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Associations between CDH13 Variants and the Initiation of Alcohol and Sexual Behavior with High-risk Hispanic and Caucasian Youth

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Abstract

Objective: Early initiation of risk behavior (e.g., alcohol use, sexual intercourse) has been associated with more adverse health outcomes for adolescents. One important factor in early initiation may be the role of genetics. However, few have investigated how these relationships may compare by ethnicity.
Methods: We evaluated these questions with a sample of high-risk justice-involved youth (N = 226; 30.1% female; 79.2% Hispanic; 20.8% Caucasian; M age = 16.18). Specifically, we examined how contextual factors (parental monitoring, peer alcohol use) and alleles within the T-Cadherin gene (CDH13) may be related to the age of initiation of alcohol and sexual behavior. We also explored the extent to which genetic factors may moderate the influence of context on youth risk behavior.
Results: Youth reported an early age of onset for both alcohol use (M age =12.74) and sexual intercourse (M age = 13.35). CDH13 SNPs did not predict age of first drink. However, main effects were found for rs7193606 on age of first intercourse. Additionally, two interactions were found, one for age of first drink (rs4389131 x parental monitoring), and another for age of first intercourse (rs12926331 x peer drinking). No ethnic differences were observed.
Conclusions: These data indicate the relevance of considering the interplay between cadherin risk alleles and contextual factors (parental monitoring, peer drinking) on adolescents' initiation of alcohol and sexual behavior, as well as the consonance of these relationships across high-risk Hispanic and Caucasian youth.

Keywords: adolescent; alcohol; sex; genetics; health disparities

Introduction

Currently comprising17% of the United States population (U.S. Census Bureau, 2013a), Hispanic Americans are expected to represent the largest minority group within the U. S. shortly (U.S. CensusBureau, 2013b). This is notable, as there is a history of health disparities for Hispanic adults across a number of health risk behaviors, including alcohol use and its related negative health sequelae (e.g., alcohol-related problems, cirrhosis) (Caetano, 2003), as well as sexual risk behaviors, including behaviors that increase risk for the transmission of sexually transmitted infections (STIs) and the human immunodeficiency virus (HIV) (CDC, 2013; Hall et al., 2013). Notably, similar patterns have been observed for Hispanic youth (Feldstein Ewing, Venner, Mead, & Bryan, 2011; Pflieger, Cook, Niccolai, & Connell, 2013).

At this time, despite drinking similar amounts as Caucasian youth, Hispanic youth report higher rates of alcohol-related risk behaviors (e.g., drinking and driving, riding with a drinking driver; CDC, 2012a). Parallel trends have been observed in adolescent sexual health. Despite comparable rates of ever having had intercourse (lifetime), Hispanic youth report higher rates of HIV/STI risk behaviors (e.g., multiple sexual partners, lower rates of condom use, less information about how to protect themselves against HIV/AIDS (CDC, 2012b). These disparities are even more pronounced among justice-involved youth, who report even higher levels of alcohol use and HIV/STI risk behaviors than their mainstream peers (Romero et al., 2007; Teplin, Mericle, McClelland, & Abram, 2003), along with much more serious and sustained long-term health consequences (Aarons, Brown, Garland, & Hough, 2004; Romero et al., 2007).

Early initiation of health risk behaviors (e.g., alcohol use, sexual activity) may be one of the most important factors in adverse health outcomes (Chassin, Pitts, & Prost, 2002; Hingson & Zha, 2009; Lee, Young Wolff, Kendler, & Prescott, 2012). This is relevant, as studies with mainstream adolescents have found that Hispanic youth are more likely to initiate health risk behaviors, including alcohol use and sexual intercourse, earlier than their Caucasian peers (before age 13) (CDC, 2012a). Moreover, these behaviors appear to co-occur. To that end, youth engaging in early alcohol use also tend to display early sexual debut (Cavazos-Rehg et al., 2012; Deardorff, Gonzales, Christopher, Roosa, & Millsap, 2005). One factor that may be particularly salient to the age of initiation for alcohol use and sexual intercourse is the role of genetics. Despite gaining ground in the field of adolescent alcohol initiation, there is still great debate regarding how genes may influence age of first drink (Agrawal et al., 2009; Prescott & Kendler, 1999). And, despite their likely co-occurrence, few studies have examined the role of genetics in sexual debut.

Explorations in genomic medicine also offer an innovative avenue to reduce existing health disparities (Feldstein Ewing, Karoly, & Hutchison, under review). While recent research on the human genome has established links between genes and a wide array of health risk behaviors (Bryan & Hutchison, 2012), existing efforts to ensure homogenous samples have resulted in Hispanic individuals often being omitted from genetic studies and related analyses (Trujillo, Castañeda, Martínez, & Gonzalez, 2006). At this time, only a handful of genetic studies include Hispanic participants (e.g., Schlaepfer et al., 2007; Viel et al., 2008; Zieger et al., 2008). And, some of those studies have found differences in genetic variation and risk behavior for Hispanic youth (Schlaepfer et al., 2007). Additionally, there is some evidence that phenotypes for risk behavior vary by ethnic group (Hasin & Grant, 2004). The result is an existing disparity in our understanding of how genetic factors may impact health risk behavior, and in particular, among Hispanic youth (Trujillo et al., 2006).

In terms of salient genetic factors, we focused our examination on a gene that has been implicated within addiction (Uhl, Drgonova, & Hall, 2014) and youth risk behavior (Franke et al., 2012; Rivero et al., 2013), known in the literature as: T-Cadherin [CDH13, H-Cadherin (heart), or Cadherein-13]. Broadly, cadherins are adhesion molecules that mediate Ca^{2+}-dependent intercell adhesion (Ivanov, Philippova, & Tkachuk, 2001). Mapped to 16q24 in the human chromosome, the CDH13 gene is anchored in the membrane via glycosylphosphatidylinositol (GPI). It has been found throughout the central nervous system (including cerebral cortex, midbrain, and medulla), and is believed to play a role in maintaining neural circuitry (Ivanov et al., 2001; Takeuchi et al., 2000).

As age of initiation of adolescent health risk behavior is also likely to be influenced by key contextual factors (Prescott & Kendler, 1999; Wichers, Gillespie, & Kendler, 2013), we also sought to examine the

contributing role of two critical contextual factors. In terms of key contextual factors, greater parental monitoring, both in terms of parents' knowledge of their youths' whereabouts, along with greater family dinner frequency, have been found to deter youths' engagement in alcohol use and risky sexual behavior (DiClemente et al., 2001; Fulkerson, Story, & Mellin, 2006). At the same time, while parents' influence may remain important for many youth, during the developmental period of adolescence, peer input begins to take primacy (Ernst, Pine, & Hardin, 2005; Sebastian, Burnett, & Blakemore, 2008), particularly for youth with difficult and/or strained family relationships (Windle et al., 2008). The increasing influence of peers during this developmental period is relevant because it is during this timeframe, and within peer contexts, that youth begin to make decisions about whether and when to engage in alcohol use and risky sexual behavior. Importantly, initiation of both behaviors by youth has been found to closely track the behavior of their peers (D'Amico & McCarthy, 2006; Santelli et al., 2004; Sieving, Eisenberg, Pettingell, & Skay, 2006).

When examining the potential contribution of genetics, it is particularly important to do so while considering the contribution of contextual factors that have been shown to influence age of health risk initiation. For example, some have found that genetic differences may be more salient than anticipated contextual factors on age of initiation (Agrawal et al., 2009). Whereas others have found that age of initiation has not been driven by genetics, but rather, by context (Prescott & Kendler, 1999). Still others have found a complex interplay between the two (Wichers et al., 2013). Thus, despite the clear importance of examining the interactions of these factors, we could find no studies that explicitly integrated these three different factors (context, genes, ethnicity) in the evaluation of Hispanic youths' age of initiation. Additionally, we could find no studies that investigated these relationships in the context of sexual debut.

Based on the current literature, we sought to compare the age of initiation for alcohol use and sexual intercourse across both Hispanic and Caucasian youth, with the expectation that Hispanic youth would show an earlier age of debut across both behaviors (alcohol use, sexual intercourse). Next, we investigated the main effects for contextual factors for youth of both ethnicities. We anticipated that greater parental monitoring would be associated with later age of onset, and more peer drinking would be associated with a younger age of onset. Similarly, we examined the main effects for genetic factors (variation in CDH13 SNPs) across youth of both ethnicities, expecting that youth with risk alleles would show an earlier age of onset, as compared to those without the risk alleles. We then explored the extent to which genetic factors moderated the influence of contextual factors on youth health risk behavior. Finally, we anticipated that genetic effects, contextual effects, and their interaction, would be influential over and above the effects of ethnicity.

Methods

Participants

Data were drawn from a larger, translational study of an alcohol-related STI/HIV risk reduction program (PI: Bryan). With the participating University's Institutional Review Board approval (including an IRB-recommended waiver of the Health Insurance Portability and Accountability Act document) and a federal Certificate of Confidentiality, participants were recruited from an alternative to incarceration program in the southwest U.S. Involvement in the study did not affect their treatment within the juvenile justice system. While components of this study have been described in prior work (Magnan et al., 2013; Thayer, Callahan, Weiland, Hutchison, & Bryan, 2013), this study is unique in its focus on Hispanic versus Caucasian youth, and its evaluation of CDH13 SNPs and contextual factors on the initiation of drinking and sexual intercourse; these relationships have not been examined within the parent study.

In terms of inclusion criteria, to participate, youth had to be 14-18 years of age, and absent the following exclusion criteria (e.g., metal implants, pregnant, claustrophobic, taking antipsychotic medication, current suicidal ideation). Consistent with other juvenile justice studies (Schmiege, Broaddus, et al., 2009), youth provided informed (written) assent and parents/guardians provided informed telephone (audiotaped) consent. All consent conversations were audio-recorded and logged for proof of consent. Paper copies of the consent documents were mailed back to parents/guardians for their records. Participants received $30 for completing the baseline set of measures and procedures ($185 for completing the total 12-month study).

Data for these analyses were drawn from the baseline assessment (N = 284), which was conducted prior to all other study procedures, including the prevention intervention. Following the methods of Culverhouse et al. (2014) to evaluate existing health disparities in adolescent health risk behaviors, we focused the current set of analyses on comparisons between Caucasian vs. Hispanic youth (N = 226).

Measures

Demographic factors. Youth completed a self-report measure to indicate their age, gender, and self-identified ethnic group.

Alcohol use was assessed by asking if youth had ever used alcohol (lifetime) and their age of first use. Alcohol dependence (past 6 months) was measured with the Alcohol Use Disorders Identification Test (AUDIT; Babor, 2006), α=.81. Alcohol use over the past three months was measured with a variation of an adolescent alcohol measure developed by White & Labouvie (1989). Participants indicated *the frequency of alcohol use* (1=never, 9=everyday), *how much they typically drank during a drinking event* (1=none, 10=more than 20), and *how often they became drunk when drinking* (1=never, 5=always). These items were summed to create a total use score with higher numbers indicating greater use over the past three months, α=.84.

Sexual risk behavior was assessed by asking youth if they had ever had sexual intercourse [defined as "*when a man puts his penis inside a woman's vagina or inside a man or woman's anus (rear end)"],* their age of first intercourse, their number of lifetime sexual partners, and the frequency of condom use (lifetime, 1=never, 5=always). Frequency of condom use was dichotomized such that a youth who did not report always using condoms was considered an inconsistent user.

Parental monitoring was assessed with three questions. *"How often do your parents/guardians know where you are?" "How often do your parents know where you are when you are not at school and away from home?"* Response options included a Likert scale ranging from 1 (never) to 5 (almost always) (DiClemente et al., 2001; Shillington et al., 2005). "*In an average week, how many times a week do you and your parents eat dinner together?"* with response options from 0 times to 7 times (Fulkerson et al., 2006). These items were summed to yield a total score with higher scores indicating greater parental monitoring, α=.55.

Peer alcohol use. Adapted from Bryan and colleagues' (Bryan, Rocheleau, Robbins, & Hutchison, 2005) evaluation of youth's perception of their peers' engagement in health risk behaviors (alcohol use and sexual risk-taking), this 5-item measure evaluates perception of peer behavior. Items include, "*Do most of your friends drink alcohol?"* (y/n); *"How often do most of your friends drink alcohol?"* (1=never, 5=always); *"Most people my age drink to get drunk"* (1=disagree a lot, 4=agree a lot); "*My friends wouldn't be friends with me if I didn't drink."* (1=disagree a lot, 4=agree a lot); "*How often do most your friends get drunk when they drink?"*

(1=never, 5=always). Following Bryan and colleagues (2005), all items were summed to yield a total score, with greater values indicating greater levels of peer alcohol use, α=.60.

DNA Collection, Extraction, Storage and Analysis. Participants were instructed to generate and deliver 5 ml of saliva in to a sterile 50 ml conical centrifuge tube. DNA was quantified using the Qbit flourimeter in conjunction with the dsDNA BR Assay Kit (Invitrogen) to obtain accurate concentrations of DNA. 200 ng of DNA were used for the Illumina® Infinium® HD Assay in conjuction with Illumina's HumanOmni1-v1-0_B Bead Chip. Summarizing, Genomic DNA underwent overnight whole genome amplification, followed by fragmentation and ethanol precipitation. The DNA was then re-suspended in hybridization buffer and applied to the bead chip array for an overnight incubation. The amplified and fragmented DNA samples annealed to locus-specific 50-mers (covalently linked to one of over 1,000,000 beadtypes) during the hybridization step. Following hybridization, the arrays were washed to eliminate unhybridized and non-specifically hybridized DNA. One bead type corresponds to each allele per SNP locus. The samples then underwent single base extension and staining followed by more washing. The arrays were allowed to dry and then scanned using the Illumina iScan system. Genotype calling was achieved using Illumina's GenomeStudio software in conjunction with the GenomeStudio genotyping module. Preprocessing and quality assurance were performed using SNP Variation Suite software, Golden Helix. We evaluated six CDH13 SNPs that were available in our genetic panel (rs8061907; rs11647879; rs4389131; rs7193606; rs12926331; rs2113148), with minor alleles combined into one group for each respective SNP. All SNPs were in Hardy-Weinberg equilibrium (see Table 1).

Statistical Analyses

Prior to analyses, all variables were checked for normality. Genotypes for each SNP were dichotomized such that any genotype that included the risk allele was coded as 1 and the genotype without the risk allele was coded as 0. For example, if the risk allele was A, the SNP would be dichotomized as AA/AG=1 and GG=0. See Table 1 for identified risk alleles and frequencies for the current sample.

Relationships were investigated using linear regression. First, to determine main effects, contextual variables (parental monitoring, peer alcohol use), ethnic group, and each CDH13 SNP were regressed individually on age of initiation of drinking and sexual behavior. To test the moderating effect of CDH13 on the effect of contextual variables on age of initiation, the individual CDH13 SNP and the contextual variable were entered in Step 1 of the regression. The multiplicative CDH13 X contextual variable was entered in Step 2 of the regression. Due to the small ethnic group X CDH13 SNP sample sizes (see Table 2), we were insufficiently powered to include ethnic group as an additional moderator in these final models.

Results

Representative of the broader juvenile justice population from which these participants were recruited, youth in this sample (N=226) were on average, 16.17 years of age, predominantly male (69.9%). Most youth self-identified as Hispanic (79.2%). In terms of alcohol use, the majority of youth (90.4%) had consumed at least one drink in their lifetime, with an average age of first drink at 12.74 years (*SD* = 2.11). Participants' average AUDIT score was 7.95 (*SD*=7.32) [cut score $\geq$ 3 indicates problem drinking in adolescents (Chung, Colby, Barnett, & Monti, 2002)], indicating the prevalence of problem drinking in this sample. In terms of sexual behavior, the majority of youth (80.7%) had also engaged in sexual intercourse at least one time in their lifetime, with an average age of 13.35 (*SD*=1.91) years at first intercourse. Youth reported an average of 6.42 (*SD*=6.81) sexual partners during their lifetime (range 0-42) with a high rate of inconsistent condom use

(85.5%). Males started drinking at a younger age, $t(190)=1.98$, $p=.05$, $d=.58$, were younger at their first intercourse, $t(176)=3.46$, $p=.001$ $d=.30$, and reported more sexual partners than females, $t(215)=3.14$, $p=.01$, $d=.39$. Table 2 presents participant characteristics by ethnic group.

There were no differences between Hispanic and Caucasian youth on any of the demographic or behavioral variables. However, in terms of genetic differences, Hispanic youth were less likely to have the risk allele for rs7193606 (χ^2 (1,N=112)=5.23, $p=.02$). Caucasian youth were less likely to have the risk allele for rs2113148 (χ^2 (1,N=148)=5.95, $p=.02$).

Table 3 displays the regression outcomes for each contextual variable, CDH13 SNP and the CDH13 X contextual interactions on age of first drink and age of first intercourse. In terms of age of first drink, there was a significant main effect of parental monitoring on age of first drink ($\beta = .36$, $p = .002$) such that greater parental monitoring was associated with an older age of first drink. There was also a significant main effect of peer alcohol use on age of first drink ($\beta = -.16$, $p = .03$) such that greater peer alcohol use was associated with a younger age of first drink. There were no main effects for any of the identified CDH13 SNPs on age of first drink. However, there was a significant CDH13 (rs4389131) x parent monitoring interaction ($\beta = .43$, $p = .02$), such that, individuals with the risk allele (AC/CC) who had greater parental monitoring were older at first drink, than individuals with the risk allele and less parental monitoring (Figure 1a).

In terms of age of sexual debut, no main effects were observed for contextual factors on age of first intercourse. There was a significant main effect of one CDH13 polymorphism (rs7193606) on age of sexual debut, such that individuals with a risk allele (TT/CT) were older at sexual debut ($\beta = .22$, $p = .02$). There was also a significant CDH13 (rs12926331) x peer alcohol use ($\beta = -.32$, $p = .002$) interaction, such that individuals with the risk allele (TT/CT), who had less peer alcohol use were older at sexual debut, than those with more peer alcohol use (Figure 1b). No differences were observed across these relationships by ethnicity. Additionally, controlling for ethnicity, age, and gender in the regression models did not influence the interpretation any of the outcomes.

Discussion

At this time, there are still notable health disparities across adolescent risk behaviors and related health outcomes; these are particularly evident among high-risk, justice-involved youth (Aarons et al., 2004; Feldstein Ewing et al., 2011; Romero et al., 2007). In an effort to advance our understanding of these differences, we sought to evaluate the interplay between targeted genetic variants (CDH13), key contextual factors (parental monitoring and peer alcohol use), and ethnicity (Hispanic and Caucasian) on high-risk youths' initiation of alcohol use and sexual intercourse. Contrary to recent work in this area (Shih, Miles, Tucker, Zhou, & D'Amico, 2010), Hispanic and Caucasian youth showed comparable patterns and prevalence of alcohol use and risky sexual behavior. To that end, both Hispanic and Caucasian youth already showed established patterns of health risk by the time they completed our baseline evaluation (at $M_{age} = 16.18$ years). In other words, by their junior year of high school, 90.4% of this high-risk sample had consumed alcohol, and 80.7% had sexual intercourse, with high problem drinking, a high number of sexual partners, and high number of unprotected sexual events. This early age of initiation ($M_{age} = 13$; ~8th grade) and very high pattern of risk, is noteworthy to consider when developing behavioral models to guide preventive programming. For example, some may argue that this age of initiation is younger than that generally observed across mainstream American youth. However, upon closer examination, these rates may not be far off from those reported by mainstream Hispanic youth, 25%

of whom have used alcohol and 7% of whom have engaged in sexual intercourse by age 13 (CDC, 2012a). This is relevant, as targeting age 13 is much earlier than the age groups generally targeted in empirically-supported HIV/STI prevention programming (Johnson, Scott-Sheldon, Hudeo-Medina, & Carey, 2011). Practically, these data suggest that existing prevention programming may be *three years too late* in getting alcohol and HIV/STI prevention messages to high-risk, justice-involved Hispanic and Caucasian youth.

In terms of contributing factors, consistent with our hypotheses and recent work in this area (Wichers et al., 2013), we found that youth with more parental monitoring and less peer alcohol use had a later age of alcohol initiation. However, contrary to expectations (Agrawal et al., 2011), but in line with other studies (Prescott & Kendler, 1999), these genetic variants were not directly associated with age of first drink. In contrast, to predictions (DiClemente et al., 2001; Fulkerson et al., 2006), contextual factors were not directly associated with age of first intercourse. However, one CDH13 variant (rs7193606) was significantly related to age of sexual debut, albeit in the opposite direction than expected (youth with the risk variant were older at sexual debut). Further work is needed to disentangle how risk alleles within this gene function (Uhl et al., 2014) to better understand the contributing role of these genetic risk and protective factors in sexual debut.

We also evaluated the extent to which genetic factors moderated the influence of contextual factors on risk initiation within this sample. Here, we found a significant interaction for two CDH13 variants (rs4389131; rs1296331). Youth with the rs4389131 risk allele who had poorer parental monitoring showed a younger age of alcohol use initiation. Similarly, youth who had the rs12926331 risk allele and more peer drinking evidenced a younger age of sexual debut. Ultimately, youth with these CDH13 risk alleles may be particularly sensitive to contextual risk factors, and that interaction may not only be relevant to the age of first drink (Agrawal et al., 2009), but also to sexual debut. Specifically, these data also highlight the importance of an attentive parent presence, in order to forestall youths' presence in peer-based and other environments where alcohol may be widely available (Wallace, 1999). In addition, while it may not be initially intuitive that peer drinking was related to youth sexual debut, this finding is consistent with studies indicating the often-intertwined role of pro-alcohol use peer environments and youth STI/HIV risk (Schmiege, Levin, & Bryan, 2009).

This study has implications for the development of adolescent health models to guide prevention programming. Most importantly, following other studies showing comparable rates of risk behavior across ethnicities (Romero et al., 2007), the outcomes from this study support the co-creation of prevention programming to serve both high-risk Hispanic and Caucasian youth. Furthermore, this study indicates the importance of incorporating factors to bolster and support parental monitoring [as found within the Family Check-Up (Van Ryzin, Stormshak, & Dishion, 2012)], and to address and decrease the perception of peer norms [as found within studies of some youth Motivational Enhancement Therapy programming (Bryan, Schmiege, & Broaddus, 2009)], particularly for high-risk youth at elevated genetic risk (youth with CDH13 SNP risk alleles). In addition, due to the entrenched patterns of risk observed by age 16, we suggest that these data indicate the importance of providing *anticipatory* preventive programming for high-risk Hispanic and Caucasian youth. Thus, while it might feel somewhat alarming to consider sharing risk prevention messages with 10- to 12-year-olds, our data suggest that if we are to effectively stave off high-risk youths' initiation of these behaviors, health risk programs need to target the late elementary to early middle school youth (Spoth, Clair, & Trudeau, in press; Spoth, Trudeau, Guyll, Shin, & Redmond, 2009), and incorporate content about both alcohol as well as STI/HIV risk (Schmiege, Broaddus, et al., 2009; Workowski, Berman, & Prevention, 2010).

Finally, while evaluation of genetic contributions to the initiation of youth health risk behaviors is gaining footing in the alcohol field (e.g., Agrawal et al., 2009), we hope that this study serves as one step towards the extension of this work to age of sexual debut. In addition, following emergent work in this area (Culverhouse et al., 2014; Sartor et al., 2013), we also hope that this work serves as footing for increased conversation around how genomics can help reduce existing health disparities for high-risk youth across all racial/ethnic backgrounds (Feldstein Ewing et al., under review).

While this study had several strengths, including the high representation of Hispanic youth, the innovative examination of adolescent genomic factors in youths' initiation of health risk behavior, and the public health relevance of better understanding these relationships, conclusions should be interpreted in light of the following limitations. This study relied on a small sample size; replication with a larger sample is requisite to validate these conclusions. This study relied on youths' retrospective report of their health behavior; future longitudinal designs observing the progression of youths' risk behavior from the elementary school years through the late teens would strengthen observed findings. In addition, these data were cross-sectional. At this time, we do not know how these risk alleles would influence subsequent risk behavior; future examination using a longitudinal design would directly address these questions. Finally, these questions were addressed with a high-risk sample. While this approach may limit generalizability to the broader youth community (non-justice involved youth), we believe that the reduction in generalizability is offset by the public health significance of evaluating factors that may exacerbate health risk behavior in this often underserved and underrepresented population.

Table 1
Summary of CDH13 SNPs

SNP	Chromosome	Position	Hardy-Weinberg equilibrium P	Minor allele frequency	Minor allele
rs8061907	16	81574017	.71	.284	G
rs11647879	16	81599134	.49	.111	T
rs4389131	16	81617265	.27	.241	A
rs7193606	16	82041019	.82	.172	T
rs12926331	16	82295173	.14	.109	T
rs2113148	16	82373088	.91	.243	A

Table 2

Participant Characteristics by Ethnic Group

	Hispanic (n=179)	Caucasian (n=47)	Total (n=226)
% Female	28.5	36.2	30.1
Age	16.13 (1.11)	16.34 (1.15)	16.18 (1.12)
Context Factors			
Parental Monitoring	11.25 (3.48)	9.29 (4.39)	10.88 (3.71)
Peer Alcohol Use	11.75 (2.57)	11.76 (2.46)	11.76 (2.54)
Drinking Behavior			
% ever drank	90.8	88.9	90.4
Age of first drink	12.79 (2.01)	12.54 (2.48)	12.74 (2.11)
AUDIT	8.11 (7.13)	7.33 (8.06)	7.95 (7.32)
3M alcohol use	8.89 (4.93)	8.20 (5.20)	8.75 (4.98)
Sexual Behavior			
% ever intercourse	78.5	89.1	80.7%
Age of first intercourse	13.30 (1.79)	13.53 (2.30)	13.35 (1.91)
Number of partners	6.33 (6.51)	8.58 (14.31)	6.79 (8.72)
% inconsistent condom use	86.2	82.9	85.5
CDH13			
rs8061907 (G risk)			
% GG/GT	50.4 (n=61)	44.4 (n=12)	49.3 (n=73)
% TT	49.6 (n=60)	55.6 (n=15)	50.7 (n=75)
rs11647879 (T risk)			
% TT/CT	23.1 (n=28)	14.8 (n=4)	21.6 (n=32)
% CC	76.9 (n=93)	85.2 (n=23)	78.4 (n=116)
rs4389131 (A risk)			
% AA/AC	42.6 (n=46)	32.0 (n=8)	40.6 (n=54)
%CC	57.4 (n=62)	68.0 (n=17)	59.4 (n=79)
rs7193606 (T risk)**			
% TT/CT	26.4 (n=32)	55.6 (n=15)	31.8 (n=47)
% CC	73.6 (n=89)	44.4 (n=12)	68.2 (n=101)
rs12926331 (T risk)			
% TT/CT	24.1 (n=28)	11.5 (n=3)	21.8 (n=31)
% CC	75.9 (n=88)	88.5 (n=23)	78.2 (n=111)
rs2113148 (A risk)*			
% AA/AG	47.9 (n=58)	22.2 (n=6)	43.2 (n=64)
%GG	52.1 (n=63)	77.8 (n=21)	56.8 (n=84)

* p = .02; **p .003. Parental monitoring scores could range from 2-17, peer alcohol use scores could range from 4-15, and three month alcohol use could range from 3-24.

Table 3

Regression Outcomes for Age of First Drink and Age of First Intercourse

	Age of First Drink				*Age of First Intercourse*			
	B	SE B	β	*p*	B	SE B	β	*p*
Ethnic Group	.25	.39	.05	.52	-.23	.34	-.05	.51
Parental Monitoring	**.20**	**.06**	**.36**	**.002**	.10	.08	.16	.22
Peer Alcohol Use	**-.14**	**.06**	**-.16**	**.03**	.06	.06	.08	.30
CDH13								
rs8061907	-.62	.40	-.14	.13	.30	.38	.07	.44
x parental monitoring	.28	.16	.29	.09	.05	.24	.04	.84
x peer alcohol use	-.25	.16	-.19	.13	.08	.17	.07	.62
rs11647879	-.84	.49	-.15	.09	.12	.45	.03	.79
x parental monitoring	.20	.19	.17	.29	-.01	.26	-.004	.99
x peer alcohol use	-.22	.21	-.11	.29	.03	.20	.02	.89
rs4389131	-.12	.44	-.03	.78	.31	.40	.08	.45
x parental monitoring	**.42**	**.16**	**.43**	**.01**	-.24	.28	-.18	.39
x peer alcohol use	.23	.18	.15	.20	-.03	.17	-.02	.89
rs7193606	.49	.44	.10	.26	**.94**	**.40**	**.22**	**.02**
x parental monitoring	.21	.17	.21	.23	.31	.24	.28	.19
x peer alcohol use	-.13	.18	-.07	.49	-.13	.17	.08	.45
rs12926331	-.23	.51	-.04	.66	-.61	.47	-.12	.20
x parental monitoring	.25	.24	.15	.31	-.30	.46	-.12	.52
x peer alcohol use	-.21	.20	-.11	.28	**-.59**	**.19**	**-.32**	**.002**
rs2113148	.24	.41	.05	.56	.15	.39	.04	.70
x parental monitoring	.12	.16	.13	.46	-.11	.28	-.07	.71
x peer alcohol use	.01	.04	.02	.90	-.05	.04	-.18	.24

Note. The interpretation of effects remained the same when controlling for age, gender, and ethnicity in the models.

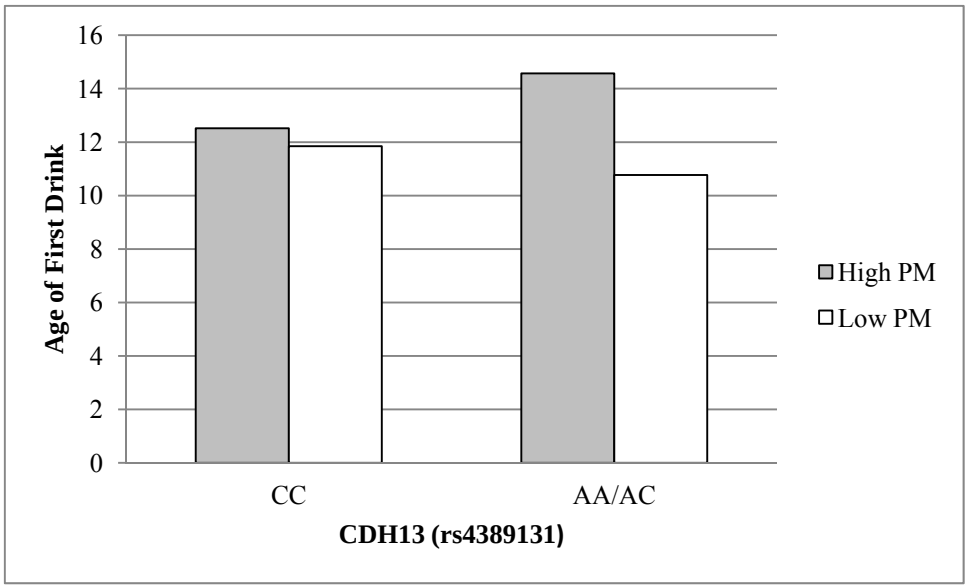

Figure 1a. CDH13 (rs4389131) x Parental Monitoring (PM) on Age of First Drink.

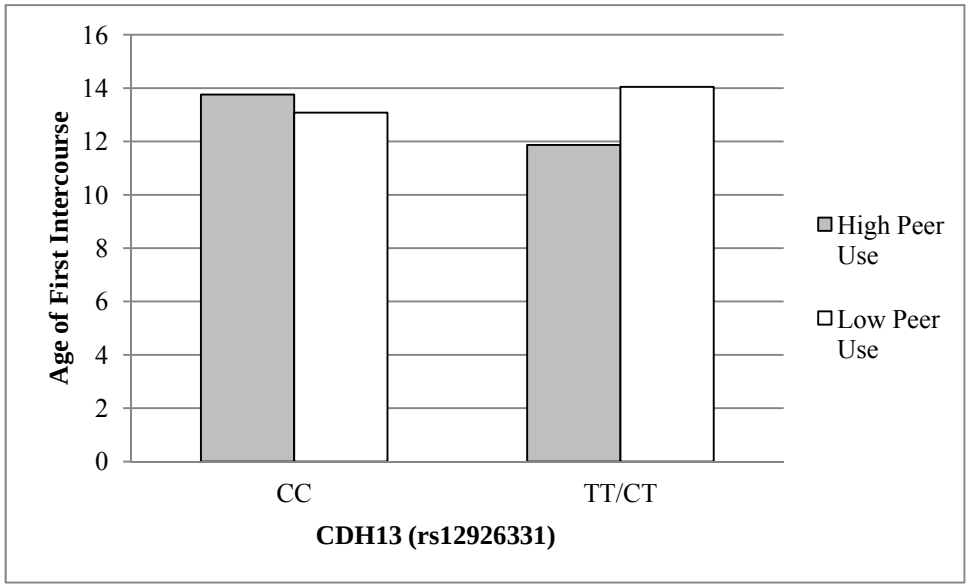

Figure 1b. CDH13 (rs12926331) x Peer Alcohol Use (Peer Use) on Age of First Intercourse.

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