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Preliminary Evidence for a Gene-Environment Interaction in Predicting Alcohol Use Disorders in Adolescents

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Abstract

Background—Emerging research suggests that genetic influences on adolescent drinking are moderated by environmental factors. The present study builds on molecular-genetic findings by conducting the first analysis of gene-environment interactions in the association between a functional single nucleotide polymorphism (SNP) of the μ-opioid receptor (*OPRM1*) gene (A118G) and risk for developing an alcohol use disorder (AUD) during adolescence. Specifically, we tested whether variation in parenting practices or affiliation with deviant peers moderated the link between the *OPRM1* gene and risk for an AUD.

Methods—Adolescents reporting European ancestry (N = 104), ages 12–19 years (M = 15.60, SD = 1.77), were interviewed to ascertain AUD diagnoses, provided a DNA sample for genetic analyses, and completed measures of parental monitoring and deviant peer affiliation. Logistic regression was used to test the effects of environmental variable sand their interactions with *OPRM1*genotype as predictors of AUD diagnosis while controlling for age and sex.

Results—Case-control comparisons showed that the proportion of youth with an AUD (n = 18) significantly differed by genotype such that 33.3% of G allele carriers met criteria for an AUD compared to 10.8% of youth who were homozygous for the A allele (p = .006). The *OPRM1* × parental monitoring (odds ratio = 0.16) and *OPRM1* × deviant peer affiliation (odds ratio = 7.64) interactions were significant predictors of AUD risk, such that G allele carriers with high levels of deviant peer affiliation or lower levels of parental monitoring had the greatest likelihood of developing an AUD (p values < .01).

Conclusions—This study provides initial evidence that the association between the A118G SNP of the *OPRM1* gene and risk for AUDs is moderated by modifiable factors. These results are limited, however, by the small sample size and require replication.

Keywords

Adolescents; *OPRM1*; Alcohol; Parental Monitoring; Deviant Peer Affiliation

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Introduction

Alcohol use during adolescence is associated with sharp increases in the risk for myriad adverse outcomes, including alcohol dependence (Grant et al., 2006). Consequently, research efforts to identify factors that affect liability for developing an alcohol use disorder (AUD) during this key developmental period have grown considerably over the past decade. Early evidence from twin and adoption studies indicates that while initiation of alcohol use during adolescence is mainly influenced by environmental factors, genetics play a primary role in the development of alcohol-related problems (Hopfer et al., 2003, Lynskey et al., 2010). Emerging research, however, illustrates the importance of elucidating the interplay between genetic and environmental influences on alcohol-related problems and other forms of psychopathology (Dick 2011, Dick et al., 2011; Nilsson et al., 2005). Specifically, recent quantitative genetic research with twin data suggests that environmental factors moderate genetic liabilities for alcohol use in youth (Dick et al., 2007).The present study builds on twin studies, which provide estimates of the combined variance explained by multiple genes (i.e., heritability or estimates of additive genetic risk for a disorder), by conducting the first analysis of gene-environment interactions in the association between a specific functional polymorphism of the μ-opioid receptor (*OPRM1*) gene, the A118G SNP, and risk for developing an AUD during adolescence. Specifically, this study tested whether variation in parenting practices and affiliation with deviant peers moderated the role of this polymorphism on the development of an AUD among youth.

The endogenous opioid system plays an integral role in the pathophysiology of alcohol misuse (Dackis and O'Brien, 2005). Alcohol consumption increases opioidergic activity, which inhibits gamma aminobutyric acid (GABA) neurotransmission and results in acute dopamine release from mesocorticolimbic neurons (Kreek, 1996).This acute dopamine release is critically involved in the rewarding and reinforcing effects of alcohol and other addictive substances (Weiss and Porrino, 2002). Given the essential role of the endogenous opioid system in the pharmacological effects of alcohol, *OPRM1* has received considerable attention as a candidate gene for alcoholism risk (for a review, see Ray et al., 2012). Although association findings between this SNP and alcohol dependence are mixed (for meta-analysis, see Arias et al., 2006), significant limitations of existing work, such as sample selection biases, clinical heterogeneity across studies, and insufficient specificity in the diagnostic phenotype of alcohol dependence, may account for disparate findings (Ray et al., 2012).

We recently reported the first evidence that the A118G SNP of the *OPRM1* gene is associated with a greater number of alcohol-related problems as well as the development of an AUD among adolescents (Miranda et al., 2010). Specifically, adolescents who met criteria for an AUD diagnosis had a higher prevalence of the G allele (51.9%) than non-AUD youth (16.3%), and the G allele accounted for 9% of the variance in alcohol-related problems experienced by youth in the past 3 months, with a medium magnitude effect size ($f = 0.31$).These findings coincide with adult studies in terms of the nature and magnitude of the association between *OPRM1* and alcoholism (Bart et al., 2005; Town et al., 1999; for a review, see Ray et al., 2012). It is important to recognize, however, that a number of adult studies did not find this association (Franke et al., 2001; Loh et al., 2004; Lou et al., 2003).

While variation in *OPRM1* appears to increase the risk for developing problems with alcohol, genetic contributions to adolescent drinking are heavily influenced by environmental factors (Rose et al., 2001a, b). One factor that has received considerable attention within this context is parenting practices or more specifically parental monitoring, which includes both supervision of youth by a parent or other adult and communication between the parent and youth (Kerr and Stattin, 2000; Stattin and Kerr, 2000). A substantial

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body of literature has consistently demonstrated that higher levels of parental monitoring are associated with reduced risk of alcohol use as well as smoking and other risk-taking behaviors among adolescents (Beck et al., 2004; Guo et al., 2001; Lahey et al., 2008). Parental monitoring has been shown to moderate the influence of genetic effects on substance use in adolescence (Chen et al., 2009; Dick et al., 2007; 2009). For example, a twin study of adolescents ages 14 and 17 years found that genetic effects on substance use were significantly decreased as parental monitoring increased (Dick et al., 2007). Thus, lower levels of parental monitoring were found to allow for greater expression of genetic predispositions demonstrating that the etiology of adolescent smoking varies dramatically as a function of parental monitoring. Similar effects were found in a prospective study that examined the association between a specific gene (GABRA2) and alcohol-related problems in a community-based sample of adolescents; the significant association between the candidate gene and alcohol misuse diminished with high levels of parental monitoring (Dick et al., 2009). These studies lend support to the role of parental monitoring as a moderator of genetic effects on substance use in adolescence.

Another environmental influence that has received much attention in the risk-behavior literature is affiliation with deviant peers. Numerous studies have provided support for the importance of peers in the development of substance use and abuse (Andrews et al., 2002; Bauman and Ennett, 1994; Curran et al., 1997).The degree to which an adolescent's peers use alcohol or illicit drugs has been identified as a strong predictor of that adolescent's own substance use behavior (Chassin et al., 2004). Emerging evidence suggests that deviant peer affiliation may moderate the genetic disposition of youth for substance use. For example, twin data have demonstrated that drinking by friends impacts the genetic effects on alcohol use; specifically higher levels of drinking by friends has been found to bring about higher levels of genetic contribution to this behavior whereas lower levels of drinking by friends suppressed the level of genetic contribution to alcohol use (Guo et al., 2009). Similar findings have been reported by Dick and colleagues (2007) who reported that as peer alcohol use increases, heritable factors associated with an adolescent's own alcohol involvement also increase. In addition to a gene by environment interaction, evidence for gene by environment correlation in which individuals with increased genetic liability for substance use are more likely to affiliate with substance-using peers has also been provided (Agrawal et al., 2010; Harden et al., 2008). Considering that the extent to which an individual affiliates with substance-using or delinquent peers has emerged as one of the strongest correlates of adolescent onset substance use and substance use problems, it is critical to consider this variable in a model of predictors of alcohol-related problems among adolescents.

The purpose of the present study is to build upon our previous findings by examining whether the influence of *OPRM1* on alcoholism risk varies depending on specific environmental factors, namely parental monitoring and deviant peer affiliation. We hypothesized that risk associated with the A118G SNP of the *OPRM1* gene would be moderated by parental monitoring and deviant peer affiliation, such that youth with lower parental monitoring and higher affiliation with deviant peers would experience greater risk for developing an AUD. In addition, given the interrelatedness of parental monitoring and deviant peer affiliation, we explored the three-way interactive effects of genotype and these environmental variables to evaluate whether an interaction between genotype and one environmental variable varies across levels of the other environmental variable. In brief, this study seeks to reach a more integrative perspective on the relative risk associated with the A118G SNP of the *OPRM1* gene by considering key environmental components known to influence the development of AUDs in youth.

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Materials and Methods

Participants

Participants (n= 104) were a subset of a larger sample of adolescents who took part in a study of biobehavioral mechanisms relating antisocial behavior and problematic substance use in youth (for additional details see Miranda et al., 2010).The present study focused on previously unreported data regarding parental practices and peer influences. All youth who enrolled in the larger project were afforded the opportunity to participate in the genetic segment of the study and 90.1% agreed. Separate informed written consent/assent was obtained for DNA collection. Informed written consent for the study was obtained from participants >18 years and from the parents/legal guardians of minors prior to participation; assent was obtained from minors. Of those who consented to the genetics study, three individuals were excluded from analyses due to an inability to successfully genotype their DNA sample and another five youths were excluded due to incomplete data. The Brown University Institutional Review Board approved all procedures. To be eligible, adolescents had no history of traumatic brain injury or hearing difficulties. Participants were also required to test negative on a urine toxicology screen on the day of assessment for the following substances: alcohol, amphetamines, barbiturates, benzodiazepines, cocaine, and opiates. Although youth who endorsed suicidal ideation or psychotic symptoms were ineligible for the study, other forms of psychopathology were not exclusionary. Adolescents who enrolled in the genetic portion of the study did not differ from those who declined in terms of age, education, racial background, ethnicity, sex, or AUDs (p values > .05). We limited the present analyses to European-American participants to control for potential confounds from population stratification. This approach, which relied on participants' self-reported ancestry, is consistent with similar studies (Hutchison et al., 2004; Park et al., 2011).

Recruitment and Procedures

Participants were recruited from the community via flyers and informational booths stationed at local recreational settings (e.g., malls) and high schools. In an effort to over sample for youth who engage in antisocial behavior and problematic substance use, adolescents were recruited primarily from disadvantaged neighborhoods and a local truancy court program. Interested volunteers telephoned the laboratory to learn about the larger project and underwent a brief screening interview to determine initial eligibility. Those who did not endorse exclusionary criteria were invited to the laboratory to obtain written informed consent/assent and to complete an in-person screening interview. Eligible youth participated in a one-day assessment session that involved administration of semi-structured clinical interviews to assess for psychopathology along with other self-report measures. Participants' parents/legal guardians were invited to take part in the study by completing semi-structured interviews and paper-and-pencil measures regarding the adolescent's developmental history and psychiatric functioning. Although informed written consent was required from parents/legal guardians of adolescents younger than age 18 years, parents/legal guardians were not required to participate in the study. This approach was chosen to allow recruitment of youth whose parents/legal guardians were unavailable or unwilling to participate in the project. Parent data, typically provided by the adolescent's mother (91.3% of cases), were obtained for 49.2% of adolescents. Participants and parents/legal guardians who took part in the study were compensated for their participation.

Domains of Assessment and Measures

Psychopathology and AUD Diagnoses—The Kiddie Schedule for Affective Disorders for School-Age Children(KSADS; Kaufman et al., 1997) is a clinician-administered semi-structured interview that was used to assess for DSM-IV-TR psychopathology, including

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substance use disorders. When a parent/legal guardian elected to participate in the study, the parent/legal guardian and adolescent were interviewed separately. Information collected from these interviews was integrated using an algorithm that identified the presence of a disorder if sufficient criteria were endorsed by either the parent or adolescent (Henin et al., 2007). In cases where a parent was unavailable to complete the assessment battery, diagnostic determinations were based on the adolescent's report. In no case did parents' reports of teenagers' AUD symptoms add to the information already gathered from the adolescents themselves. Interviewers received systematic training in diagnostic assessment with adolescents to achieve a high level of inter-rater reliability (kappa > 0.90) at the item severity level prior to conducting interviews independently. Two clinical psychologists (RM, AJ) reviewed all cases at weekly case consensus meetings to minimize potential drift in item severity ratings by interviewers. All symptom severity level and diagnostic decisions were derived by case consensus with the interviewer(s) and both psychologists present. For the purpose of this study, our primary dependent measure of interest was the binary classification of youth based on the presence or absence of an AUD (i.e., abuse or dependence).

Parental Monitoring—Adolescents completed a 19-item measure that assessed how frequently, on a 5-point scale (never to always), their parents: (i) require knowledge of their whereabouts, activities, and associations; (ii) exert control over their behavior (e.g., requires permission to stay out late); and (iii) solicit information from others regarding their school performance, recreational activities, and friendships (Kerr and Stattin, 2000). Means were calculated for each scale. An overall parental monitoring score was computed by averaging all 19 items (Cronbach's α =0.93).

Deviant Peer Affiliation—Consistent with previous research (Marshal and Molina, 2006), deviant peer affiliation was assessed using a measure adapted by Chassin and colleagues (1993) from the Monitoring the Future study (Johnston et al., 1988). Adolescents used a 6-point scale (none to all) to report how many of their friends engaged in six forms of substance use: occasional and regular use of alcohol, marijuana, and other drugs. Adolescents also rated on a 6-point scale how their close friends would feel if they engaged in these six forms of substance use, as well as "weekend heavy alcohol use," ranging from strongly disapprove to strongly approve. Similar to other studies (Marshal and Molina, 2006), the zero-order intercorrelation between the mean of the peer use items and the mean of the peer tolerance of use items was fairly strong (r= 0.81, $p < 0.001$), therefore an overall peer deviance score was computed by averaging all items (Cronbach's α = 0.96).

Genotyping—Genomic DNA was collected and isolated from buccal swabs using standard procedures (Freeman et al., 1997; Walker et al., 1999). The A118G SNP in the *OPRM1* gene was assayed using a commercially available instrument and TaqMan assays (Applied Biosystems, Foster City, California). To ensure accurate data, genotypes for all participants were determined by two independent laboratory technicians blinded to participants' characteristics. In addition, a randomly selected subset of samples (10%) was assayed again to assess reliability (kappa = 1.0).

Statistical Analysis

Analyses were performed using the SPSS statistical package, version 19.0 (IBM, Armonk, NY). Variables were first checked for distributional assumptions. Multicollinearity was assessed and the Variance Inflation Factor for all independent variables and covariates (i.e., deviant peer affiliation, *OPRM1* genotype, parental monitoring, age, and sex) was less than 2, indicating acceptable statistical associations between explanatory variables. A series of *t*-tests and χ^2 tests compared the two groups on AUD diagnostic status, deviant peer

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affiliation, and parental monitoring. To test whether the association between the candidate gene and the development of an AUD was influenced by specific environmental circumstances, a backward stepwise logistic regression equation was conducted. The dependent variable was the binary categorization of AUD diagnosis as the presence (1) or absence (0) of either alcohol abuse or dependence. Predictors were the candidate gene (coded as AG/GG versus AA), the moderators (i.e., deviant peer affiliation, parental monitoring), and the candidate gene × moderator interactions. Continuous independent variables (deviant peer affiliation, parental monitoring) were centered prior to being entered into the models. Potential confounding effects of sex and age were controlled by entering these variables as covariates. The most parsimonious model was identified using the backward elimination method ($\alpha = 0.10$).The Bonferroni method was used to control for inflation of Type I error by adjusting the threshold of significance ($\alpha = 0.05$) for each hypothesized gene × moderator interaction (Dar et al., 1994),yielding a modified threshold of significance ($\alpha = 0.025$).

Results

Participant Characteristics

Descriptive statistics on the sample by genotype are shown in Table 1. Among the sample of 104 European-American youth, 30 adolescents (28.8%) carried the G allele [AG = 24% (n = 25), GG = 4.8% (n = 5)]; the remainder were homozygous for the A allele [71.2% (n = 74)].Allele frequencies were consistent with Hardy–Weinberg equilibrium ($\chi^2 = 2.07$, df = 1, $p = .15$).In terms of AUD diagnoses, 18 adolescents (17.31%) met diagnostic criteria either alcohol abuse [5.8% (n = 6)] or dependence (11.5% (n = 12)].The proportion of youth diagnosed with an AUD in this sample was comparable to prevalence rates reported for European-American youth (ages 12-17 years) in a large representative sample of adolescents in the U.S. (Wu et al., 2011).As illustrated in Table 1, case-control comparisons showed that the proportion of youth with an AUD significantly differed by genotype such that 33.3% of G allele carriers met criteria for an AUD compared to 10.8% of youth who were homozygous for the A allele($\chi^2 = 7.57$, df = 1, p = .006). In addition, compared to youth who were homozygous for the A allele, carriers of the G allele reported significantly higher levels of deviant peer affiliation (t = −2.44, df = 102, p = .02; see Table 1). Conversely, carriers of the G allele reported marginally lower levels of parental monitoring than those homozygous for the A allele (t= 1.99, df = 102, p = .05; see Table 1). There was no difference in age between G allele and non-G allele carriers (t = 0.47, df = 102, p = .64; see Table 1).

Zero-order Pearson correlations among study variables are shown in Table 2.Diagnosis of an AUD was significantly correlated with deviant peer affiliation, parental monitoring, and *OPRM1* in the expected directions (*p* values < .01). *OPRM1* was significantly correlated with deviant peer affiliation and parental monitoring, such that carriers of the G allele tended to have higher levels of deviant peer affiliation and lower levels of parental monitoring (*p* values < .05).

Gene and Environment Interactions

To test whether the association between *OPRM1* and the development of an AUD in adolescence was moderated by two environmental influences we used logistic regression with a hierarchical backward elimination procedure to determine the most parsimonious model. Interaction effects of the *OPRM1* genotype with environmental variables were calculated by multiplying the *OPRM1*variable by each centered environmental variable. Potential confounding effects of sex and age were controlled by entering these variables as covariates. The main and interaction effects of *OPRM1* genotype, deviant peer affiliation,

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and parental monitoring were entered into the logistic regression model simultaneously. The final backward elimination logistic regression model was significant ($\chi^2 = 64.41$, df = 3, p = .000, Nagelkerke $R^2 = .77$, see Table 3) and included sex, the *OPRM1* × parental monitoring interaction, and the *OPRM1* × deviant peer affiliation interaction. These predictors remained significant after controlling for multiple testing using the Bonferroni correction (adjusted $\alpha = 0.025$). As hypothesized, decomposition of the *OPRM1* × parental monitoring interaction indicated that carriers of the G allele who reported relatively high levels parental monitoring were least likely to develop an AUD. Conversely, youth with a copy of the G allele and relatively high levels of deviant peer affiliation were more likely to develop an AUD than G allele carriers with relatively low levels of deviant peer affiliation. Decomposition of the effect of sex showed that more girls (26%) meet diagnostic criteria for an AUD than boys (9%).

Discussion

This study provides initial evidence that parenting practices and affiliation with deviant peers moderate the effect of *OPRM1* on risk for developing an AUD during adolescence, such that genotypic risk for an AUD was significantly lower when parental monitoring was higher and significantly heightened when youth affiliated with more deviant peers. While preliminary, our findings suggest there is heterogeneity in AUD risk in adolescents carrying the G allele and that parental monitoring may play a protective role against vulnerability for AUDs in youth at elevated risk based on *OPRM1* genotype. Similarly, there was a significant genotype by deviant peer affiliation interaction, such that adolescent carriers of the G allele who reported high levels of deviant peer affiliation were more likely to develop an AUD. This effect was less pronounced in youth who were homozygous for the A allele and low levels of deviant peer affiliation were associated with a low prevalence of AUDs regardless of genotype. These data build on recent findings from longitudinal twin studies that indicate that genetic influences on adolescent substance use are strongest when parental monitoring is relatively low and when teenagers have a larger number of deviant peers (Dick et al., 2007; Guo et al., 2009). On the whole, these findings add to a growing body of evidence, now observed in both quantitative and molecular genetic research, which shows that well-supervised and non-permissive family environments can restrict manifestation of genetic predispositions for alcoholism while affiliation with deviant peers can potentiate this risk. Our findings provide further support for intervention strategies designed to decrease teenage alcohol use by increasing affiliation with non-deviant peers. Such interventions may in effect delay the development of heavy use and problems, and this may be effective across levels of alcoholism diathesis.

The association between the *OPRM1* gene and deviant peer affiliation is especially noteworthy in light of mounting evidence from animal models and more recently from human data that the A118G SNP of the *OPRM1* gene modulates individual differences in the capacity to experience social reward and the need for affiliation, with carriers of the G allele demonstrating greater tendencies to engage in and experience reward from social situations (Troisi et al., 2011a). At the same time, research also shows that individuals carrying the G allele experience heightened sensitivity to social rejection on self-report measures as well as increased neuronal activity in response to social rejection across multiple brain regions that govern the processing of physical pain (Troisi et al., 2011b; Way et al., 2009). Although this work was done with adult samples and requires further study among adolescents, the possible implications of these findings for the present study are intriguing. Adolescent carriers of the G allele may be prone to affiliating with deviant peers in part due to their heightened sensitivities to social reward and to fear of social rejection. These liabilities may in turn increase susceptibility to peer influences on initiation of

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drinking and escalation to problematic use. This possibility is purely speculative at this time, however, and warrants empirical testing in future research.

Despite the potential importance of these findings, several important limitations must be noted. First, a primary shortcoming of this study is that our sample size is modest, which increases the likelihood that our results reflect false-positive findings (see Duncan and Keller, 2011). Although the threshold for significance was adjusted (i.e., modified α level) to attenuate the inflation of Type I error, we must emphasize the importance of independent and direct replication of these findings. Second, we must consider that parental monitoring and deviant peer affiliation are themselves likely to be genetically influenced. There is growing evidence that parental monitoring is complex, affected by both genetic and environmental factors (Neiderhiser et al., 2004). Genetic influences include the genotypic characteristics of the parents and the genetically influenced characteristics of the adolescents that influence their interactions with their parents. Similarly, twin studies indicate that genetic factors influence adolescents' selection of peers with similar temperament and drinking patterns (Fowler et al., 2007). Because genotypic factors influence susceptibility to alcoholism as well as parental monitoring and peer selection, the association between these factors may be spurious and attributable to a shared genetic liability. In addition, modest correlations were observed between genotype and parental monitoring and deviant peer affiliation, such that carriers of the G allele tended to experience lower levels of parental monitoring and affiliate with more deviant peers. In the case of our findings, causal variants need to be examined in future research while including passive gene-environment correlations (rGE) in the model, by which children inherit both genes and environment from their parents, which is particularly important with regard to our parental monitoring findings. In addition, future studies need to examine active rGE, by which children with genetically oriented tendencies to drink select a social environment in which drinking is normative or rewarded – this is especially important with regard to our findings on peer affiliation. Such associations could have important implications. For example, it may be that adolescent carriers of the G allele are more susceptible to developing an AUD when parental monitoring is low compared to youth who are homozygous for the A allele. Alternatively, carriers of the G allele may evoke lower levels of parental monitoring, which in turn set the stage for these youth to develop an AUD. The first example suggests that carriers of the G allele might benefit disproportionately from interventions aimed at increasing parental monitoring. In the second example, however, the key mechanism of risk involves parental monitoring and not direct genetic effects on alcohol outcomes, and therefore interventions would be appropriately aimed at all youth with low levels of parental monitoring, regardless of genotype. While our findings provide initial evidence of interplay between *OPRM1* genotypes and environmental variables, elucidating the precise nature of these relationships is an important area for future research.

In summary, the findings of this study provide the first evidence that environmental factors, namely parental monitoring and deviant peer affiliation, moderate the influence of an opioid-related gene in the development of AUDs in adolescents. Specifically, these findings highlight the importance of examining interactions between genotype and parental monitoring and deviant peer affiliation, as our data suggest that genetic influences the development of AUDs in adolescents vary dramatically as a function of these factors. Importantly, these environmental factors are tractable and amenable to behavioral intervention, providing an important buffer against the development AUDs in youth.

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Table 1

Sample Descriptive Statistics by *OPRM1* Genotype

	AG/GG (*n*= 30)	AA (*n*= 74)	Total (*n*= 104)
Demographic Variables:			
Age [M(sd)]	15.47 (2.03)	15.65 (1.67)	15.60 (1.77)
Sex (% Female)	46.7	50.0	49.0
Deviant Peer Affiliation [M (SD)] *	1.91 (1.23)	1.39 (0.86)	1.54 (1.00)
Parental Monitoring [M (SD)]	3.34 (0.89)	3.70 (0.77)	3.60 (0.82)
AUD Status (% met criteria for an AUD) **	33.33	10.81	17.31

Note. AUD = Alcohol use disorder; M = Mean; SD = Standard Deviation;

* $p < .05$;

** $p < .01$

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Table 2

Pearson Correlations Among Study Variables

Variable	1	2	3	4	5	6
1. Age						
2. Sex[a]	0.13					
3. AUD status[b]	0.45***	0.21*				
4. Deviant peer affiliation	0.57***	0.16	0.63***			
5. Parental monitoring	–0.51***	0.06	–0.49***	–0.47***		
6. *OPRM1* genotype[c]	–0.05	–0.03	0.27**	0.24*	–0.19*	

Note. AUD = Alcohol Use Disorder;

[a] 0 = male, 1 = female;

[b] 0 = not present, 1 = present (i.e., alcohol abuse or dependence);

[c] *OPMR1* genotype coded as 1 = AA, 2 = AG/GG (risk status);

* $p < .05$;

** $p < .01$;

*** $p < .001$

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Table 3

Final Backward Elimination Logistic Regression Model – Predicting the Odds of an Alcohol Use Disorder Diagnosis (N = 104)

Variables	β	OR	95% Confidence Interval		p value or order of elimination
			Lower	Upper	
Age (years)					–5
Sex (male = 0, female = 1)	–3.66	0.03	0.00	0.48	.014
Genotype (GG/AG = 0, AA = 1)					–3
Deviant Peer Affiliation					–4
Parental Monitoring					–1
Genotype × Deviant Peer Affiliation	2.03	7.64	2.30	25.40	.001
Genotype × Parental Monitoring	–1.65	0.19	0.06	0.59	.004
Genotype × Deviant Peer Affiliation × Parental Monitoring					–2

Note. Continuous measures were centered before their inclusion in both models;the main effect also refers to the effect of the centered version of the variable. Standardized β presented; OR = Odds ratio

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