DIFFERENTIAL SUSCEPTIBILITY TO THE EFFECTS OF PEER PRESSURE AND POSITIVE FRIEND SUPPORT ON ALCOHOL USE

A Thesis in
Human Development and Family Studies
by
Amanda M. Griffin

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The thesis of Amanda M. Griffin was reviewed and approved* by the following:

H. H. Cleveland  
Associate Professor of Human Development and Family Studies  
Thesis Advisor

David J. Vandenbergh  
Associate Professor of Biobehavioral Health

Douglas M Teti  
Professor of Human Development and Family Studies  
Department Head of the Department of Human Development and Family Studies

*Signatures are on file in the Graduate School.
ABSTRACT

Adolescents’ peer relationships have been shown to influence alcohol use, however, not all peer relationships equally influence adolescents. This study draws from the in-home subsample of the PROSPER Project to investigate the association between peer relationships (both positive and negative) and adolescent alcohol use, and the moderating role of DRD4. I hypothesize that the DRD4 candidate gene (7-vs.7+) moderates the impact of both Peer Deviance Pressure and Positive Peer Activity on 12th grade alcohol use. Results revealed significant main effects for both peer measures, but no main effects for the DRD4 variant, on 12th grade alcohol use. In addition, DRD4 moderated the association between negative peer relationships and alcohol use. For individuals who carried at least one copy of the DRD4 7+ variant, Peer Deviance Pressure was associated with increases in both overall alcohol use and recent alcohol use. However, DRD4 status did not moderate the effect of Positive Peer Activity on alcohol use for DRD4 7+ individuals.
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INTRODUCTION

Early alcohol use is linked to reduced educational attainment, increased risky sexual practices, and amplified mental health risk (US Department of Health and Human Services, 2013). Alcohol use in early adolescence also dramatically increases the odds of alcohol abuse and alcohol dependency beyond age 21 (DeWit, Adlaf, Offord, & Ogborne, 2000). These findings demonstrate that alcohol use during early adolescence indicates risks over a broad range of negative outcomes, both general and substance use related.

Positive and negative peer relationships are both critical influences on adolescent alcohol use. Their significance is expected given the general increased importance of peer relationships during early adolescence, as time spent with peers increases and time spent with parents decreases (Csikszentmihalyi & Larson, 1984; Larson, Richards, Moneta, Holmbeck, & Duckett, 1996). Early adolescent peer relationships have the opportunity to establish and transmit behavioral norms and attitudes regarding activities, including alcohol use. Thus, it is not surprising that affiliating with delinquent peers is linked to adolescents’ own alcohol use (Hawkins, Catalano, & Miller, 1992).

Although exposure to peer delinquency can generally predict adolescent alcohol use, susceptibility to peer influence on adolescents’ own behaviors can differ across individuals (Dielman, Campanelli, Shope, & Butchart, 1987; Dielman, Kloska, Leech, Schulenberg, & Shope, 1992). Varying levels of susceptibility to peer influence have been related to individual characteristics such as perceived harm of substance, sensation seeking, self-esteem, and magnitude of non-use social values (Hawkins, Catalano, & Miller, 1992; Petraitis, Flay, & Miller, 1995).

Susceptibility to peer influences on alcohol use may also be influenced by genetics.
Recent research guided by Differential Susceptibility Theory (DST) (Belsky, Bakermans-Kranenburg, & van IJzendoorn, 2007; Belsky & Pluess, 2009; Belsky & Pluess, 2013; Ellis, Boyce, Belsky, Bakermans-Kranenburg, & van IJzendoorn, 2011) has provided substantial evidence that genetic variants can confer different amounts of sensitivity to experiences ranging from interventions (see Brody, Beach, Philibert, Chen & Murry, 2009; Beach, Brody, Lei, & Philibert, 2010) to parenting (see Bakermans-Kranenburg & Van IJzendoorn, 2006). Most pertinent to the current inquiry are findings that genetic variants can modify the impact of experimentally manipulated peer influence on alcohol use (Creswell, Sayette, Manuck, Ferrell, Hill, & Dimoff, 2012; Larsen et al., 2010).

Based upon longstanding research demonstrating peers’ impact on adolescent risk behaviors, including but not limited to alcohol use, as well as recent research demonstrating the effect of specific genetic variants, this study investigates how the DRD4 gene may moderate the influence of positive and negative peer relationships on adolescent alcohol use. Before providing specific hypotheses, pertinent literature regarding DST, the biological role DRD4 plays in peer influence, and how peer influence is related to adolescent alcohol use will be reviewed.

**Differential Susceptibility Theory**

A growing body of research, guided by Differential Susceptibility Theory (DST), focuses on the effects of variability in individual environmental experiences (Belsky, Bakermans-Kranenburg, & van IJzendoorn, 2007; Belsky & Pluess, 2007; Belsky & Pluess, 2013; Ellis, Boyce, Belsky, Bakermans-Kranenburg, & van IJzendoorn, 2011). DST posits that individuals may be more susceptible to environmental contexts due to genetic differences. At its most basic level, DST is rooted in evolutionary theory. The core concept behind DST is that environmental uncertainty results in parents “hedging their bets” by providing offspring with different biological traits that would help them survive in a multitude of environmental contexts (Belsky,
1997; Boyce & Ellis, 2005). As a result, some offspring will be relatively less sensitive to environmental influences compared to their siblings who will be relatively more sensitive to them. For example, in adverse environments, offspring with low environmental sensitivity manifest reduced impacts of the negative experiences encountered. Likewise, in adverse environments, offspring with high environmental sensitivity manifest increased impacts of the negative experiences encountered. Conversely, in favorable environments, these highly sensitive offspring tend to flourish, while less sensitive offspring are relatively unaffected by the favorable environmental contexts.

One major implication of DST is that increased sensitivity to the environment does not necessitate genetic main effects. Rather, DST suggests genes will moderate the impact of environmental contexts. Thus, according to DST, offspring who receive a “sensitive” genetic makeup from their parents will be more “vulnerable” to both adverse and favorable environmental contexts, which results in negative consequences in adverse environments and positive consequences in favorable environments. The net result of such sensitivity to both negative and positive environments is no direct effects of specific genes on individuals, when averaged across all environmental contexts.

**Dopamine and Peer Influences**

Candidate gene research on DST has used various genetic variants, including the *DRD2* (Berman, Ozkaragoz, Young, & Noble, 2002) and *DAT1* genes (Kahn et al., 2003), but the genetic variant most commonly studied has been the *DRD4* gene (Bakermans-Kranenburg, van IJzendoorn, Pijlman, Mesman, & Juffer, 2008; Gervai et al., 2007; van IJzendoorn, Bakermans-Kranenburg, & Mesman, 2008). *DRD4* is a critical candidate gene because it regulates signaling in the dopamine system, which significantly affects activation.

*DRD4*, the dopamine receptor D4 gene, contains a 48-base pair Variable Number of
Tandem Repeats (VNTR) in the third exon of the D4 gene (Van Tol et al., 1992). This \textit{DRD4} locus has ten alleles that vary from two to eleven repeats, with the 4- and 7-repeats being the most common. In this study, the \textit{DRD4} gene is analyzed by comparing the presence or absence of the 7-repeat allele (7+ vs. 7-, respectively). \textit{DRD4} is often classified by the presence or absence of the 7-repeat allele because the presence of the sensitive variant (7+) is associated with less concentration-dependent inhibition of forskolin-stimulated cyclic AMP (cAMP) levels (Schoots & Van Tol, 2003) and decreased ligand binding (Asghari et al., 1994).

Changes in dopamine activation encompass several midbrain structures (i.e., ventral tegmental area and substantia nigra) and project to the ventral striatum and prefrontal cortex. In these brain structures, changes in dopamine production are linked to the processing of reward salience and magnitude (Apicella, Ljungberg, Scarnati, & Schultz, 1991; Hikosaka & Watanabe, 2000; Wise, 2002). Changes in dopamine activation due to genetic variants, such as \textit{DRD4}, are linked with reinforcing the value and salience of stimuli (Montague, Dayan, & Sejnowski, 1996; Schultz, 1998), enabling neurological change in response to environment (Tobler, Fiorillo, & Schultz, 2005), and anticipating rewards (Kelley, Schiltz, & Landry, 2005). For example, dopamine activation is related to the stimulatory and rewarding effects of alcohol (Littleton & Little, 1994; Samson & Harris, 1992).

\textit{DRD4} has been associated with multiple behavior outcomes. The \textit{DRD4} 7+ variant has been associated with increased susceptibility to alcohol use (Namkoong et al., 2008), addiction behavior (McGeary, 2009), novelty-seeking personality traits (Ebstein et al., 1996; but also see Malhotra, Virkkunen, Rooney, Eggert, Linnoila, & Goldman, 1996), and attention deficit/hyperactive disorder (Faraone & Mick, 2010). \textit{DRD4} 7+ individuals have been found to possess both an increased “urge” to drink after being primed with a dose of alcohol (Hutchinson,
McGeary, Smolen, Bryan, & Swift, 2002; Ray et al., 2010) and increased neurological responses to alcohol taste cues (Filbey et al., 2008), when compared to individuals who possess the less sensitive DRD4 7- gene.

Of particular importance to the current study is research demonstrating the role of the DRD4 7+ variant in moderating the impact of social experiences. Experimental research has shown that the sensitive DRD4 7+ variant increases individuals’ sense of reward from alcohol consumption when in a group context (Creswell et al., 2012). For individuals who possess this variant, the increased sense of reward is theorized to be due to an increase in perceived social bonding. Related research has found that the DRD4 7+ variant is associated with an increased susceptibility to alcohol related cues, such as being in the presence of a same-age individual who drinks heavily (Larsen et al., 2010). Thus, individuals with the DRD4 7+ variant are more likely to consume alcohol in an attempt to conform to their social contexts (Larsen et al., 2010). Theoretical literature also suggests that adolescents who possess the 7+ variant are particularly susceptible to the company of peers because of a heightened desire to conform due to the important role peers play in autonomy development (Warr, 2002).

Contrary to the experimental findings above, one study failed to find a significant moderating effect of the DRD4 7+ variant on the association between best friend alcohol use and adolescents’ own alcohol use (van der Zwaluw, Larsen, & Engels, 2012). This inconsistent result may be due to the use of youth self-report of friends’ alcohol consumption and that peer influences on alcohol use differ depending on whether youth are adolescent or college-age. Additionally, this result may be due to lower alcohol consumption rates for adolescent samples in comparison to college-age samples (i.e., Creswell et al., 2012; Larsen et al., 2010).
Peers and Adolescent Alcohol Use

Peer relationships result in social contexts with novel sources of deviant and/or prosocial influences. Associating with deviant peers is linked to an increase in problem behavior such as delinquency and substance use (Patterson, Dishion, & Yoerger, 2000; Scaramella, Conger, Spoth, & Simons, 2002; Rowe, Woulbroun, & Gulley, 1994). Conversely, associating with prosocial peers is linked to abstinence from alcohol (Spoth, Redmond, Hockaday, & Yao, 1996). Although ample research focuses on the negative effects of peer influences, prosocial peer relationships have been shown to be equally as important, but rather in reducing the likelihood of alcohol use during adolescence (i.e., Hawkins, Catalano, & Miller, 1992; Kandel & Andres, 1987; Newcomb, Maddahian, & Bentler, 1986). Prosocial peer relationships, conceptualized as affiliating with prosocial peers, are associated with direct and long-term effects on youth abstaining from alcohol (Spoth, Redmond, Hockaday, & Yao, 1996). Additionally, friends’ prosocial behavior was negatively associated with adolescent violence and substance use (Prinstein, Boergers, & Spirito, 2001). Prosocial peer relationships are theorized to influence adolescents by prompting youth to share in prosocial attitudes and norms (Bandura, 1986). These relationships provide opportunities for youth to practice egalitarian social exchanges and acquire behavioral and emotional competencies (Bukowski, Buhrmester, & Underwood, 2011).

The reviewed literature suggests that both positive and negative peer experiences can have important influences on adolescents’ alcohol use behaviors. DST research has shown that specific genes can moderate the impact of these individual environmental experiences. Thus, it is possible that individuals with different genotypes will experience different effects from these peer experiences. To investigate this possibility, the current study examines how the DRD4 gene may moderate the effects of peer relationships on adolescent alcohol use. Based on the reviewed
peer influence literature, I expect to find main effects on alcohol use for both negative and positive peer relationships. Specifically, 7th grade Peer Deviance Pressure will be associated with greater alcohol use, while 7th grade Positive Peer Activity will be associated with lower alcohol use. I do not expect main effects for DRD4 status. Finally, I expect to find that DRD4 will moderate the effect of peer relationships on alcohol use, both for Peer Deviance Pressure and Positive Peer Activity.

Analytic Challenge to G x E Research

An analytic challenge when doing gene by environment research (G x E) is addressing the potential effects of population stratification. Population stratification refers to differences in allele distribution across different ancestral population groups. Such differences in allele distribution can create spurious, rather than causal, associations between alleles and phenotypes of interest (Freedman et. al., 2004). Therefore, if the population structure within a sample is not accounted for, research findings can be false positives (Cardon & Palmer, 2003).

To assess and control for population stratification, this study conducted a principal coordinates analysis (PCoA). This method has been used previously to assess genetic differences in multiple populations due to geographical ancestry and admixture (Halder, Shriver, Thomas, Fernandez, & Frudakis, 2008). Allele-sharing distances are used to extract principal coordinates (PCs) that describe the dimensions of the sample. PCs are used in two ways: 1) To assess the extent to which population stratification contributes to variation in analysis variables, and 2) To determine whether the study’s results were robust against population stratification controls (i.e., not spurious). These approaches are outlined in the methods section.
METHODS

PROSPER Project. The data used to investigate the above specified research questions are drawn from the PROSPER Project. PROSPER (PROmoting School-community-university Partnerships to Enhance Resilience) is an evidence-based intervention program aimed at reducing future substance use by targeting middle school-aged youth and their families. The PROSPER Project consists of 28 communities in Iowa and Pennsylvania randomized into 14 control and 14 intervention units (for more information on intervention design see Spoth, Redmond, Shin, Greenberg, Clair, & Feinberg, 2007; Spoth, Redmond, Shin, Greenberg, Feinberg, & Schainker, 2013). PROSPER investigates the effectiveness of interventions on a variety of substance use outcomes, such as alcohol, tobacco, and marijuana use. In-school assessments included pre-test assessments during the fall semester of the 6th grade, post-test assessments during the spring semester of the 6th grade, and annual follow-ups assessments until the completion of high school.

In addition to the in-school assessments, participants were subsampled to participate in detailed in-home data collection. In-home assessments were provided to a subsample of PROSPER youth who were randomly selected and invited to take part in in-home interviews. Of the initial 2,267 youth who were invited, 977 (43.1%) agreed to participate in in-home data collection. In-home assessments were conducted twice in the 6th grade (once in the fall and once in the spring) and annually thereafter until the 9th grade (Waves 3, 4, and 5). The in-home assessments included written questionnaires completed independently by the participant and one (typically the mother) or both parents/guardians. The in-home subsample provided extensive, phenotypically rich data measurements of participants’ environments, and a unique opportunity
to examine gene by environment interplay. The in-home sample measured peer relationships in detail.

**Sample and participants.** The data analyzed in this study were from youth who provided DNA and had valid data for in-home and in-school variables. Predictor items were surveyed during the 7th grade in-home assessment at Wave 3 (Mean age=13.44), while outcome items were surveyed during the 12th grade in-school assessment at Wave 8 (Mean age=18.16). During the Wave 5 (9th grade) in-home data collection, DNA was collected from 594 (74.2%) of the 740 families who took part in the Wave 5 data collection. Of the 594, 340 (57.2%) provided in-school data during the 7th and 12th grade. The sample was predominantly self-identified Caucasians (92.6%), with a limited number of self-identified Hispanics/Latinos (4.4%), African Americans (0.6%), Asians (0.6%), and other (1.6%) individuals. Sources of missing data for each variable will be explained below.

**Measures**

**DRD4 Genotyping.** DNA was collected using buccal swabs and extracted using a modified phenol-chloroform technique (Freeman et al., 2003). The 3730XL DNA Analyzer and Genotyper software v4.0 (Applied Biosystems, Foster City, CA) were used to analyze amplification products of the extracted DNA. The 48-base pair VNTR in the third exon of the D4 gene (Anchordoquy, McGeary, Liu, Krauter, & Smolen, 2003; Sander et al., 1997) was genotyped by the Penn State Genomics Core using primer sequences developed by Lichter et al. (1993). Of the total sample, 98.5% were successfully genotyped for the *DRD4* polymorphism (n=584). An error rate of 7.5% was determined by re-genotyping 10% of the entire sample. The error rate is a by-product of the difficulty in genotyping *DRD4* heterozygous individuals. Errors occur when amplifying the 7-copy allele in the presence of the 4-copy allele. Hardy-Weinberg Equilibrium was tested [$\chi^2(1) = 0.03$, ns], and indicated genotyping was consistent with
population level statistics. *DRD4* status was coded as those who possessed the 7+ variant (1) (N = 120, 35.3%), and all other youth (0) (7-; N = 220 64.7%). Before analysis, I tested for differences in gender, intervention condition, and ethnicity by *DRD4* status (see Table 1).

**PC1 Controls for Population Stratification.** Principal Coordinates Analysis (PCoA) was conducted to assess and control for population stratification. Allelic distances were used to identify dimensions of population ancestry stratification (for details see Cleveland et al., in press). Single Nucleotide Polymorphisms (SNPs) were selected from the Affymetrix Exome Array using PLINK (v1.07, Purecell et al., 2007). To estimate genetic ancestry, SNPs with a minor allele frequency greater than 0.05 (~47,000 SNPs) were used to generate allele-sharing vectors between all pairs of participants. Of the total in-home sample of 594, Affymetrix data were available for 511 (93.5%) participants. Using the statistical package R, PCoA was performed on the allelic distance matrix to generate multiple PCs representing the major axes of genetic variation in the sample. The first PC (PC1) accounted for approximately 10% of total allele-sharing distance, while the second PC (PC2) accounted for approximately 6%. Biplots of the PCs were then merged with self-reported ancestry to visualize the axis of genetic variation represented by each PC.

PC1 provided an index of non-European ancestry that complimented information from self-reported ethnicity. The highest PC1 scores belonged to individuals who self-reported African-American ethnicity. Comparing PC1 means across self-reported non-Hispanic Whites (M = -0.008, SD=0.008, n=493) and those reporting a different ethnicity (i.e., Hispanic and African-American; M = 0.067, SD=0.035, n=53) revealed a significant difference between self-reported Whites and minorities (t(544)=39.79, p<0.001). The Cohen’s D for this difference was 3.0. PC2 distinguished African-Americans and Hispanics compared to self-report status. The
overlap of PC1’s and PC2’s distinguishing ability resulted in PC1 being selected as the primary linear indicator of European ancestry.

First, correlations were computed between PC1 and the predictor and outcome variables. As mentioned above, if population stratification significantly covaries with predictors and outcome variables, there is a possibility that the candidate-gene and phenotype associations are spurious and due to genetic ancestry. Second, after fitting the full model of all cases with valid candidate gene and phenotype data, models were re-run in two ways: 1) On the full sample using PC1 as the control, and 2) On a European descent only subsample constructed by removing PC1-identified non-Europeans.

The subsample of genetically identified Europeans was classified based on the criteria of being one standard deviation below the mean PC1 score of all self-reported non-Europeans (0.0664). This value, 0.031, classified 507 participants as having European ancestry, and 48 participants as having significant non-European ancestry. The PC1-informed classification strongly agreed with adolescent self-report. Using the PC1 criteria, 6 of 7 individuals who self-reported as African-American, 26 of 27 who self-reported as Hispanic, and 3 of 4 who self-reported as Asian matched their self-report classification as non-European. The PC1 derived cutoff classified two self-reported Caucasians as having significant non-European ancestry. PCoA also identified three sets of siblings; one sibling from each pair was randomly removed from the sample.

**Data Analysis.** The assumption of independence was violated because children were nested within school districts. To address the correlated structure of the data, the analyses applied multilevel (mixed model) analysis of covariance with the REPEATED statement in SAS PROCMIXED and restricted maximum likelihood estimation.
**Intervention Status.** Among the 340 participants in the analysis sample, 202 (59.4%) attended and participated in the school intervention, while the remaining 138 (40.6%) were in the control condition. Intervention status was dummy coded as either “control” (0) or “intervention” (1) (See Table 1). Once intervention status differences by genotype were tested, further analysis controlled for intervention status.

**Peer Deviance Pressure.** Early adolescent Peer Deviance Pressure was assessed with a seven-item self-reported measure during 7th grade (Wave 3) in-home interviews (Mean age=13.44). Items asked about the frequency of friends’ attempts to persuade the interviewed youth to engage in delinquent behavior. Example items included, “Do your friends try to…get you to skip school without an excuse” and “…do things at school that can get you into trouble.” Items were coded on a four-point scale from “Never” (1) to “Often” (4) and showed positive internal consistency. The scale was non-normally distributed with a skewness of 4.11. Thus, the scale was Winsorized so that all responses of 4 were recoded as 3 to correct for skewness, thereby affecting the range of responses (Cronbach’s α = 0.93, M = 1.15, SD = 0.30, range = 1 to 3).

**Positive Peer Activity.** Early adolescence Positive Peer Activity was assessed with a two-item self-reported measure during 7th grade (Wave 3) in-home interviews (Mean age=13.44). The items asked youth to think about the activities their friends participate in. Example items included “How often in the past month have you spent time with kids who take school seriously and complete their homework?”. Items were coded on a five-point scale from “Never” (1) to “Always” (5) (Cronbach’s α = 0.76, M = 3.71, SD = 1.02, range = 1 to 5).

**Alcohol Use Cumulative Index (AUCI).** Annual in-school assessments included items regarding personal alcohol use. A cumulative index of six items regarding alcohol use was
created from the 12th grade assessment (Wave 8; mean age=18.16). The index was sensitive to early and later adolescence alcohol use. Example items included, “Have you ever drunk more than just a few sips of alcohol?” and “During the past year, how many times have you been drunk from drinking wine, wine coolers, or other liquor?” All six items were dichotomized, with answers of “Yes” (1) or “No” (0). The index was created by summing the dichotomized responses from all six items, yielding a measure with values ranging from 0 to 6 (Cronbach’s $\alpha = 0.78$, $M = 2.59$, $SD = 0.33$, range = 0 to 6).

**Past Month Drunkenness.** In-school assessments included an item regarding 12th grade recent adolescent drunkenness (Wave 8; mean age=18.16). The item, “During the past month, how many times have you been drunk from drinking wine, wine coolers, or other liquor?”, was coded on a scale of “Not at all” (0) to “More than once a week” (4) ($M = 0.67$, $SD = 1.25$, range = 0 to 4).
RESULTS

Preliminary Analysis

Three sets of preliminary analyses were conducted. First, I analyzed the distribution of **DRD4** genotypes for Hardy-Weinberg Equilibrium. These analyses indicated that **DRD4** allele distribution was in equilibrium \( \chi^2(1) = 0.03, \text{ns} \). Second, I tested for sample differences in demographic variables (i.e., age, intervention status, ethnicity, and PC1 ethnicity control) across genotype. These analyses showed that the demographic variables did not differ based on **DRD4** 7+ vs. 7- status (see Table 1). Finally, I attempted to find associations between PC1 and the primary study variables. Analyses revealed that primary study variables were not related to European ancestry, and therefore population stratification was unlikely to be a confound.

Peer Deviance Pressure

A two-step analysis was run on both outcomes of interest: Model 1 estimated the main effects of Peer Deviance Pressure and **DRD4** status, and Model 2 added the two-way interactions between Peer Deviance Pressure and **DRD4**. Table 2 provides Peer Deviance Pressure results for both AUCI and Past Month Drunkenness outcomes. AUCI models are presented on the left of the table and Past Month Drunkenness models are presented on the right.

The first set of hypotheses tested were the effects of Peer Deviance Pressure on both alcohol use outcomes, AUCI and Past Month Drunkenness. Model 1 presents the main effect results for both outcomes; Peer Deviance Pressure significantly predicted both AUCI (b=0.55, p<.01) and Past Month Drunkenness (b=0.24, p<.01). These main effects indicated that higher levels of peer pressure predict increases in both overall and recent 12\textsuperscript{th} grade alcohol use. As hypothesized, the main effects of the **DRD4** 7+ genotype on AUCI (b=0.13, ns) and Past Month Drunkenness (b=0.06, ns) were not significant. Model 2 added the effects of the two-way interaction between Peer Deviance Pressure and **DRD4** on both alcohol use outcomes. These
two-way interactions between Peer Deviance Pressure and DRD4 were significant for both AUCI (b=1.01, p<.05) and Past Month Drunkenness (b=.41, p<.05), indicating that increases in both overall and recent 12th grade alcohol use were dependent on early adolescent peer pressure and DRD4 status.

To investigate the meaning of the two-way interactions between Peer Deviance Pressure and DRD4 on AUCI, probing techniques were used to analyze the conditional main effects (see Frazier, Tix, & Barron, 2004). DRD4 status was reverse coded (i.e., 1 = 7- vs. 0 = 7+) and Peer Deviance Pressure was re-centered (i.e., ±1SD). The associations between Peer Deviance Pressure and AUCI are shown separately for DRD4 7+ vs. 7- youth in Figure 1. Among 7- youth, there was no significant difference in AUCI based on the level of Peer Deviance Pressure. However, for youth who possess the 7+ variant, Peer Deviance Pressure was positively associated with AUCI, with levels of AUCI increasing from 0.91 to 2.35 to 3.78 across low, mean, and high levels of Peer Deviance Pressure. At low levels (-1SD) of Peer Deviance Pressure, there was a significant difference in AUCI between DRD4 7+ and 7- youth (0.92 vs 1.89). At high levels (+1SD) of Peer Deviance Pressure, this difference was near significance (p=0.051).

Using the same recoding methods, I examined the 2-way interaction between Peer Deviance Pressure and DRD4 on Past Month Drunkenness (see Figure 2). Among 7- youth, there was no significant difference in Past Month Drunkenness based on the level of Peer Deviance Pressure. Among 7+ youth, however, Peer Deviance Pressure was positively associated with Past Month Drunkenness, with levels of Past Month Drunkenness increasing from 0.21 to 0.81 to 1.40 across low, mean, and high levels of Peer Deviance Pressure. At high levels (+1SD) of Peer
Deviance Pressure, there was a significant difference in Past Month Drunkenness between DRD4 7+ and 7- youth (1.4 vs. 0.87).

**Positive Peer Activity**

The second set of models examined the association between early Positive Peer Activity and both alcohol use outcomes. Similar to Peer Deviance Pressure, a two-step analysis occurred for both outcomes of interest: Model 1 contained the main effects for Positive Peer Activity and DRD4 status, and Model 2 added the two-way interactions between Positive Peer Activity and DRD4. Table 3 presents the Positive Peer Activity model results for both AUCI and Past Month Drunkenness outcomes. AUCI models are presented on the left of the table and Past Month Drunkenness models are presented on the right.

The hypotheses tested in the second set of models were the effects of Positive Peer Activity on both alcohol use outcomes, AUCI and Past Month Drunkenness. Model 1 presents the main effects for both outcomes; Positive Peer Activity significantly predicted both AUCI (b=-0.22, p<.01) and Past Month Drunkenness (b=-0.15, p<.05). The negative direction of these main effects indicates that higher amounts of positive peer influence are associated with a decrease in overall and recent 12th grade alcohol use. As expected, the main effects for the DRD4 7+ genotype on AUCI (b=-0.22, ns) and Past Month Drunkenness (b=-0.02, ns) were not significant. Model 2 added the effects of the two-way interaction between Positive Peer Activity and DRD4 on both alcohol use outcomes. Contrary to my hypotheses, the two-way interactions were not significant for either AUCI (b=0.35, ns) or Past Month Drunkenness (b=0.16, ns). The non-significant interactions indicated that the effect of Positive Peer Activities on overall and recent alcohol use did not differ by DRD4 genotype.
DISCUSSION

This study was the first to focus on whether inter-individual genetic differences affect adolescent susceptibility to negative and positive peer relationships. I examined whether \textit{DRD4} moderated the association between 7\textsuperscript{th} grade negative and positive peer relationships, Peer Deviance Pressure and Positive Peer Activity, and two 12\textsuperscript{th} grade alcohol use outcomes, AUCI and Past Month Drunkenness.

As hypothesized, analyses revealed main effects of Peer Deviance Pressure that resulted in an increase in alcohol use, specifically increases in 12\textsuperscript{th} grade AUCI and Past Month Drunkenness. Also as hypothesized, analyses revealed no main effects for \textit{DRD4} on either alcohol use outcome; the lack of genetic main effects is congruent with DST. DST postulates that rather than genetic variation directly causing differences in outcomes, genetic variation only contributes to individuals’ overall sensitivity to environmental experiences. Genetic sensitivity to environmental experiences is theorized to lead to differential negative or positive outcomes depending on the experiences encountered (Belsky, Bakermans-Kranenburg, & van IJzendoorn, 2007; Belsky & Pluess, 2009, 2013; Bakermanss–Kranenberg & van IJzendoorn, 2011).

The specific results of this study include finding a significant difference in AUCI between \textit{DRD4} 7- and \textit{DRD4} 7+ adolescents at low levels of Peer Deviance Pressure. For Past Month Drunkenness, there was a significant difference between \textit{DRD4} 7- and \textit{DRD4} 7+ adolescents at high levels of Peer Deviance Pressure. While the effects of Peer Deviance Pressure on AUCI and Past Month Drunkenness are similar, the effects vary by the level of Peer Deviance Pressure. This difference is possibly due to the fact that AUCI measured multiple drinking behaviors indexed over time, while Past Month Drunkenness only measures recent alcohol use.
Previous literature supports the finding that the *DRD4* gene moderates the effect of peer deviance on alcohol use. Research has found that the dopamine system mediates social rewards and the reinforcement of alcohol use (Krach, Paulus, Bodden, & Kircher, 2010). Specifically, *DRD4* research has found that 7+ individuals have increased sensitivity to dopamine responses triggered by priming doses of alcohol (Hutchinson, McGeary, Smolen, Bryan, & Swift, 2002). Experimental research has found that 7+ individuals do not have increased euphoric effects of alcohol consumption, but rather have an increased perceived ability to bond with peers while consuming alcohol (Larsen et al., 2010). Related research has found that the *DRD4* 7+ variant increases the sense of reward from alcohol consumption when in a group context (Creswell et al., 2012).

As hypothesized, analyses revealed main effects of Positive Peer Activity that resulted in reduced levels of both AUCI and Past Month Drunkenness. Consistent with my hypotheses, analyses again revealed a lack of main effects of *DRD4* on both alcohol use outcomes. However, associations between Positive Peer Activity and both AUCI and Past Month Drunkenness did not differ between youth who carried at least one copy of the *DRD4* 7-repeat allele (7+) and those who were homozygous for the *DRD4* short allele (7-).

A number of reasons may explain why the *DRD4* gene did not moderate the effect of Positive Peer Activity on alcohol use. First, during early adolescence, prosocial peer relationships are considered a normative environmental context (Hartup, 1993). Prosocial peer relationships have been found to be stable over time, with the percentage of reciprocal friendships that last a year or more being roughly 70% (Berndt, Hawkins, & Hoyle, 1986). Second, positive and negative peer relationships are not mutually exclusive, meaning youth may experience both positive and negative peer socialization from the same, or different, group of
friends. The social contexts created by peers have been shown to stem from situational activities and characteristics (Power, Stewart, Hughes, & Arbona, 2005). Finally, my measure of positive peer relationships did not operationalize positive behaviors meaningfully equivalent to my measure of negative peer relationships.

To reiterate, DST postulates that individuals vary in their susceptibility to environmental contexts (i.e., peers) both “for better” and “for worse” (Belsky, Bakermans-Kranenburg, & van IJzendoorn, 2007). Evidence supporting DST has shown that environmental factors have the ability to influence individuals differently (Belsky, 1997). While DST was the framework that guided these research questions, diathesis–stress is a corresponding theory. In contrast to DST, diathesis–stress hypothesizes that environmental stressors (i.e., peer deviance pressure) have an increased impact on the development of sensitive individuals when “triggered” by poor experiences (Zuckerman, 1999). The diathesis–stress theory states that in the absence of an environmental trigger there should be no differences between vulnerable and resilient individuals. In the context of this study, Peer Deviance Pressure may be the trigger for youth with the DRD4 7+ variant that results in increased alcohol use.

The results of this study should be interpreted in the context of its limitations. First, the PROSPER sample relied on a school-based sample, which risks excluding the population that may be at the greatest risk for alcohol use (i.e., dropouts; Berk, 1983). Within the context of G x E research, it is particularly important to study a sample with individuals who experience the full range of environmental contexts in order to avoid the danger of false positives and negatives (Moffitt, Caspi, & Rutter, 2005). Second, this sample was predominantly of European descent and located within rural and semi-rural towns. The sample’s demographics limit the generalizability of the findings to similar populations. Finally, peer relationship measures were
based on youth self-reports, which are subject to social desirability bias. Using network data or parent-reports on peer relationships in the future may increase the quality of peer relationship measures.

This study was limited to focusing on the effect of peer social influence. Future directions include further elucidating the mechanism behind how peer relationships are genetically influenced. By using network data, such as PROSPER Peers, future studies can utilize youth nominations of friends to determine what aspects of the social networks are moderated by genetic difference.

In conclusion, this study found that adolescents’ alcohol use in 12th grade increased as negative peer relationships increased, and this finding was moderated by DRD4 genotype. Adolescents with the DRD4 7+ allele were more affected by negative peer relationships than DRD4 7- adolescents. Adolescents’ alcohol use in 12th grade decreased as positive peer relationships increased, and this relationship was not moderated by DRD4 genotype. Future research should examine how genetic influences may moderate different aspects of negative peer relationships.
### APPENDIX: TABLES AND FIGURES

Table 1. Demographic comparisons by DRD4 genotype and for analytic sample

<table>
<thead>
<tr>
<th>Variable</th>
<th>Categories/Unit</th>
<th>DRD4 7-</th>
<th>DRD4 7+</th>
<th>Total (n=340)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td>%(n)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td>66.1 (121)</td>
<td>33.9 (62)</td>
<td>53.8 (183)</td>
</tr>
<tr>
<td>Condition</td>
<td></td>
<td>66.8 (135)</td>
<td>33.2 (67)</td>
<td>54.9 (202)</td>
</tr>
<tr>
<td>European</td>
<td></td>
<td>66.9 (194)</td>
<td>33.1 (96)</td>
<td>85.2 (290)</td>
</tr>
<tr>
<td>Race</td>
<td>White</td>
<td>65.1 (205)</td>
<td>34.9 (110)</td>
<td>91.6 (315)</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
<td>40 (6)</td>
<td>60 (9)</td>
<td>4.4 (15)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>50 (1)</td>
<td>50 (1)</td>
<td>0.6 (2)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>100 (2)</td>
<td>0 (0)</td>
<td>0.6 (2)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>100 (6)</td>
<td>0 (0)</td>
<td>1.8 (6)</td>
<td></td>
</tr>
</tbody>
</table>

Note: % European is based on PC1, Race is based on participant self-report. PC1 is reported here in standard deviation units.
Table 2. Parameter estimates and standard errors for peer deviance pressure models.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Parameter Estimate (Standard Errors)</th>
<th>AUCI</th>
<th>Past Month Drunkenness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Model 1</td>
<td>Model 2</td>
<td>Model 1</td>
</tr>
<tr>
<td><strong>Main Effects</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PDP</td>
<td>.55(.13)*</td>
<td>.42(.14)**</td>
<td>.24(.06)*</td>
</tr>
<tr>
<td>DRD4 7R</td>
<td>-.12(.27)</td>
<td>.03(.28)</td>
<td>.06(.13)</td>
</tr>
<tr>
<td><strong>Two-Way Interaction</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PDP*D4</td>
<td>1 .01(.39)**</td>
<td></td>
<td>.41(.19)*</td>
</tr>
</tbody>
</table>

Note: PDP = Peer Deviance Pressure, D4 = DRD4 7R, AUCI= Alcohol Use Cumulative Index. *p < .05, *p < .01.
Table 3. Parameter estimates and standard errors for positive peer activity models

<table>
<thead>
<tr>
<th>Variables</th>
<th>Parameter Estimate (Standard Errors)</th>
<th>AUCI</th>
<th>Past Month Drunkenness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Model 1</td>
<td>Model 2</td>
<td>Model 1</td>
</tr>
<tr>
<td><strong>Main Effects</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPA</td>
<td>- .22(.13)** - .37(.17)* - .15(.06)* - .22(.08)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DRD4 7R</td>
<td>- .22(.27) - .30(.27) - .02(.13) .00(.13)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Two-Way Interaction</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPA*D4</td>
<td></td>
<td>.35(.27)</td>
<td></td>
</tr>
</tbody>
</table>

Note: PPA = Positive Peer Activity, D4 = DRD4 7R, ACUI = Alcohol Use Cumulative Index. *p < .05, **p < .01.
Figure 1. Differential Effects of Peer Deviance Pressure on Alcohol Use Cumulative Index by DRD4 Genotype.
Figure 2. Differential Effects of Peer Deviance Pressure on Past Drunkenness by $\text{DRD}4$ Genotype.
REFERENCES


polymorphism (DRD4 VNTR) moderates intervention effects on toddlers’ externalizing behavior in a randomized control trial. *Developmental Psychology, 44*, 293–300.


