Genetic and Environmental Predictors of Alcohol Use in Asian American Young Adults

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ABSTRACT. Objective: Among Asian American young adults, variations in alcohol-metabolizing genes (i.e., aldehyde dehydrogenase [*ALDH2*] and alcohol dehydrogenase [*ADH1B*]) are protective, whereas Korean ethnicity, family history of alcohol problems (FH), and acculturation represent risk factors for alcohol misuse. This study aims to integrate these genetic and environmental factors in a sample of Asian Americans expressing a wide range of alcohol use behaviors and problems. **Method:** Participants were 97 Asian American young adults (42% female) recruited as heavy and light drinkers (n = 49 and 48, respectively). Participants completed the Alcohol Use Disorders Identification Test, Timeline Followback, Vancouver Acculturation Index, and Family Tree Questionnaire. All participants provided buccal cell samples for DNA analysis. **Results:** Family history–positive (FH+) subjects reported greater alcohol use than family history–negative (FH−) subjects. A FH × *ALDH2* interaction was observed such that FH− subjects demonstrated no *ALDH2* effect, yet in FH+ subjects, the *ALDH2*2* genotype was associated with increased alcohol use. A significant main effect of acculturation was also moderated by FH such that the positive association between acculturation and alcohol use was greater among FH+ subjects and, in particular, among FH+ men. **Conclusions:** Although preliminary, these results suggest that the potential protective effects conferred by *ALDH2* and *ADH1B* are moderated by FH, such that a positive FH appeared to abolish the protective effect of these genes. Further, acculturation was associated with greater alcohol use in FH+ subjects only. If replicated in larger samples, these data suggest that alcohol-metabolism genes may not be protective in the context of high environmental risk. (*J. Stud. Alcohol Drugs, 76,* 690–699, 2015)

EACH YEAR IN THE UNITED STATES, 1,700 college students die because of alcohol-related accidents including motor vehicle crashes, and approximately 600,000 college students are injured as a result of alcohol use (Hingson et al., 2005). According to the National Institute on Alcohol Abuse and Alcoholism (NIAAA), 4 in 5 college students, including a majority of underage students, engage in drinking behavior (NIAAA, 2013). Moreover, adolescent and young adult alcohol use has been linked to the development of subsequent alcohol use disorders (Grant & Dawson, 1997).

However, Asian American young adults are unique in their experiences with alcohol. On average, Asian Americans drink less than Whites, yet some studies show alcohol use among Asian Americans to be on the rise (Harachi et al., 2001). To effectively address alcohol use among this population, predictive factors, both genetic and environmental, must be examined and integrated. As such, the present study aims to synthesize genetic and environmental predictors of alcohol use in a population of Asian American young adults expressing a wide range of alcohol use behaviors and problems.

Among identified risk factors for alcohol use/problems, particularly in ethnically Asian populations, are the genes encoding for alcohol-metabolism enzymes, which are among the most robustly supported genetic factors related to alcohol use (e.g., Wall, 2005). In particular, the aldehyde dehydrogenase gene (*ALDH2*) has been widely linked to both alcohol use (Sun et al., 2002) and the development of clinically significant alcohol use disorders (Luczak et al., 2004). A polymorphism of the *ALDH2* gene, *ALDH2*2,* is present in between 30% and 50% of individuals of Northeast Asian descent.

The *ALDH2*2* allele codes for an inactive mitochondrial aldehyde dehydrogenase enzyme, which results in less than optimal metabolism of acetaldehyde and consequently a significant increase in acetaldehyde levels after alcohol consumption (for review, see Wall, 2005). Studies have linked increased acetaldehyde levels to a heightened physiological response to alcohol, characterized by a flushing response and tachycardia (Hendershot et al., 2009a; Wall, 2005). Consequently, compared with *ALDH2*1* homozygotes, *ALDH2* heterozygotes are about one fourth as likely to develop alcohol dependence, and **2* homozygotes have effectively no risk (Luczak et al., 2006). *ALDH2*2* has also been linked to significant reductions in heavy episodic drinking (Luczak et al., 2001; Wall et al., 2001).

Hendershot et al. (2009a) proposed alcohol expectancy theory as a framework for the effects of *ALDH2* on alcohol use. According to this model, sensitivity to alcohol strongly

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influences one's experience with alcohol, which in turn translates into learned alcohol expectancies. Alcohol expectancies, therefore, serve as an intermediary process between genetics and the development of problematic patterns of alcohol use. As a result of their increased physiological response to alcohol, *ALDH2*2* carriers report more negative global alcohol expectancies (McCarthy et al., 2000). Consequently, *ALDH2*2* carriers are more likely to alter their drinking habits to be congruent with their alcohol expectancies (Hendershot et al., 2009b).

In addition to *ALDH2,* the gene encoding for one of the alcohol dehydrogenase enzymes (*ADH1B*) has also been linked to alcohol consumption in Asian Americans (for review, see Wall, 2005). The theoretical mechanism of action for *ADH1B* is that the **2* allele codes for a more potent ADH enzyme, which results in an increase in acetaldehyde levels (Luczak et al., 2006; Wall, 2005). As is the case with *ALDH2*2,* elevated levels of acetaldehyde as a result of *ADH1B*2* will theoretically predict lower alcohol consumption. Evidence in favor of this hypothesis is mixed, however (Whitfield, 1997), with some studies finding the effect of *ADH1B* on subjective and physiological responses to alcohol to be moderated by *ALDH2* genotype (Cook et al., 2005).

In addition to genetic polymorphisms, psychosocial and/or cultural predictors such as ethnicity, acculturation, and family history of alcohol problems (FH) have been shown to predict drinking in the general population and in Asian Americans specifically. In terms of vulnerability to alcohol use disorders, ethnicity has been shown to be significantly associated with alcohol use, such that Korean Americans drink significantly more and generally have lower alcohol sensitivity than either Chinese or Japanese Americans (Duranceaux et al., 2008). There are population-level *ALDH2* allele frequency differences between Korean and Chinese populations, such that Korean Americans are significantly less likely to possess the *ALDH2*2* allele than are Chinese Americans. Thus, ethnicity and FH may represent a case of gene–environment correlation. It is unclear at present, however, whether the impact of ethnicity on alcohol use, alcohol sensitivity, and alcohol use problems is a direct result of population stratification (in other words, fully explained by gene–environment correlation) or if other cultural attitudes and beliefs also may explain these findings (Hendershot et al., 2009b). In the present study, we examined whether there exist independent—or even potentially interactive—effects of these familial factors and genetic variants.

Furthermore, acculturation may represent a risk factor for alcohol use in Asian Americans (Price et al., 2002). Although international data are sparse, alcohol use appears to be more widespread and culturally accepted among college students and young adults in the United States than in most of Asia (Karam et al., 2007). As such, acculturation toward social drinking norms in the United States may represent a risk factor for heavy alcohol use among Asian American college students. However, this may vary as a function of the culture of origin norms of specific East Asian groups. Research suggests that rates of alcohol use and misuse are higher among Korean Americans compared with Chinese Americans (Weatherspoon et al., 1994), and Korean men have higher rates of heavy drinking than North American men (Helzer et al., 1990). Indeed, ethnicity appears to moderate the effects of acculturation on Asian American alcohol use, with acculturation being a risk factor for Chinese Americans but a protective factor for Korean Americans (Hendershot et al., 2008).

The present study examined the effect of acculturation on alcohol misuse and tested whether this effect is moderated by genetic factors. In addition, this study examined parental alcohol use (representing FH of alcohol misuse), as it has been linked to adolescent and young adult alcohol consumption among Asian Americans (Hendershot et al., 2005; Shih et al., 2010). In the general population, parental alcohol use has been shown to be a significant predictor of adolescent drinking (White et al., 2000); however, this effect was found to be particularly strong among Asian American adolescents (De Moor et al., 1989; Hu et al., 1995).

In summary, there are notable important gaps in the literature with respect to genetic, cultural, and psychosocial predictors of heavy alcohol use in Asian American young adults. Most studies on Asian American alcohol use lack statistical power for assessing heavy alcohol use because they do not specifically target heavy alcohol users, thus resulting in samples in which rates of heavy or problematic alcohol use are generally low. In addition, a large number of studies investigating risk factors were conducted with underage populations with limited alcohol exposure. Given alcohol expectancy theory and its relation to *ALDH2* and *ADH1B* genotypes, studies of underage individuals are less likely to fully capture genetic influences, as a large percentage of adolescent samples lack exposure to alcohol and thus have not had the opportunity to develop alcohol expectancies informed by their biobehavioral response to alcohol. The present study sought to address these shortcomings by targeting heavy alcohol users and comparing them with a group of non–heavy users, thus capturing the full range of alcohol use/problems and allowing for a more complete assessment of relevant predictor variables (i.e., genetic and cultural factors).

The primary aim of the present study was to integrate genetic, psychosocial, and cultural predictors of heavy alcohol use among Asian American young adults. The genetic factors investigated are *ALDH2* and *ADH1B* (rs671 and rs1229984, respectively). Environmental factors to be investigated included acculturation and ethnicity, and FH represents a hybrid factor with elements of both environmental and genetic risk. Based on previous research, it was expected that *ALDH2*2* and *ADH1B*2* carriers would express lower rates of alcohol use than would **1* homozygotes. Korean ethnicity

and FH+ were expected to be associated with greater alcohol consumption. Last, it was hypothesized that genetic effects would be moderated by psychosocial and/or cultural factors, such that at high psychosocial risk (e.g., Korean ethnicity and FH+), the protective effect of *ALDH2*2* and *ADH1B*2* would be attenuated.

Method

Participants

This study was approved by the Institutional Review Board at the University of California, Los Angeles. Participants were 97 Asian American young adults (42% female) recruited from the Los Angeles community. To ensure a wide distribution of alcohol use and problems, participants were recruited into two groups. The first group consisted of heavy drinkers (n = 49) who were recruited for a laboratory trial of naltrexone in non–treatment-seeking Asian American heavy drinkers (Ray et al., 2012). Inclusion criteria included (a) Chinese, Korean, or Japanese descent; (b) age between 21 and 35 years; (c) currently taking no psychoactive medications; (d) having no major psychiatric disorder; and (e) current heavy alcohol use as identified by the Alcohol Use Disorders Identification Test (AUDIT), with a cutoff score of 8 or above (Allen et al., 1997).

Participants in the light drinking group were recruited by one of two methods. First, participants who were not heavy drinkers but were otherwise eligible for the naltrexone study were recontacted and informed of the present study. Interested participants were then screened over the phone using an identical screening script. Light drinking participants were also recruited via flyer and Internet postings in the same locations and avenues from which heavy drinking participants were recruited. Flyer information and recruitment methods were consistent with the heavy drinking study in order to equalize recruitment procedures. Eligibility criteria were precisely the same as in the naltrexone study, except for an AUDIT score requirement of greater than or equal to 1 and less than 8 and a minimum of one drinking occasion in the past month of at least one standard drink.

Procedures

All participants were initially screened over the phone by a trained research assistant. Eligible participants were then scheduled for a 1- to 2-hour in-person laboratory visit. Participants then provided informed consent and provided a breath alcohol analysis sample to ensure current breath alcohol concentration (BrAC) of .000 g/dl before data collection. Participants with BrAC's greater than .000 g/dl were asked to reschedule their appointment. Participants then supplied a DNA sample through a buccal cell sample and completed a series of self-report questionnaires.

Measures

Alcohol use. Several indicators of alcohol use were collected. First, alcohol use was assessed through a 30-day Timeline Followback (TLFB; Sobell et al., 1988). The TLFB is a calendar-assisted interview developed for the retrospective assessment of alcohol use. Participants are asked to catalogue every alcohol-containing drink they have had in the last 30 days in order to assess real-world drinking behavior. Specific variables to be analyzed include number of drinking days (drink days), drinks per drinking day (DPDD), percentage of drinking days that were heavy episodic drinking days (% HEDD; *heavy episodic drinking* was defined as at least five drinks per drinking occasion for men and four for women). In addition, the AUDIT was used to assess alcohol use as well as alcohol-related consequences.

To reduce the possibility of alpha inflation and to examine a more robust index of alcohol use, these four variables (drinking days, DPDD, % HEDD, and AUDIT score) were subjected to a principal component analysis, which revealed one meaningful factor (eigenvalue ≥ 1), which explained 68.8% of the variance in the indicator variables. Furthermore, all indicator variables had factor loadings ≥ 0.67 on the alcohol use factor score. Factor scores were used as the dependent variable in all subsequent analyses.

Acculturation. Acculturation was assessed via the Vancouver Index of Acculturation (Ryder et al., 2000). The Vancouver Index of Acculturation measures acculturation along two dimensions, namely, association with one's heritage culture and association with the mainstream culture. For the purpose of this study, standardized scores on the mainstream culture subscale were used as indices of acculturation to mainstream American culture.

Parental history of alcohol problems. Parental alcohol misuse was assessed via the Family Tree Questionnaire (FTQ; Mann et al., 1985). The FTQ was designed to assess alcohol-related consequences (e.g., "legal problems," "health problems," "social problems," or "receiving treatment for alcoholism") in first-degree blood relatives and has demonstrated good reliability for first-degree relatives (Mann et al., 1985). For the present study, a binary variable was constructed indicating whether subjects had one or more parents with significant alcohol-related problems (FH+) or parents with no such problems (FH−).

DNA collection and genotyping

DNA was collected via buccal cell samples using either Oragene saliva collection kits or a cheek swab. Genotyping was performed at the UCLA Genotyping and Sequencing Core, using polymerase chain reaction (PCR) techniques. Primers were labeled with fluorescent dye, and PCR was performed on Applied Biosystems (Life Technologies, Grand Island, NY) dual block PCR thermal cyclers. Genotype was

Table 1. Drinking group, *ALDH2* and *ADH1B* allele frequency, ethnicity, and level of acculturation by family history (FH) of alcohol problems

Variable	FH− (n = 76)	FH+ (n = 20)	Statistical test
Drinking group (% HD)	36 (47%)	13 (65%)	Fisher Exact p = .21
ALDH2 (**2* Carriers)	27 (36%)	5 (25%)	Fisher Exact p = .44
ADH1B			Fisher Exact p = .19
**1*1*	7 (9%)	2 (10%)	
**1*2*	26 (34%)	11 (55%)	
**2*2*	43 (57%)	7 (35%)	
Ethnicity			Fisher Exact p = .001
Chinese	47 (62%)	4 (20%)	
Japanese	3 (4%)	0 (0%)	
Korean	19 (25%)	14 (70%)	
Mixed ethnicity	7 (9%)	2 (10%)	
Acculturation (*SD*)	54.89 (7.23)	54.50 (5.62)	F = 0.05, p = .82

Notes: FH− = family history–negative; FH+ = family history–positive; HD = heavy drinking.

established via an AB 7900HT Fast Real-Time PCR System and was then analyzed using the Sequence Detection Systems software Version 2.3 (Life Technologies, Grand Island, NY). Each run included two positive control samples to ensure accuracy. Genotypes were initially scored by the genotyping software and then double-checked by visual inspection. Complete genetic data on the two SNPs of interest (*ALDH2:* rs671; *ADH1B:* rs1229984) were available for all participants.

Data analytic strategy

Statistical analyses were conducted in SAS Version 9.4 for Windows (SAS Institute Inc., Cary, NC). Hypothesis testing was conducted using PROC GLM. To reduce the number of statistical comparisons and produce a reliable indicator of alcohol use/misuse, alcohol variables were subjected to principal component analysis (described above). Alcohol use as indicated by this factor score served as the principal outcome variable of interest throughout the study. After significant interactions were observed, post hoc re-centering analyses were conducted to describe the nature of the moderation effects. Alpha rate was set at .05 for all statistical tests. Standardized regression coefficients (β) are presented as a measure of effect size.

Results

Sample characteristics

A total of 97 subjects (41 female) completed the study. Mean age for this sample was 22.8 years (*SD* = 2.5). In terms of ethnicity, 51 subjects endorsed a Chinese ethnicity, 3 endorsed a Japanese ethnicity, 33 endorsed Korean ethnicity, and 9 reported mixed ethnicity within the three ethnicities included. For the analyses in this study examining ethnicity effects, subjects were either coded as Korean or non-Korean in order to have reasonably large cell sizes for statistical testing and based on existing literature showing ethnicity-level differences. Participants reporting multiple ethnicities were dropped from these analyses. One subject was missing data on this ethnicity variable and thus was dropped from the analyses on ethnicity.

Twenty subjects were FH+. In terms of allele frequency, 33% of subjects (n = 32) were *ALDH2*2* carriers. Nine percent of subjects (n = 9) were homozygous for *ADH1B*1,* 39% (n = 37) were heterozygous, and 52% (n = 50) were homozygous for *ADH1B*2.* To test for violations of Hardy–Weinberg equilibrium (HWE) in the context of small expected cell counts, we used nonparametric exact tests described in Wigginton et al. (2005). Violations of HWE were not detected in this sample for *ALDH2* or *ADH1B* (p = .07 and .62, respectively). *ALDH2, ADH1B,* and ethnicity frequencies and acculturation scores by FH status are displayed in Table 1. A wide range of alcohol use and problems were reported. Means, standard deviations, and ranges for all alcohol use/problem indicator variables are presented in Table 2. Bivariate correlations between alcohol use outcomes and drinking group are presented in Table 3.

Genetic and psychosocial predictors of alcohol use

A significant effect of sex was observed, $F(1, 90) = 7.53$, $p < .01$, β = .28, such that men had significantly greater

Table 2. Means, standard deviations, and range for alcohol use/problem variables. Factor score from a unidimensional principal component analysis (factor loadings reported) was the primary dependent variable for analyses reported herein.

Variable	*M*	*SD*	Min.	Max.	Factor loading
AUDIT	8.63	5.69	1	23	0.85
Drink days	7.58	4.99	1	22	0.67
DPDD	3.86	2.33	0.50	9.87	0.89
% HEDD	35%	33%	0%	100%	0.89

Notes: Min. = minimum; max. = maximum; AUDIT = Alcohol Use Disorders Identification Test; DPDD = drinks per drinking day; HEDD = heavy episodic drinking days.

TABLE 3. Bivariate correlations between drinking group (i.e., light vs. heavy drinkers) and all alcohol use outcomes. All correlations are significant at $p \leq .001$.

Variable	1.	2.	3.	4.
1. Group	–			
2. AUDIT	.83	–		
3. Drink days	.56	.59	–	
4. DPDD	.51	.62	.36	–
5. % HEDD	.47	.62	.32	.87

Notes: AUDIT = Alcohol Use Disorders Identification Test; DPDD = drinks per drinking day; HEDD = heavy episodic drinking days.

alcohol use than women. Thus, all further results controlled for sex. Contrary to our hypotheses, no significant main effects of *ALDH2* or *ADH1B* were observed (*p*s = .82 and .85, respectively). Further, no interaction between *ALDH2* and *ADH1B* was observed ($p = .84$). A significant association between ethnicity (Korean vs. non-Korean ethnicity) and FH was observed (Fisher Exact $p < .001$), such that 42% of Korean participants reported a positive FH of alcohol problems, whereas only 9% of Chinese or Japanese subjects were FH+. As a result of this significant association between ethnicity and FH, these variables were examined as moderators in separate models to avoid multicollinearity. A significant main effect of FH on alcohol use was observed, $F(1, 89) = 5.31$, $p < .05$, $\beta = .23$, yet no significant main effect of ethnicity was observed ($p = .97$).

A significant interaction between FH and *ALDH2* genotype was observed, $F(1, 86) = 9.19$, $p < .01$; Figure 1. This interaction was followed by post hoc tests examining the effect of *ALDH2* genotype in FH− and FH+ subjects separately. These post hoc tests showed a simple effect of *ALDH2* genotype among FH+ subjects, $t(1) = 2.79$, $p < .01$, $\beta = .67$, such that FH+ carriers of *ALDH2*2* had greater alcohol use/severity compared with FH+ *ALDH2*1* homozygotes. No simple effect of *ALDH2* genotype was observed among FH− subjects ($p = .27$, $\beta = -.12$). The interaction between FH and *ALDH2* remained significant after we controlled for drinking group—Group: $F(1, 86) = 77.23$, $p < .001$; FH × *ALDH2:* $F(1, 85) = 5.71$, $p < .05$—suggesting that this effect was not simply a product of recruitment differences between groups.

Furthermore, a significant interaction between FH and *ADH1B* genotype was observed, $F(1, 84) = 4.06$, $p < .05$ (Figure 2). In post hoc tests, trend-level differences between *ADH1B*1* homozygotes and *ADH1B* heterozygotes were observed in FH− and FH+ subjects in opposite directions, $t(1) = -1.82$, $p = .07$; $t(1) = 1.83$, $p = .07$, respectively. *ADH1B*2* homozygotes and heterozygotes did not significantly differ from each other in either FH− or FH+ subjects (*p*s ≥ .11). In light of the small number of *ADH1B*1* homozygotes ($n = 9$) and empirical support for a partial-dominance model of *ADH1B* (Luczak et al., 2006), we conducted additional analyses to determine whether the FH ×*ADH1B* interaction was robust to dropping of *ADH1B*1* homozygotes from the model. These analyses still revealed a significant FH × *ADH1B* interaction, $F(1, 77) = 3.95$, $p = .05$, although no post hoc tests of *ADH1B* were significant (*p*s ≥ .11). Ethnicity was not found to moderate the effect of *ALDH2* or

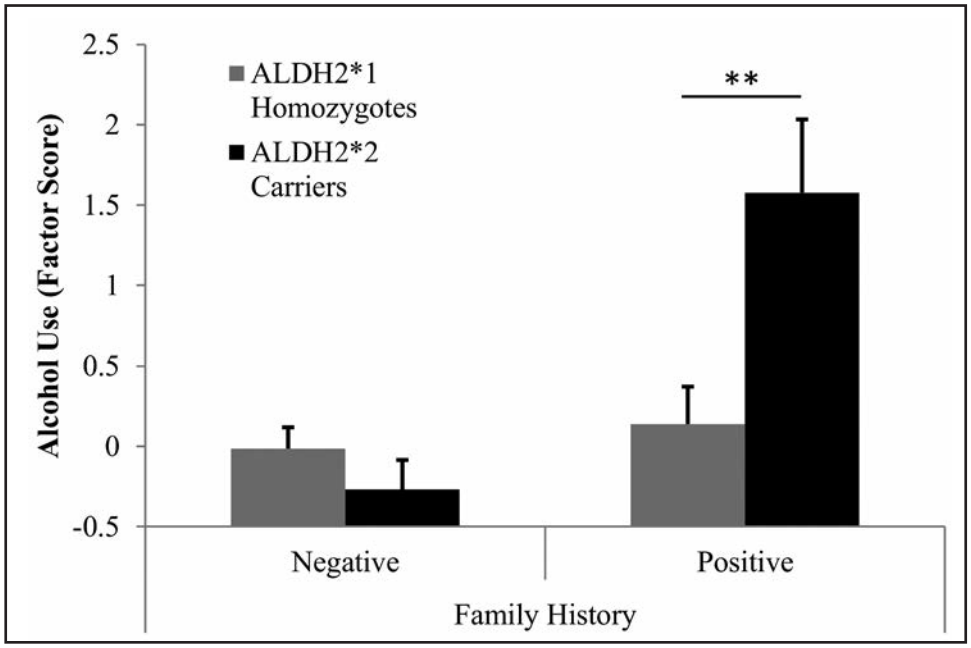

FIGURE 1. *ALDH2,* family history, and alcohol use: Alcohol use and problems as predicted by participants' *ALDH2* genotype, family history of alcohol problems, and their interaction, controlling for sex
**post hoc test $p < .01$.

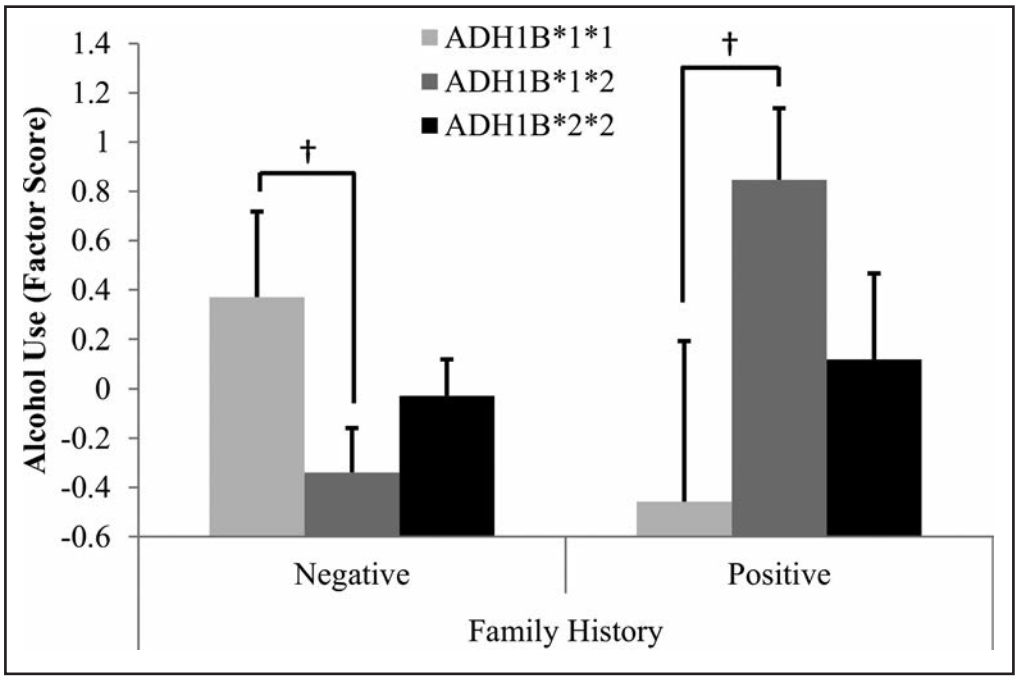

FIGURE 2. *ADH1B,* family history, and alcohol use: Alcohol use and problems as predicted by participants' *ADH1B* genotype, family history of alcohol problems, and their interaction, controlling for sex
†post hoc test $p < .10$.

ADH1B genotype on alcohol use—Ethnicity × *ALDH2:* $p = .12$; Ethnicity × *ADH1B:* $p = .61$.

Acculturation

A significant and positive main effect of acculturation was observed on alcohol use, $t(1) = 3.04$, $p < .01$, $\beta = .29$. Furthermore, a significant two-way interaction between FH and acculturation was found, $B = 0.67$, $t(1) = 2.46$, $p < .05$, such that among FH+ subjects a significant simple effect was observed between acculturation and alcohol use, $t(1) = 3.46$, $p < .001$, $\beta = .89$, yet among FH− subjects this effect was blunted, $t(1) = 2.18$, $p = .03$, $\beta = .22$.

As part of an exploratory analysis, a marginal three-way Sex × FH × Acculturation interaction suggested that the FH × Acculturation interaction may be further moderated by participant sex, $B = 1.37$, $t(1) = 1.81$, $p = .07$ (Figure 3). This three-way interaction was decomposed into two simple two-way interactions, which revealed a significant simple FH × Acculturation interaction among men, $B = 0.89$, $t(1) = 2.80$, $p < .01$, yet no significant FH × Acculturation interaction among women, $B = -0.48$, $t(1) = -0.70$, $p = .48$. The significant FH × Acculturation simple interaction in men was further decomposed into simple effects of acculturation in FH− and FH+ men. These analyses revealed a significant association between acculturation and alcohol use among male FH+ subjects, $\beta = 1.12$, $t(1) = 3.74$, $p < .001$, yet this association was blunted among male FH− subjects, $\beta = .22$, $t(1) = 1.84$, $p = .07$. Neither ethnicity nor genotype significantly moderated the effect of acculturation (ps ≥ .19).

Discussion

The aims of this study were to integrate several prominent predictors of problematic alcohol use in Asian American young adults, including genetic factors (i.e., *ALDH2* and *ADH1B*) and psychosocial factors (i.e., FH of alcohol problems, acculturation, and ethnicity). To fully capture the impact of these predictors, a sample of Asian American young adults was recruited that expressed a wide range of alcohol problems, including a large percentage (~50%) expressing hazardous alcohol use. Furthermore, in light of alcohol expectancy theory (Hendershot et al., 2009b), all subjects were required to have at least past-month alcohol experiences, thus ensuring that all participants have had the opportunity to learn alcohol expectancies in part from their own personal experience of alcohol's subjective effects.

A significant main effect of FH was observed, with FH+ participants reporting greater alcohol use. Contrary to our hypotheses, no significant main effects of *ALDH2* or *ADH1B* genotype were observed, yet FH was found to interact with both genotypes. Specifically, among FH− subjects, no significant *ALDH2* effect was observed, yet among FH+ subjects there was a significant effect of *ALDH2* genotype such that *ALDH2*2* carriers reported greater alcohol use than did **1* homozygotes.

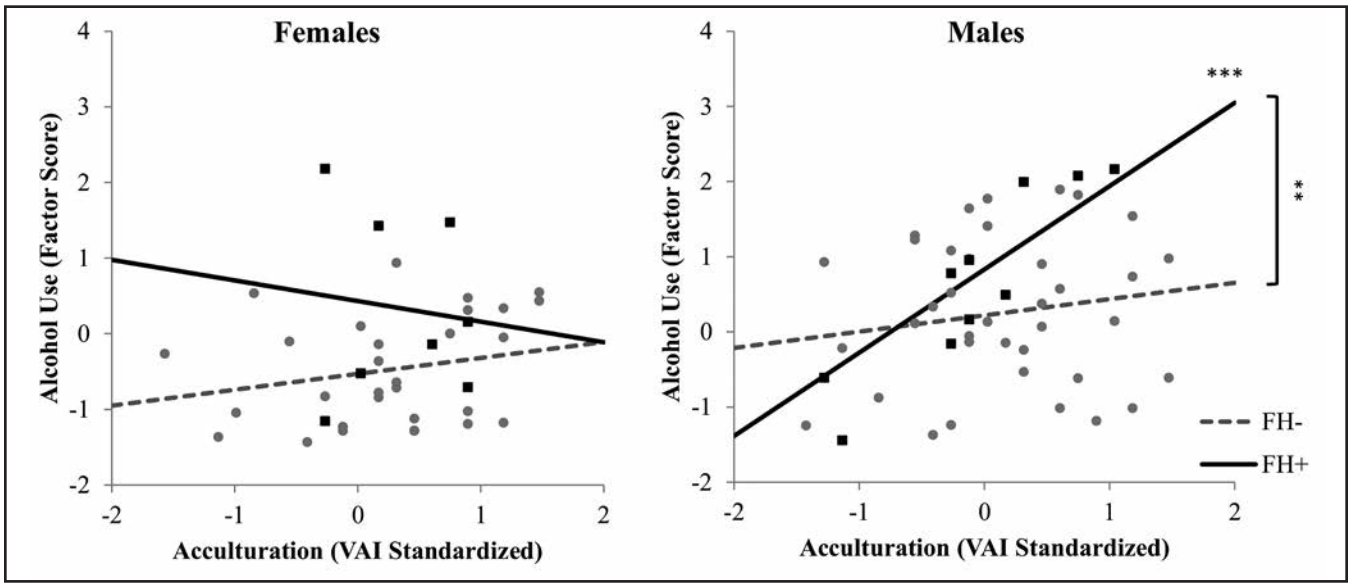

FIGURE 3. Acculturation level, family history, sex, and alcohol use: Alcohol use and problems as predicted by acculturation to mainstream American culture, family history of alcohol problems, sex, and their interactions
$^{**}p < .01$; $^{***}p < .001$.

In terms of *ADH1B,* differences between *ADH1B*1* homozygotes and *ADH1B* heterozygotes were marginal in both FH− and FH+ subjects, yet the direction was reversed. Among FH− subjects, being heterozygous for *ADH1B* was associated with a marginal decrease in drinking, and this effect was reversed in FH+ subjects. Of note, the number of participants with a positive family history in this study is small ($n = 20$), and thus these Gene × FH effects should be interpreted with caution and require replication in larger samples. However, these preliminary results suggest that the potential protective effects conferred by these alcohol-metabolizing genes are modulated by FH, with potentially a change of direction from protection to risk.

Unfortunately in this sample, parental genotype was not available. Therefore, we are unable to directly disentangle the effect of parental genetic factors from other family-based effects. As a consequence, future studies will be required to disentangle whether the observed parental alcohol use effect is related to gene–environment correlation, or whether the effect is perhaps reflective of perceived normativity of heavy drinking. Although based on few subjects, these data do not appear to support a simple gene–environment correlation because the direction of genetic effects changed based on FH, suggesting that the two variables do not merely represent two indicators of a single shared etiological factor.

A third, yet speculative, possibility is that unmeasured genetic factors interact with alcohol-metabolizing genes, leading to a reversal of protective effect of acetaldehyde buildup. Of note, significant debate exists about the ubiquity of acetaldehyde's aversiveness, with some studies suggesting that brain-derived acetaldehyde may actually partially mediate alcohol's rewarding effects (Israel et al., 2013; Ledesma & Aragon, 2013; Rodd et al., 2005), whereas peripheral acetaldehyde causes the aversive physiological effects (Israel et al., 2013; Mizoi et al., 1983; Shimoda et al., 1996). Although speculative at this point and in need of direct empirical examination in future studies with large samples, the results of this study are consistent with the possibility that brain acetaldehyde may actually be reinforcing. For example, FH may modulate the relative levels of peripheral versus brain acetaldehyde, such that FH+ young adults experience greater brain acetaldehyde levels and thus more acetaldehyde-induced reward from drinking.

In this study, acculturation to mainstream American culture was also investigated as a potential predictor of alcohol use in Asian American young adults. Results revealed a significant, yet moderate in magnitude, main effect of acculturation such that greater acculturation was associated with greater alcohol use. This main effect was, however, found to be moderated by FH, with the effect of acculturation being significantly greater among FH+ subjects compared with FH− subjects ($\beta = .89$ and .22, respectively).

This interaction was then found to be further moderated by sex at the trend level such that the interaction between FH and acculturation was significant only in male subjects. Specifically, only male FH+ subjects showed a significant effect of acculturation on alcohol use, with all other subjects failing to show a significant association. Thus, as with the genetic results described above, the effect of acculturation appeared to be dependent on FH such that acculturation was only predictive of alcohol problems among FH+ subjects. As with the Gene × FH effects discussed above, these ac-

culturation findings should be treated as preliminary, in need of replication in larger studies. That said, one possible interpretation of these results is that a positive FH puts young adults at risk for peer influence on alcohol use (Curran et al., 1997). Further, the observation that adolescent alcohol use is more prevalent in men (Substance Abuse and Mental Health Services Administration, 2013) may lead FH+ men to be particularly susceptible to acculturation-related peer-mediated risk of alcohol misuse (Bacio et al., 2013).

Based on the literature (Duranceaux et al., 2008; Hendershot et al., 2008; Luczak et al., 2004), we hypothesized ethnic differences in terms of alcohol use. Although Korean ethnicity was associated with a greater likelihood of positive FH, no effect of ethnicity was observed as either a main effect or a moderator of either genetic factors or acculturation. Thus, in terms of familial-based predictors, FH appears to be a more salient predictor of alcohol misuse among Asian American young adults than was ethnicity. This lack of ethnic differences is in contradiction to those reported by others in the literature (Duranceaux et al., 2008; Hendershot et al., 2008). Differences between the present study and prior studies may account for these disparate findings, most notably our sampling strategy that resulted in a sample that was older and consumed more alcohol.

These results should be interpreted in light of some strengths and limitations. This study benefits from a sample of Asian American young adults expressing a wide range of alcohol use from very moderate social drinking (e.g., < 5 drinks a month) to those with significant alcohol-related problems. Given the purported mechanism of action of alcohol-metabolizing genes in modifying alcohol expectations, protective effects of alcohol-metabolizing genes would be most pronounced in subjects with alcohol experiences. A further strength of this study is the use of a single alcohol use factor informed from numerous alcohol-related variables, thus reducing the number of statistical tests and the probability of a false positive.

Limitations of the study include its cross-sectional nature, which impairs our ability to examine risk factors prospectively. Furthermore, the small number of subjects with a positive FH of alcohol problems warrants replication in a larger sample with more balanced FH rates. Larger samples would also allow for testing of possible interactions between ethnicity and FH. We were unable to examine this interaction in this study because of multicollinearity concerns, which were exacerbated by the relatively small sample size.

The same sample size weakness is noted in terms of *ADH1B* genotype. Although there exists controversy about sample size requirements in behavioral genetics (Burmeister et al., 2008), there is a robust literature on these functional polymorphisms in alcohol-metabolizing genes, including their biobehavioral mechanism of action. As a result, *ALDH2* and ADH are among the most widely studied and supported polymorphisms in alcoholism genetics (for review, see Eng et al., 2007; Wall, 2005), thus justifying their evaluation in this sample.

As noted previously, the lack of genetic data for participants' parents limits our ability to dissociate genetic effects from FH and ethnicity. Last, the measure of FH is somewhat dated (Mann et al., 1985). Thus, comparisons with other studies should make note of possible FH assessment differences.

On balance, this study extends the literature on alcohol use in Asian American young adults by suggesting that FH may be a particularly salient predictor of alcohol problems among Asian American young adults and a significant moderator of several key risk/protective factors in this population (i.e., *ALDH2* and *ADH1B* genotype and acculturation). This is consistent with the conclusions in Hu et al. (1995), wherein parental influence may be more salient in Asian American populations relative to other ethnic groups. Further research is warranted to expand on these findings by examining the influence of parental genotype as a potential moderator or mechanistic factor explaining the influence of parental history of alcohol problems on alcohol use and problems among Asian American young adults.

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