *Circ J.* 2011; 75(4):911–918. DOI: 10.1253/circj.CJ-10-0774 [PubMed: 21372407]
12. Quillen EE, Chen X-D, Almasy L, Yang F, He H, Li X, et al. ALDH2 is associated to alcohol dependence and is the major genetic determinant of “daily maximum drinks” in a GWAS study of an isolated rural chinese sample. *Am J Med Genet B Neuropsychiatr Genet.* 2014; 165(2):103–110. DOI: 10.1002/ajmg.b.32213
13. Edenberg HJ. The genetics of alcohol metabolism: role of alcohol dehydrogenase and aldehyde dehydrogenase variants. *Alcohol Res Health.* 2007; 30(1):5–13. [PubMed: 17718394]
14. Thomasson HR, Beard JD, Li T-K. ADH2 gene polymorphisms are determinants of alcohol pharmacokinetics. *Alcohol Clin Exp Res.* 1995; 19(6):1494–1499. DOI: 10.1111/j.1530-0277.1995.tb01013.x [PubMed: 8749816]
15. Eriksson CJ. The role of acetaldehyde in the actions of alcohol (update 2000). *Alcohol Clin Exp Res.* 2001; 25(5):15s–32s. DOI: 10.1111/j.1530-0277.2001.tb02369.x [PubMed: 11391045]
16. Luo X, Kranzler HR, Zuo L, Wang S, Schork NJ, Gelernter J. Diplotype trend regression analysis of the ADH gene cluster and the ALDH2 gene: multiple significant associations with alcohol dependence. *Am J Hum Genet.* 2006; 78(6):973–987. DOI: 10.1086/504113 [PubMed: 16685648]
17. Sartor CE, Wang Z, Xu K, Kranzler HR, Gelernter J. The joint effects of ADH1B variants and childhood adversity on alcohol related phenotypes in African-American and European-American women and men. *Alcohol Clin Exp Res.* 2014; 38(12):2907–2914. DOI: 10.1111/acer.12572 [PubMed: 25410943]
18. Ehlers CL, Montane-Jaime K, Moore S, Shafe S, Joseph R, Carr LG. Association of the ADH1B*3 allele with alcohol-related phenotypes in Trinidad. *Alcohol Clin Exp Res.* 2007; 31(2):216–220. DOI: 10.1111/j.1530-0277.2006.00298.x [PubMed: 17250612]

19. McCarthy DM, Pedersen SL, Lobos EA, Todd RD, Wall TL. ADH1B*3 and response to alcohol in African-Americans. *Alcohol Clin Exp Res*. 2010; 34(7):1274–1281. DOI: 10.1111/j.1530-0277.2010.01205.x [PubMed: 20477764]
20. Cox WM, Klinger E. A motivational model of alcohol use. *J Abnorm Psychol*. 1988; 97(2):168–180. DOI: 10.1037/0021-843X.97.2.168 [PubMed: 3290306]
21. Kuntsche E, Knibbe R, Gmel G, Engels R. Why do young people drink? A review of drinking motives *Clin Psychol Rev*. 2005; 25(7):841–861. DOI: 10.1016/j.cpr.2005.06.002 [PubMed: 16095785]
22. Madson MB, Villarosa MC, Moorer KD, Zeigler-Hill V. Drinking motives and alcohol use behaviors among African American college students: the mediating role of protective behavioral strategies. *J Ethn Subst Abuse*. 2015; 14(2):133–150. DOI: 10.1080/15332640.2014.973627 [PubMed: 25984955]
23. O'Hara RE, Boynton MH, Scott D, Armeli S, Tennen H, Williams C, et al. Drinking to cope among African-American college students: an assessment of episode-specific motives. *Psychol Addict Behav*. 2014; 28(3):671–681. DOI: 10.1037/a0036303 [PubMed: 25134052]
24. Bachrach RL, Merrill JE, Bytschkow KM, Read JP. Development and initial validation of a measure of motives for pregameing in college students. *Addict Behav*. 2012; 37(9):1038–1045. DOI: 10.1016/j.addbeh.2012.04.013 [PubMed: 22591951]
25. Neighbors C, Lee CM, Lewis MA, Fossos N, Larimer ME. Are social norms the best predictor of outcomes among heavy-drinking college students? *J Stud Alcohol Drugs*. 2007; 68(4):556–565. DOI: 10.15288/jsad.2007.68.556 [PubMed: 17568961]
26. LaBrie JW, Lac A, Kenney SR, Mirza T. Protective behavioral strategies mediate the effect of drinking motives on alcohol use among heavy drinking college students: gender and race differences. *Addict Behav*. 2011; 36(4):354–361. DOI: 10.1016/j.addbeh.2010.12.013 [PubMed: 21215529]
27. Hendershot CS, Lindgren KP, Liang T, Hutchison KE. COMT and ALDH2 polymorphisms moderate associations of implicit drinking motives with alcohol use. *Addict Biol*. 2012; 17(1):192–201. DOI: 10.1111/j.1369-1600.2010.00286.x [PubMed: 21309949]
28. McCarthy DM, Wall TL, Brown SA, Carr LG. Integrating biological and behavioral factors in alcohol use risk: the role of ALDH2 status and alcohol expectancies in a sample of Asian Americans. *Exp Clin Psychopharmacol*. 2000; 8(2):168–175. DOI: 10.1037/1064-1297.8.2.168 [PubMed: 10843299]
29. Beach SRH, Brody GH, Lei M-K, Philibert RA. Differential susceptibility to parenting among African American youths: testing the *DRD4* hypothesis. *J Fam Psychol*. 2010; 24(5):513–521. DOI: 10.1037/a0020835 [PubMed: 20954761]
30. Brody GH, Beach SRH, Philibert RA, Chen Y-f, Murry VM. Prevention effects moderate the association of 5-HTTLPR and youth risk behavior initiation: gene × environment hypotheses tested via a randomized prevention design. *Child Dev*. 2009; 80(3):645–661. DOI: 10.1111/j.1467-8624.2009.01288.x [PubMed: 19489894]
31. Goyal N, Aliev F, Latendresse SJ, Kertes DA, Bolland J, Byck GR, et al. Genes involved in stress response and alcohol use among high-risk African American youth. *Subst Abuse*. 2016; 37(3):450–458. DOI: 10.1080/08897077.2015.1134756 [PubMed: 26751645]
32. Kranzler HR, Scott D, Tennen H, Feinn R, Williams C, Armeli S, et al. The 5-HTTLPR polymorphism moderates the effect of stressful life events on drinking behavior in college students of African descent. *Am J Med Genet B Neuropsychiatr Genet*. 2012; 159B(5):484–490. DOI: 10.1002/ajmg.b.32051 [PubMed: 22488930]
33. Aliev F, Latendresse SJ, Bacanu S-A, Neale MC, Dick DM. Testing for measured gene-environment interaction: problems with the use of cross-product terms and a regression model reparameterization solution. *Behav Genet*. 2014; 44(2):165–181. DOI: 10.1007/s10519-014-9642-1 [PubMed: 24531874]
34. Cooper ML. Motivations for alcohol use among adolescents: development and validation of a four-factor model. *Psychol Assess*. 1994; 6(2):117–128. DOI: 10.1037/1040-3590.6.2.117
35. Kuntsche E, Stewart SH, Cooper ML. How stable is the motive-alcohol use link? A cross-national validation of the drinking motives questionnaire revised among adolescents from Switzerland,

- Canada, and the United States. *J Stud Alcohol*. 2008; 69(3):388–396. DOI: 10.15288/jsad.2008.69.388
36. Sobell, LC., Sobell, MB. Timeline Follow-Back. In: Litten, R., Allen, J., editors. *Measuring alcohol consumption: psychosocial and biochemical methods*. Totowa, NJ: Humana Press; 1992. p. 41–72.
 37. National Institute on Alcohol Abuse and Alcoholism [Internet]. Recommended alcohol questions. 2004. Available from: <http://www.niaaa.nih.gov/research/guidelines-and-resources/recommended-alcohol-questions>
 38. Tabachnick, BG., Fidell, LS. *Using multivariate statistics*. Boston, MA: Pearson; 2007.
 39. Neal DJ, Simons JS. Inference in regression models of heavily skewed alcohol use data: a comparison of ordinary least squares, generalized linear models, and bootstrap resampling. *Psychol Addict Behav*. 2007; 21(4):441–452. DOI: 10.1037/0893-164X.21.4.441 [PubMed: 18072826]
 40. Byers AL, Allore H, Gill TM, Peduzzi PN. Application of negative binomial modeling for discrete outcomes: a case study in aging research. *J Clin Epidemiol*. 2003; 56(6):559–564. DOI: 10.1016/S0895-4356(03)00028-3 [PubMed: 12873651]
 41. Keller MC. Gene $\times$ environment interaction studies have not properly controlled for potential confounders: the problem and the (simple) solution. *Biol Psychiatry*. 2014; 75(1):18–24. DOI: 10.1016/j.biopsych.2013.09.006 [PubMed: 24135711]
 42. Weitzman ER, Nelson TF, Wechsler H. Taking up binge drinking in college: the influences of person, social group, and environment. *J Adolesc Health*. 2003; 32(1):26–35. DOI: 10.1016/S1054-139X(02)00457-3 [PubMed: 12507798]
 43. Agrawal A, Dick DM, Bucholz KK, Madden PAF, Cooper ML, Sher KJ, et al. Drinking expectancies and motives: a genetic study of young adult women. *Addiction*. 2008; 103(2):194–204. DOI: 10.1111/j.1360-0443.2007.02074.x [PubMed: 18199298]
 44. Hendershot CS, Witkiewitz K, George WH, Wall TL, Otto JM, Liang T, et al. Evaluating a cognitive model of ALDH2 and drinking behavior. *Alcohol Clin Exp Res*. 2011; 35(1):91–98. DOI: 10.1111/j.1530-0277.2010.01325.x [PubMed: 21039630]
 45. Kristjansson SD, Agrawal A, Lessov-Schlaggar CN, Madden PAF, Lynne Cooper M, Bucholz KK, et al. The relationship between rs3779084 in the dopa decarboxylase (DDC) gene and alcohol consumption is mediated by drinking motives in regular smokers. *Alcohol Clin Exp Res*. 2012; 36(1):162–170. DOI: 10.1111/j.1530-0277.2011.01596.x [PubMed: 21797889]
 46. Lee SL, Chau GY, Yao CT, Wu CW, Yin SJ. Functional assessment of human alcohol dehydrogenase family in ethanol metabolism: significance of first-pass metabolism. *Alcohol Clin Exp Res*. 2006; 30(7):1132–1142. DOI: 10.1111/j.1530-0277.2006.00139.x [PubMed: 16792560]
 47. Prescott CA, Cross RJ, Kuhn JW, Horn JL, Kendler KS. Is risk for alcoholism mediated by individual differences in drinking motivations? *Alcohol Clin Exp Res*. 2004; 28(1):29–39. DOI: 10.1097/01.ALC.0000106302.75766.F0 [PubMed: 14745300]
 48. Juarez P, Walters ST, Daugherty M, Radi C. A randomized trial of motivational interviewing and feedback with heavy drinking college students. *J Drug Educ*. 2006; 36(3):233–246. DOI: 10.2190/753N-8242-727T-G63L [PubMed: 17345916]
 49. Borsari B, Carey KB. Two brief alcohol interventions for mandated college students. *Psychol Addict Behav*. 2005; 19(3):296–302. DOI: 10.1037/0893-164X.19.3.296 [PubMed: 16187809]
 50. Carey KB, Carey MP, Maisto SA, Henson JM. Brief motivational interventions for heavy college drinkers: a randomized controlled trial. *J Consult Clin Psychol*. 2006; 74(5):943–954. DOI: 10.1037/0022-006X.74.5.943 [PubMed: 17032098]
 51. Borsari B, Carey KB. Effects of a brief motivational intervention with college student drinkers. *J Consult Clin Psychol*. 2000; 68(4):728–733. DOI: 10.1037/0022-006X.68.4.728 [PubMed: 10965648]
 52. Darkes J, Goldman MS. Expectancy challenge and drinking reduction: experimental evidence for a mediational process. *J Consult Clin Psychol*. 1993; 61(2):344–353. DOI: 10.1037/0022-006X.61.2.344 [PubMed: 8473588]

53. Darkes J, Goldman MS. Expectancy challenge and drinking reduction: process and structure in the alcohol expectancy network. *Exp Clin Psychopharmacol*. 1998; 6(1):64–76. DOI: 10.1037/1064-1297.6.1.64 [PubMed: 9526147]
54. Carey KB, Scott-Sheldon LAJ, Carey MP, DeMartini KS. Individual-level interventions to reduce college student drinking: a meta-analytic review. *Addict Behav*. 2007; 32(11):2469–2494. DOI: 10.1016/j.addbeh.2007.05.004 [PubMed: 17590277]
55. Scott-Sheldon LA, Carey KB, Elliott JC, Garey L, Carey MP. Efficacy of alcohol interventions for first-year college students: a meta-analytic review of randomized controlled trials. *J Consult Clin Psychol*. 2014; 82(2):177–188. DOI: 10.1037/a0035192 [PubMed: 24447002]
56. Arranz MJ, de Leon J. Pharmacogenetics and pharmacogenomics of schizophrenia: a review of last decade of research. *Mol Psychiatry*. 2007; 12(8):707–747. DOI: 10.1038/sj.mp.4002009 [PubMed: 17549063]
57. Hughes AR, Brothers CH, Mosteller M, Spreen WR, Burns DK. Genetic association studies to detect adverse drug reactions: abacavir hypersensitivity as an example. *Pharmacogenomics*. 2009; 10(2):225–233. DOI: 10.2217/14622416.10.2.225 [PubMed: 19207023]
58. van Ijzendoorn MH, Bakermans-Kranenburg MJ. Genetic differential susceptibility on trial: meta-analytic support from randomized controlled experiments. *Dev Psychopathol*. 2015; 27(1):151–162. DOI: 10.1017/s0954579414001369 [PubMed: 25640837]
59. Duncan LE, Keller MC. A critical review of the first 10 years of candidate gene-by-environment interaction research in psychiatry. *Am J Psychiatry*. 2011; 168(10):1041–1049. DOI: 10.1176/appi.ajp.2011.11020191 [PubMed: 21890791]

Figure 1. Mean levels of alcohol consumption variables as a function of presence of *ADH1B*3* and drinking motives (high = upper 50%; low = lower 50%) on alcohol consumption. Error bars represent standard error of the mean.

Table 1
Means (and Standard Deviations) or Percentages of All Study Variables and Their Bivariate Correlation Coefficients

Study Variable (possible range)	<i>M (SD)</i>	1.	2.	3.	4.	5.	6.	7.
1. <i>ADHIB</i> [*] (1 = carrier; 0 = noncarrier)	34%	—						
2. Sex (1 = male; 0 = female)	34%	-.10	—					
3. Age	20.04 (4.11)	.00	.03	—				
4. Social drinking motives (5 – 25)	16.00 (4.93)	-.03	.03	-.07	—			
5. Coping drinking motives (5 – 25)	9.07 (4.20)	-.08	-.10	.05	.40 ^{***}	—		
6. Enhancement drinking motives (5 – 25)	13.66 (5.25)	-.05	-.00	-.08	.66 ^{***}	.39 ^{***}	—	
7. Past-30-day drinking frequency	6.19 (4.28)	-.10	.16 [*]	.17 [*]	.24 ^{***}	.21 ^{**}	.38 ^{***}	—
8. Past-30-day typical drinking quantity	4.05 (2.48)	-.03	.31 ^{***}	-.04	.28 ^{***}	.10	.26 ^{***}	.25 ^{***}
9. Past-30-day binge drinking frequency	2.93 (3.59)	-.07	.14 [*]	.08	.35 ^{***}	.20 ^{**}	.42 ^{***}	.77 ^{***}
								.61 ^{***}

Note. *N* = 239 – 241 due to missing values.

*
p < .05.

**
p < .01.

p < .001.

Table 2
Hierarchical Negative Binomial Regressions Predicting Alcohol Use from *ADH1B* Genotype and Drinking Motives

	Drinking frequency			Drinking quantity			Binge drinking frequency		
	IRR	[95% CI]	<i>p</i>	IRR	[95% CI]	<i>p</i>	IRR	[95% CI]	<i>p</i>
<i>Block 1</i>									
<i>ADH1B*3</i>	0.90	[0.76,1.07]	.24	1.02	[0.89,1.18]	.77	0.95	[0.68,1.33]	.76
Social motives	0.99	[0.97,1.02]	.56	1.02 [1.01,1.04]	.01		1.04	[1.00,1.09]	.08
Coping motives	1.01	[0.99,1.03]	.25	1.00	[0.98,1.02]	.91	1.01	[0.97,1.05]	.70
Enhancement motives	1.05 [1.03,1.07]	.00		1.02 [1.00,1.04]	.05		1.08 [1.04,1.13]	.00	
Male sex	1.21 [1.02,1.43]	.03		1.43 [1.24,1.65]	.00		1.22	[0.88,1.70]	.24
Age	1.03 [1.01,1.04]	.01		1.00	[0.98,1.01]	.66	1.02	[0.98,1.06]	.31
<i>Block 2</i>									
<i>ADH1B*3</i> × Male sex	0.73	[0.50,1.07]	.11	1.24	[0.90,1.70]	.19	0.91	[0.43,1.95]	.81
<i>ADH1B*3</i> × Age	0.94 [0.89,0.99]	.02		0.99	[0.95,1.04]	.66	0.90	[0.78,1.03]	.13
Social motives × Male sex	1.04	[0.99,1.08]	.15	1.01	[0.97,1.05]	.54	1.09	[0.99,1.20]	.08
Social motives × Age	1.00	[1.00,1.01]	.25	1.00	[0.99,1.01]	.89	1.01	[0.99,1.02]	.55
Coping motives × Male sex	0.99	[0.94,1.03]	.56	1.01	[0.97,1.05]	.79	0.98	[0.90,1.07]	.69
Coping motives × Age	1.00	[0.99,1.00]	.14	1.00	[1.00,1.01]	.56	1.00	[0.99,1.01]	.90
Enhancement motives × Male sex	0.99	[0.95,1.04]	.68	1.00	[0.96,1.04]	.96	1.00	[0.91,1.09]	.91
Enhancement motives × Age	1.00	[1.00,1.01]	.31	1.00	[0.99,1.00]	.33	1.00	[0.99,1.01]	.70
<i>Block 3</i>									
<i>ADH1B*3</i> × Social motives	1.00	[0.96,1.05]	.92	0.95 [0.92,0.99]	.01		0.95	[0.87,1.04]	.25
<i>ADH1B*3</i> × Coping motives	1.06 [1.01,1.11]	.02		1.03	[0.99,1.07]	.20	1.08	[0.99,1.18]	.09
<i>ADH1B*3</i> × Enhancement motives	0.99	[0.95,1.04]	.75	1.01	[0.97,1.05]	.63	0.99	[0.91,1.07]	.74

Note. *N* = 239 due to missing data. IRR = incidence rate ratio; CI = confidence interval. Significant statistics at *p* < .05 are highlighted in bold.