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Parent and Youth Dopamine D4 Receptor Genotypes Moderate Multilevel Contextual Effects on Rural African American Youth's Risk Behavior

Junhan Cho and Steven M. Kogan

Department of Human Development and Family Science and the Center for Family Research, University of Georgia

Abstract

The present investigation extends research on gene by environment ($G \times E$) interactions and youth risk behavior by linking multilevel contextual factors, such as community disadvantage and protective parenting practices, to both parental and youth dopamine D4 receptor (*DRD4*) genotypes. We expected community disadvantage to influence youth risk behavior via a series of indirect effects involving protective parenting and youth's planful future orientation when both parents' and youth's *DRD4* status was considered. Genetic moderation processes also were tested to determine whether they conformed to a diathesis-stress or a differential susceptibility model. Hypotheses were investigated with data from 361 rural African American youth and their parents assessed 3 times when youth were ages 16 to 19. Community disadvantage interacted with parental *DRD4* status to predict low levels of protective parenting. Protective parenting, in turn, interacted with youth *DRD4* status to forecast increases in youth's planful future orientations, a proximal influence on changes in risk behavior. The parental *DRD4* $\times$ community disadvantage interaction, but not youth *DRD4* $\times$ protective parenting, conformed to a differential susceptibility model. Indirect effect analyses revealed a significant indirect path linking community disadvantage to youth risk behavior through a series of multilevel $G \times E$ interaction processes.

Keywords

gene by environment interaction; community disadvantage; protective parenting; future orientation; risk behavior

Adolescents engage in numerous risk behaviors that compromise their health and well-being, including substance use, risky sexual activity, and delinquency. These risk behaviors frequently co-occur (Hair, Park, Ling, & Moore, 2009; Wu, Witkiewitz, McMahon, & Dodge, 2010) and engagement in multiple forms of risk behavior has been found to have an additive influence on poor health and suboptimal development in young adulthood (Hair et al., 2009; Mason et al., 2010). The present study focuses on risk behaviors reported by African American youth living in resource poor communities in the rural South. Historically, rural residence protected youth from engagement in many risk behaviors. Recent data

indicate, however, that rural youth engage in risk behavior at rates that equal or exceed those of urban youth (Kogan, Berkel, Chen, Brody, & Murry, 2006; Milhausen et al. 2003). For African Americans, studies reveal that involvement in risk behaviors during adolescence disproportionately affects their education, employment, involvement with the criminal justice system, mental health, and physical health (Brook et al., 2004; Chatterji, 2006; Massoglia, 2008).

In the ecological-systems perspective, adolescents are viewed as developing within a set of embedded social contexts (Bronfenbrenner, 1986). For example, adolescents develop within families, and families select into and are influenced by community contexts. The bioecological model further emphasizes that individual-level biological factors can interact with a broad array of multiple-level contexts to affect human development (Bronfenbrenner & Ceci, 1994). Despite calls for inclusion of the intricate interplay among multiple levels of social contexts and personal biological characteristics, including genotype (Ellis, Boyce, Belsky, Bakermans-Kranenburg, & van IJzendoorn, 2011), little research has considered this complexity.

The present study investigates genetic moderation processes in the development of rural African American youth's risk behavior. It responds to the need for increasing sophistication in the characterization of gene and environment interaction ($G \times E$) processes by investigating pathways linking multiple contextual levels and multiple family members' genotypes (Mills-Koonce et al., 2007; Rutter, Moffitt, & Caspi, 2006). Consistent with bioecological theory focusing on the interaction of individuals and their proximal contexts (Bronfenbrenner & Morris, 2006), we hypothesized that, among rural African American families, disadvantaged community environments would interact with parental genotype to predict parenting behavior. Parenting behavior was hypothesized to interact with youth genotype to affect youth's outlook on the future, which in turn would predict risk behavior. We further hypothesized that community disadvantage would influence youth risk behavior indirectly via this series of $G \times E$ interactions.

Environmental Influences on Rural African American Youth's Risk behavior

Risk behaviors such as substance use, sexual risk, and delinquency pose significant concurrent and downstream threats to adolescents' psychosocial and physical well-being (D'Amico, Ellickson, Collins, Martino, & Klein, 2005; Hair et al., 2009; Oesterle et al., 2004). These risk behaviors frequently co-occur, particularly in early adolescence (Biglan, Brennan, Foster, & Holder, 2004; Krueger, Markon, Patrick, Benning, & Kramer, 2007); however, substance use, sexual risk, and delinquency remain strongly associated throughout the high school years (Hair et al., 2009; Mustanski et al., 2013; Wu et al., 2010). Moreover, recent research indicates that engagement in multiple forms of risk behavior may have a particularly deleterious effect, forecasting increases in physical and mental health problems as well as poor academic and employment outcomes in young adulthood (Hair et al., 2009).

A substantial body of research documents the influence of community environments on youth's involvement in substance use (Brooks, Magnusson, Spencer, & Morgan, 2012;

Lambert, Brown, Philips, & Ialongo, 2004), risky sex (Browning, Burrington, Leventhal, & Brooks-Gunn, 2008), and delinquency (Leventhal & Brooks-Gunn, 2000; Sampson, Morenoff, & Gannon-Rowley, 2002). African American families disproportionately reside in disadvantaged communities, characterized by racial segregation, an important driver of multiple institutional disadvantages (Williams & Collins, 2001). This is true in the rural South, where many African American communities are characterized by elevated proportions of single-parent households, receipt of public assistance, and low household income (Boatright, 2009; Sampson, 2012; Williams & Collins, 2001; Wilson, 2012). Community disadvantage potentially affects youth risk behavior via a range of pathways including peer group influence, risk behavior opportunities, educational quality, and access to structured, after-school leisure activities (Chuang, Ennett, Bauman, & Foshee, 2005; Wallace & Muroff, 2002).

Studies of rural African American families suggest that a key pathway linking community disadvantage to youth risk behavior involves community effects on parenting practices (Brody et al., 2006; Kogan et al., 2011, 2013). For many African American parents, the daily stress associated with living in a disadvantaged community undermines their ability to engage in a set of risk-reducing *protective parenting practices* that include high levels of parental monitoring, involvement with youth's academic activities, consistent discipline, and high levels of nurturance (Brody et al., 2001; Kogan et al., 2013; Mrug & Windle, 2009). This constellation of parenting practices has been linked to African American youth's avoidance of substance use (Brody et al., 2009, 2014), sexual risk (Kogan et al., 2011), and conduct problems (Brody, Kogan, Chen, & Murry, 2008). Conversely, youth who experience low levels of protective parenting are at elevated risk for engagement in multiple risk behaviors (Brody, Chen, & Kogan, 2010).

Direct effects of protective parenting on risk behavior are evident particularly in early- and mid-adolescence (East, Khoo, & Reyes, 2006; Farmer et al., 2004). As youth exhibit greater autonomy in late adolescence, however, attitudes and self-regulatory competencies internalized through interactions with parents become increasingly important (Brook & Brook, 1996; Brook, Brook, Gordon, Whiteman, & Cohen, 1990; Kogan et al., 2011). A *planful future orientation* is one such intrapersonal mechanism hypothesized to link protective parenting practices to risk behavior among rural African American youth during the high school years. A planful future orientation combines positive expectations about the future with an orientation toward setting goals and persisting in their accomplishment (Aronowitz, 2005; Brody et al., 2004; Kogan, Brody, & Chen, 2011; Wills, Sandy, & Yaeger, 2001). A planful future orientation locates adolescents' primary set of psychological influences beyond their current circumstances, which renders them more attentive to the lasting consequences of their behaviors, enhancing their goal setting and persistence (Routledge & Arndt, 2005). In contrast, youth who lack a planful future orientation are influenced more by immediate situational factors and are less likely to inhibit emotional responses to negative environments. Investigations of planful future orientations among African American youth in rural and urban contexts reveal negative associations with substance use (Li et al., 2001; Wills et al., 2001), sexual risk behaviors (Bolland, 2003; Kogan et al., 2010; Li et al., 2001), and delinquency (Bolland et al., 2007; Caldwell, Wieber, & Cleveland, 2006; Kerpelman, Eryigit, & Stephens, 2008).

Disadvantaged communities have been hypothesized to affect rural African American youth's risk behavior by undermining protective parenting, which in turn influences youth's development of a planful future orientation (Kogan et al., 2013). Prior research suggests that harsh environmental conditions lead youth to perceive their futures as unpredictable, undermining their development of a planful future orientation. This is a proximal risk factor for risk behavior (see Ellis, Figueredo, Brumbach, & Sclover, 2009; Hill, Ross, & Low, 1997). Studies indicate that adolescents hold more optimistic views about their futures when they receive parental support (Dubow, Arnett, Smith, & Ippolito, 2001; Kenny, Blustein, Chaves, Grossman, & Gallagher, 2003; McCabe & Barnett, 2000), and that close relationships with parents are positively related to youth future orientation (Nurmi & Pulliainen, 1991; Seginer, Vermulst, & Shoyer, 2004). A planful future orientation may be particularly important for African American youth living in disadvantaged rural environments because they are exposed to few educational and vocational opportunities within their communities (Gore & Aseltine, 2003; Sum et al., 2002).

Dopamine Receptor 4 Polymorphism and Susceptibility to Environmental Factors

Recent studies indicate that both parents and youth vary considerably in the extent to which proximal environmental factors such as community disadvantage and protective parenting practices affect their behavior (Belsky & Pluess, 2009). A number of candidate genes that affect neurotransmitter activity are thought to modulate the influence of environmental input on individual behavior. Interactions between specific polymorphisms and family environments have been detected for youth substance use (Brody et al., 2009; Brody et al., 2014), sexual risk behavior (Guo, Tong, & Cai, 2008), and delinquent behavior (Caspi et al., 2002; Simons et al., 2011; Simons et al., 2012). A more modest literature suggests that genetic status may interact with aspects of parents' proximal environments to affect their parenting behavior (Beach et al., 2012; van IJzendoorn, Bakermans-Kranenburg, & Mesman, 2008).

The majority of $G \times E$ studies investigating youth risk behavior conceptualize the interaction effect from a *diathesis-stress* perspective. This perspective focuses on the extent to which particular alleles confer vulnerability to adverse social conditions. In contrast, Belsky and Pluess (2009) suggested that some alleles may act to amplify both positive and negative environmental input. From this *differential susceptibility* perspective, persons who are more vulnerable to adverse social environments also benefit more from positive environments (Belsky, Bakermans-Kranenburg, & van IJzendoorn, 2007; Belsky & Pluess, 2009; Ellis et al., 2011).

The dopamine receptor 4 polymorphism, *DRD4*, is associated with neurocognitive systems that regulate risk and reward (Spear, 2011). Evidence is accumulating that supports the possibility that the *DRD4* gene confers differential susceptibility to the environment (Bakermans-Kranenburg & van IJzendoorn, 2007, 2011). *DRD4* is a variable nucleotide tandem repeat (VNTR) polymorphism composed of 16 amino acid (48-bp) repeat polymorphisms that range from 2 to 11 repeats. The 2, 3, 4, and 7 repeat versions account

for about 98% of allelic variability (Lichter et al., 1993). Studies characterize *DRD4* alleles as either “short” (*s*) or “long” (*l*), with the *s* category defined as having 6 or fewer repeats and the *l* category as having 7 or more repeats (Beach et al., 2012; Brody et al., 2012; Eisenberg et al., 2007; Laucht, Becker, Blomeyer, & Schmidt, 2007; McGeary, 2009). *DRD4-l* alleles appear to function in a way that yields a protein structure that produces less reactive D4 receptors in both *in vitro* and *in vivo* tests of responsiveness, resulting in weaker transmission of intracellular signals for those with at least one *l* allele versus two *s* alleles (Levitan et al., 2006; Asghari et al., 1995).

Dopamine regulation is a promising focus for understanding youth risk behavior. Dopamine is released in response to rewarding stimuli, including sexual activity and stimulant drugs. Reward signals initiate a phasic burst of mid-brain dopamine neurons, which induce positive emotional states and organize the learning of cues that predict future rewards (Spear, 2000a). The dopaminergic system is thus engaged in attentional, motivational, and reward mechanisms (Robbins & Everitt, 1999). Reduced dopaminergic signaling impedes learning based on negative feedback (Klein et al., 2007), which in turn may lead to a relative insensitivity to environmental cues and rewarding stimuli (Spear, 2000b). This results in a strong preference for immediate reinforcement from the environment and elevated reactivity to high-intensity environmental cues (Tripp & Wickens, 2008).

Multiple studies support the hypothesis that *DRD4-l* alleles confer differential sensitivity to environmental input. For example, Beach et al. (2010) found that African American youth carrying *DRD4-l* were more responsive to the effects of protective parenting practices, which included child management skills and nurturant-involved parenting practices, on diminished substance use than were those with the *s* allele. Additional evidence is summarized in a recent review and meta-analysis by Bakermans-Kranenburg and van IJzendoorn (2011). In the present study, we hypothesized that $G \times E$ effects involving *DRD4* status would demonstrate a pattern conforming to differential susceptibility effects.

Indirect Effects of Community Disadvantage on Risk Behavior via Multilevel $G \times E$ Interactions

To date, most $G \times E$ research on youth development and risk behavior has focused on the ways in which proximal family environments interact with youth genotype. Far fewer studies, however, have considered the interaction of parental genotype with the environment in affecting the kind of parenting to which youth are exposed in the family system (for exceptions see Beach et al., 2012; Mills-Koonce et al., 2007; van IJzendoorn et al., 2008). In the present investigation, we extended the research base on $G \times E$ interactions by linking multilevel contextual factors, such as community disadvantage and protective parenting practices, to both parental and youth genotype. Our hypotheses are summarized in Figure 1.

We expected community disadvantage to influence youth risk behavior via a series of indirect effects involving protective parenting and youth’s planful future orientations when both parents’ and youth’s *DRD4* status were considered. We predicted that community disadvantage would interact with parental *DRD4* status to forecast their engagement in protective parenting practices. Protective parenting, in turn, was hypothesized to interact

with youth *DRD4* status to predict changes in youth's planful future orientations, which would affect changes in risk behavior. In each case, we also determined whether specific $G \times E$ interactions would be best characterized as differential susceptibility or diathesis-stress models.

Methods

Participants

Study hypotheses were tested with 361 African American youth (159 male and 202 female) and their primary caregivers who resided in six counties in Georgia selected on the basis of their rurality (> 50% of census tracts designated rural) and the proportion of the population that was African American (> 20%). The communities are representative of the Southern "Black Belt" (Wimberly & Morris, 1997), a geographic concentration of rural poverty characterized by the nation's worst economic and child health disparities by race (Hartley, 2004). Families were recruited randomly from lists that public schools provided. Data were collected within the context of a family-based prevention study at intervals timed to evaluate the prevention program. Because the present study hypotheses were not focused on intervention efficacy, random assignment to the intervention program or to an attention control program was controlled. Three waves of data spanning 3 years were obtained in 2006, 2008, and 2009. Youth's mean ages were 16 years at Time 1 (T1; $SD = .56$), 17.5 years at Time 2 (T2; $SD = .54$), and 18.6 years at Time 3 (T3; $SD = .56$).

The families' demographic characteristics were representative of the areas in which they lived (Boatright, 2009). Of the primary caregivers, 88.5% were the youth's biological mothers, 33.8% of whom were married at baseline. The remaining caregivers were grandparents (7%), aunts/uncles (2%), siblings (0.6%), and other adults (1.9%). The caregivers' mean age was 43 years ($SD = 8.29$) at T1, and their educational backgrounds ranged from less than a high school diploma (25%) to a bachelor's or graduate degree (6%); the modal education level (69%) was a high school diploma or GED. Mean family income was \$1,761 per month.

Procedures

Families were contacted and enrolled in the study by African American community liaisons who resided in the counties where the participants lived. The community liaisons were selected on the basis of their social contacts and standing in the community; they worked with the researchers on participant recruitment and retention. At all data collection points, parents gave written consent to minor youth's participation, and youth gave written assent or consent to their own participation. During each assessment, one home visit lasting 2 hours was made to each family. At the visits, self-report questionnaires were administered to the primary caregiver and target youth via audio computer-assisted self-interviewing (ACASI) technology on laptop computers. Caregivers were paid \$100 and youth were paid \$50 at each assessment.

Measures

Community disadvantage—Community disadvantage was assessed using the 2006 census tract data from the American Community Survey. Participants' residential addresses at T1 were geocoded and matched to census tracts. Census tracts generally include 1,500 to 8,000 residents and are designed to be as homogenous as possible regarding population characteristics, living conditions, and economic status (U.S. Bureau of the Census, 2000). Tract boundaries reflect significant physical (e.g., roads, rivers, and railroads) and demographic (e.g., ethnic composition) features of neighborhoods, which are delineated with the advice of local community members. A total of 36 census tracts were identified in this study; the number of participants residing in a tract ranged from 1 to 41. Median household income in these census tracts ranged from \$13,018 to \$60,417; median income across the 36 tracts was \$29,918. Consistent with prior research (Leventhal & Brooks-Gunn, 2000; Sampson, Raudenbush, & Earls, 1997; Simons et al., 2005), we developed a community disadvantage index using four indicators: percentage of female-headed households, percentage of households receiving Temporary Assistance for Needy Families (TANF), per capita annual income, and the proportion of African American families residing in the community. On the basis of studies of both physical morbidity and psychological dysfunction that support the basic concept of cumulative SES risk (see Brody et al., 2013, 2014), an index of cumulative community disadvantage was developed. Risk factor thresholds were set at the first quartile for percentages of female-headed households, receipt of TANF, and African American families, and at the fourth quartile for per capita annual income. Each indicator was coded dichotomously (0 if absent, 1 if present). Scores were summed to indicate the extent of community disadvantage, yielding an index that ranged from 0 to 4 ($M = 1.27$, $SD = 1.38$).

Protective parenting—At T1, parents completed a 14-item scale about three aspects of protective parenting practices that have been linked with adolescent adjustment and risk behavior in previous research (Brody et al., 2014; Cleveland et al., 2005). The measure included items about parental monitoring (4 items; e.g., “How often do you know when your teen gets in trouble at school or someplace else away from home?” and “How often do you know who your teen is with when he/she is away from home?”), nurturant parenting (5 items; e.g., “How often does your teen talk to you about things that bother him/her?” and “How often do you ask your teen what he/she thinks before making decisions that affect him/her?”), and parental academic involvement (5 items; e.g., “How often do you talk about the importance of finishing high school?” and “How often do you discuss going to college with your teen?”). The response set for parental monitoring and nurturant parenting ranged from 1 (*never*) to 4 (*always*); the items for parental academic involvement were rated on a scale ranging from 1 (*never*) to 6 (*4 or more times per week*). The items were standardized and summed to form the protective parenting scale ($M = .00$, $SD = 2.18$, $\alpha = .78$).

Planful future orientation—At T1 and T2, youth reported their planful future orientation using the perceived life chances scale and the state hope scale. The perceived life chances scale (Jessor, Donovan, & Costa, 1996) includes 10 items that measure one's estimation of achieving certain adaptive life goals, on a 5-point scale from 1 (*very low*) to 5 (*really high*). Items assessed perceived chances of outcomes such as going to college, having

a job that I enjoy doing, having a job that pays well, and having a happy family life. Cronbach's alpha was .93. The State Hope Scale (Snyder et al., 1996) included 6 items that addressed youth's beliefs in their capacity to initiate actions and to generate routes for reaching goals. Example items include, "At this time, I am meeting the goals that I have set for myself" and "I can think of many ways to reach my current goals." The response set ranged from 1 (*really false*) to 5 (*really true*); Cronbach's alpha was .87. The measures were standardized and summed to form the planful future orientation construct ($\alpha = .78$). The mean scores for the planful future orientation variable were .00 ($SD = 1.73$) for T1 and .00 ($SD = 1.74$) for T2.

Risk behavior—We assessed youth's risk behavior at T1 and T3 using self-reports of substance use, delinquent behavior, and sexual risk. A three item scale was used to assess substance use per prior research with African American youth (Brody, Kogan, & Chen, 2012; Brody et al., 2014). Youth indicated the number of times during the past 3 months they had used alcoholic beverages (beer, wine, wine cooler, or other liquor), drunk a lot of alcohol at one time, and used marijuana. The response set ranged from 0 (*none*) to 6 (*more than 30 times*); Cronbach's alpha was .69. Delinquent behavior was measured using 8 questions from the National Youth Survey (Elliott, Huizinga, & Ageton, 1985). The scale indicated how many times during the past 6 months youth committed acts such as theft, truancy, fighting, and vandalism, and how many times they were suspended from school; Cronbach's alpha was .69. Youth's sexual risk behavior was assessed using 3 items for which youth provided specific numbers: "In the past 3 months, how many people have you had sex with?", "In the past 3 months, how many times have you had sex?", and "In the past 3 months, out of the times you have had sex, how many times did you have sex while high on alcohol or drugs?" Items were standardized and then summed to produce the sexual risk behavior index. Cronbach's alpha was .78. Confirmatory factor analysis of the three indicators of risk behavior indicated a single factor with loadings that ranged from .62 for delinquent behavior to .78 for substance use at T1 and T3. We subsequently used the factor score to form a global assessment of youth's risk behavior.

Genotyping—Participants' DNA was obtained using Oragene™ DNA kits (DNA Genotek, Kanata, Ontario). Parents and youth rinsed their mouths with tap water and then deposited 4 ml of saliva in the Oragene sample vial. The vial was sealed, inverted, and shipped via courier to a central laboratory in Iowa City, Iowa, where samples were prepared according to the manufacturer's specifications. The genotype at *DRD4* was determined for each participant using the primers F-GGCGTTGCCGCTCTGAATGC and R-GAGGGACTGAGCTGGACAACCAC, standard Taq polymerase and buffer, and standard deoxynucleotide triphosphates with the addition of 100 mM 7-deaza GTP and 10% DMSO (Bradley, Dodelzon, Sandhu, & Philibert, 2005). The resulting polymerase chain reaction products were electrophoresed on a 6% nondenaturing polyacrylamide gel, and the products were visualized using silver staining. The genotype was then called by two individuals blind to the study hypotheses and other information about the participants. For tests of the $G \times E$ hypotheses, *DRD4* status was dummy coded; participants with at least one *l* allele were assigned a code of 1 (43.8% of parents; 47.4% of target youths), and participants who were homozygous for the *s* allele were assigned a code of 0 (56.2% of parents; 52.6% of target

youths). Using the Hardy-Weinberg equilibrium test, the observed distribution of *DRD4* did not differ significantly from that predicted on the basis of simple Mendelian inheritance.

Control variables—Three variables were controlled that might have influenced the relations among study variables. Consistent with our past research (Brody et al., 2014; Kogan et al., 2012), an index of family SES was developed using five dichotomous variables: family poverty based on federal guidelines, caregiver unemployment, receipt of TANF, female-headed households, and caregiver education level less than high school graduation. Each indicator was coded dichotomously (0 if absent, 1 if present), and the scores were summed to form an index that ranged from 0 to 5 ($M = 1.83$, $SD = 1.22$). Youth gender (0 = female; 1 = male) was controlled. Finally, in all analyses we controlled for intervention program assignment in the randomized prevention trial. Families were assigned to one of two family-centered, five-session programs. A dichotomous variable was specified (1 = *treatment*, 0 = *attention control*).

Analysis plan

The hypotheses for the present study were tested using structural equation modeling (SEM) with complex designs as implemented in Mplus (Muthén & Muthén, 1998–2010). Because respondents were clustered within census tracts, the error terms of regression models were not independent, leading to an underestimation of standard errors. To avoid this problem, we used the complex analysis to adjust parameter standard errors for interdependence in the data. Interaction terms were used to test the $G \times E$ pathways. To produce a common scale, standardized regression weights were used in which all study variables were standardized (a mean of 0 and a standard deviation of 1) before the interaction terms were calculated. Benefits of standardized weights in the interaction model include making coefficients easier to interpret, reducing multicollinearity, and making the simple slope easier to test (Dawson & Richter, 2006). We conducted post hoc analyses of significant interaction terms using the Johnson-Neyman (J-N) technique (Hayes & Matthes, 2009). This procedure identifies regions of significance for interactions between continuous (i.e., community disadvantage and protective parenting) and categorical (i.e., genotypes) variables. We tested the conditional indirect effects of community disadvantage on youth's risk behavior when both parent and youth have *DRD4-I* using Monte Carlo integration methods (Hayes, 2013; Preacher, Rucker, & Hayes, 2007). This approach can estimate the power of a test for each individual parameter of the model and account for specific data characteristics when a sampling design includes multiple levels (Thoemmes, MacKinnon, & Reiser, 2010).

To assess goodness-of-fit, we used Root Mean Square Error of Approximation (RMSEA; Browne & Cudeck, 1992), comparative fit index (CFI; Bentler, 1990), and chi-square divided by its degrees of freedom (fit ratio). CFI was truncated to range from 0 to 1; values close to 1 indicated a very good fit (Bentler, 1990). An RMSEA smaller than .05 indicates a close fit; an RMSEA between .05 and .08 suggests a reasonable fit (Browne & Cudeck, 1992).

Results

Preliminary analyses

Attrition analyses were conducted to evaluate predictors of non-participation based on project attrition and refusal to provide DNA. The original sample at T1 comprised 502 youth and their parents. At T3, the 464 youth and their parents remaining in the study were asked to provide DNA. Study hypotheses were tested with the 361 youth and their parents who agreed to provide DNA. We investigated differences on all study variables at T1 between retained participants and those who left the study by T3, and between participants at T3 who agreed or refused to provide DNA. No differences were detected. We next checked for evidence of gene-environment correlations, rGE, a non-random distribution of environments among people with different genotypes. Importantly, rGE likely confounds $G \times E$ effects (Caspi & Moffitt, 2006). Table 1 presents zero-order correlations for the study variables; no associations of parent or youth genotype with the study variables were significant, ruling out potential rGE effects. Finally, we assessed racial admixture using the Structure program version 2.3.4 (Falush, Stephens, & Pritchard, 2007) with a panel of 24 ancestrally informative markers to infer the number of ancestral populations and to estimate an ancestry proportion for each participant. The average proportion of African ancestry among 24 ancestral populations in this sample was 50.2%. Including the racial admixture variable as a covariate did not change any results; we thus report our findings without ancestry controlled.

Multilevel $G \times E$ interaction processes predicting changes in risk behavior

Figure 2 presents the SEM for hypothesized indirect pathways. In the sections that follow, we first describe the portion of the model representing the interaction of community characteristics and parental genotype on protective parenting. Then, we focus on the interaction effect of protective parenting and youth genotype on a planful future orientation, an outcome proximal to risk behavior. After this, we present the results of indirect effect tests.

Community disadvantage $\times$ parent's *DRD4* effects on protective parenting

The results presented in Figure 2 indicate that the parameter representing the interaction between community disadvantage and parent's *DRD4* status significantly predicted protective parenting ($\beta = -.19, p < .01$). Figure 3a depicts the effect of parent's *DRD4* on protective parenting for levels of community disadvantage ranging from -2 to $+2$ standard deviations from the mean. The slope indexing the effect of community disadvantage on protective parenting for parents carrying *DRD4-I* was significantly different from zero ($b = -.17, p < .05$), whereas the slope for parents carrying only *DRD4-s* was not significantly different from zero ($b = .10, p = .18$). Thus, the effect of community disadvantage on protective parenting emerged only for parents carrying *DRD4-I*.

The graph of the interaction depicted in Figure 3a demonstrated the crossover pattern that suggests a differential susceptibility effect. The J-N technique (Preacher et al., 2006) was used to assess regions of significant difference attributable to different alleles of *DRD4*. A differential susceptibility model produces relatively equal regions of significance on both sides of the graph. The shaded areas in Figure 3a represent the regions of significant

difference for the $G \times E$ interaction effect. The J-N technique yields an index that addresses the equality of the regions of significance, called the proportion of the interaction areas (PoI); scores near .50 indicate relatively equal significance on both sides of the interaction. The PoI in this case was .58, which is within the range consistent with differential susceptibility effects (Roisman et al., 2012).

Protective parenting $\times$ youth *DRD4* effects on a planful future orientation

Consistent with our hypotheses, the data presented in Figure 2 demonstrated that the interaction term between protective parenting and youth genotype at *DRD4* was associated significantly with increases in planful future orientation ($\beta = .15, p < .05$), which, in turn, was associated with youth risk behavior at age 19 ($\beta = -.16, p < .01$). Analyses of the simple slopes (see Figure 3b) indicated that protective parenting enhanced a planful future orientation only for youth with a *DRD4-I* allele (*DRD4-I*, $b = .23, p < .01$; *DRD4-s*, $b = .02, p = .73$). The J-N technique identified a region of significant difference confined to one side of the interaction effect. This indicated that *DRD4* conferred vulnerability to low levels of protective parenting when protective parenting was less than $-.48$ *SD* below the sample mean; however, high levels of protective parenting for *DRD4-I* youth did not result in increases in planful future orientation. In this case, the $G \times E$ interaction was more consistent with a diathesis-stress model than a differential susceptibility model (PoI = .25).

Indirect effects linking community disadvantage to youth risk behavior

Table 2 presents the conditional indirect effects linking multilevel $G \times E$ processes to youth's planful future orientation and subsequent changes in youth risk behavior. A significant indirect effect linked community disadvantage to changes in youth's planful future orientation via protective parenting when both parent and youth carried *DRD4-I*; $\beta = -.03, 95\% \text{ CI } [-.060, -.008]$. A significant indirect effect also linked protective parenting to changes in risk behavior through planful future orientation when youth carried *DRD4-I*; $\beta = -.03, 95\% \text{ CI } [-.063, -.007]$. Finally, the indirect effect of community disadvantage on risk behavior via protective parenting and planful future orientation was significant only when *DRD4* status of both parents and youth are considered; $\beta = .01, 95\% \text{ CI } [.003, .015]$.

Discussion

Drawing on bioecological (Bronfenbrenner & Ceci, 1994) and differential susceptibility (Belsky et al., 2007; Belsky & Pluess, 2009) perspectives, we tested a series of multilevel $G \times E$ hypotheses predicting African American youth's risk behavior from ages 16 to 19. Consistent with our hypotheses, the effects of community disadvantage on protective parenting and the effects of protective parenting on youth's planful future orientation were moderated by parent and youth *DRD4* status. Specifically, parents' exposure to community disadvantage predicted their provision of protective parenting practices only when parents carried *DRD4-I*. Protective parenting, in turn, predicted youth's development of a planful future orientation, a proximal predictor of risk behavior, when youth carried *DRD4-I*. We subsequently tested the hypothesis that the pathway linking community disadvantage to youth risk behavior via protective parenting and planful future orientation would be evident

only when both parents' and youth's *DRD4* status was considered. The indirect effect analysis supported this hypothesis.

Informed by research on differential susceptibility to environmental exposures, we also examined the possibility that parent and youth *DRD4* operated to increase environmental sensitivity in a "for better and for worse" manner or conferred vulnerability to negative environments. Results were mixed for parent and youth genotypes. For the interaction effect of community disadvantage and parents' *DRD4* on protective parenting, this association emerged as a differential susceptibility effect. For the effect of protective parenting on increases in youth's planful future orientation, however, the evidence was consistent with the diathesis-stress perspective.

Most research on $G \times E$ interaction effects on youth development has focused on a range of proximal environments interacting with youth genotypes. In this study, we extended this literature by examining the ways in which community environments interacted with parental genotype at *DRD4* to forecast parenting behavior. We found that exposure to community disadvantage did not predict parenting behavior among parents who did not carry *DRD4-I*. In contrast, among parents who carried 1 or 2 copies of the *I* allele, community disadvantage predicted diminished protective parenting characterized by monitoring, nurturance, and academic involvement. We are aware of two other studies that have examined parent genotype by environment interaction effects on parenting behavior. Van IJzendoorn et al. (2008) found that, among parents of infants, dopamine-related genes moderated the influence of daily hassles on parenting behavior. Similar to the present study, parents displayed less sensitivity to their children's needs when they were stressed by daily hassles, but only in the group of parents who had the *DRD4-I* and catechol-O-methyltransferase (*COMT*)-*val* alleles. A second study also yielded results consistent with the present study. Beach et al. (2012) found that parents with *DRD4-I* who were exposed to community stress developed patterns of negative emotionality that affected their relationships with their children. Taken together, these studies, in which different sources and methods were used, suggest that *DRD4* genotype may interact with contextual circumstances to affect parenting behavior.

Our finding that youth's *DRD4* status moderated the influence of protective parenting on planful future orientation is consistent with a number of studies investigating youth *DRD4* and family environments. Most of this research, however, has focused on the interaction effects of youth *DRD4* genotypes $\times$ family environments on risk behaviors without consideration of intermediate phenotypes such as planful future orientations (Bakermans-Kranenburg & van IJzendoorn, 2006; Bakermans-Kranenburg & van IJzendoorn, 2007; Beach et al., 2010; Propper, Willoughby, Halpern, Carbone, & Cox, 2007). Our focus on the intermediate phenotype, planful future orientation, is a response to recent requests for investigations of intermediate mechanisms that account more precisely for $G \times E$ interactions. For example, Brody et al. (2012) found the effect of *DRD4* $\times$ life stress on substance use was mediated by changes in substance use vulnerability cognitions and increases in affiliations with substance-using peers. Our findings suggest that a planful future orientation is a plausible intermediate mechanism linking *DRD4* $\times$ rearing environment to youth risk behavior.

We also sought to determine whether the $G \times E$ effects were consistent with the diathesis-stress or the differential susceptibility perspective. The parent genotype $\times$ community disadvantage interaction effect on protective parenting was consistent with the differential susceptibility perspective. Protective parenting among parents carrying *DRD4-I* was undermined in highly disadvantaged community environments but was enhanced in favorable environments. This finding is consistent with Beach et al. (2012) who documented a “for better and for worse” effect for *DRD4* $\times$ community context in predicting parents’ negative arousal, a proximal determinant of parenting behaviors. Van IJzendoorn et al. (2008) reported that combinations of *COMT* and *DRD4* moderated the influence of daily hassles on maternal sensitivity; however, evidence for differential susceptibility is unclear (Belsky, 2011). Additional research involving parenting behaviors is needed to clarify further the role of *DRD4* in conferring differential susceptibility.

The effects of protective parenting on youth’s planful future orientations were moderated by youth *DRD4* in a “for worse” manner indicative of a diathesis-stress effect. Youth with the *DRD4-I* allele who received little protective parenting reported diminished planful future orientations. There was, however, no evidence emerged for a “for better” effect in which heightened protective parenting led to significant enhancement of planful future orientation among youth with the *DRD4-I* allele. Relatively few studies, however, investigate intermediate phenotypes, and among those we aware of, only two tested for differential sensitivity. Simons et al. (2011) found that a combined assessment of community and family environments interacted with youth’s cumulative gene index to predict youth hostility in a manner consistent with differential susceptibility. Similarly, Belsky and Beaver (2011) found differential susceptibility effects of parenting practices and a cumulative gene index on male adolescents’ self-regulation. Contradictory findings in our study may be the result of prior studies using cumulative gene index rather than a single genotype. However, given the paucity of $G \times E$ studies on intermediate phenotypes, additional research is warranted to determine the specific environmental conditions under which various kinds of measures detect differentially sensitive effects for *DRD4-I*.

To date, little research has considered the joint effects of parent and youth genotypes interacting with environmental factors to forecast youth behavior. Our analyses suggested that community environments affected youth risk behavior indirectly via a series of indirect effects involving protective parenting and youth’s planful future orientations when the *DRD4* statuses of both parents and youth are considered. Significant indirect effects were detected across the pathways linking community disadvantage $\times$ parental *DRD4* status effects on protective parenting to protective parenting $\times$ youth *DRD4* status effects on planful future orientation (linking parent $G \times E$ processes to youth $G \times E$ processes). The indirect effects model, operating through both parental and youth $G \times E$ processes, underscores the need to document the pathways through which members of a family system with varying genotypes shape the environment in which others’ development and behavior take place.

Several methodological strengths in the present study are noteworthy. We used multi-informant and multi-method assessments gathered from the U.S. Census, parents, and youth. Census tract data were used to obtain an objective assessment of community disadvantage.

We also used both parent and youth reports and alternated these reports to minimize self-report bias in the links between parenting and planful future orientation. Both planful future orientation and risk behavior were assessed by youth report, producing the potential for self-report bias to inflate the association of these factors. This concern was mitigated somewhat by the evaluation of these variables at different time points and the use of a baseline control. Some limitations of the research also should be noted. Only one genetic polymorphism was examined in this study. A number of genetic variants are under investigation that may alter risk or environmental sensitivity, although *DRD4* is among the best documented and characterized polymorphisms (Bakermans-Kranenburg & van IJzendoorn, 2006; Brody et al., 2012; Propper et al. 2007). It also should be noted that, although we coded *DRD4* alleles as 6 or fewer repeats versus 7 or more repeats, some studies focus on the 4-repeat allele versus the 7-repeat allele (Beach et al., 2010) or on the 7-repeat allele versus all others (Bakermans-Kranenburg & van IJzendoorn, 2006). Also, the findings focused on rural community contexts; thus, the results may not generalize to other settings. These limitations notwithstanding, the present study demonstrates the ways in which community disadvantage, protective parenting, and both parents' and youth's *DRD4* status combine to influence youth risk behavior via a planful future orientation. The results suggest a continued need for studies that integrate transactional developmental perspectives and $G \times E$ research. Such research expands the focus of individual differences to include exposure to environmental characteristics in accounting for complex transactions among family members and communities over time.

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Figure 1.
Conceptual model.

Figure 2.

Test of study hypotheses; $\chi^2 = 54.73$, $df = 47$, $p = .20$. RMSEA = .03. CFI = .98. $N = 361$. Standardized coefficients are shown. Family SES, target gender, and program intervention effects were controlled.

* $p < .05$. ** $p < .01$

Figure 3. (a) Community disadvantage $\times$ parental *DRD4* effects on protective parenting; (b) Protective parenting $\times$ youth *DRD4* effects on a planful future orientation.

Table 1

Correlations among the research variables (N = 361)

Variable	1	2	3	4	5	6	7	8	9	10	11
1. Youth gender	–										
2. Family SES	–.04	–									
3. Intervention	–.01	–.07	–								
4. Community disadvantage	–.02	.11*	–.09	–							
5. Protective parenting T1	–.02	–.18**	–.05	–.06	–						
6. Planful future orientation T1	–.07	–.04	.03	.06	.13*	–					
7. Planful future orientation T2	–.06	–.06	–.05	.05	.17**	.40**	–				
8. Risk behavior T1	.06	.02	–.01	.04	–.01	–.13*	–.19**	–			
9. Risk behavior T3	.25**	.01	.02	.14**	–.12*	–.08	–.21**	.28**	–		
10. <i>DRD4</i> : Parent	.02	–.01	–.01	.05	–.05	.05	.01	–.01	.03	–	
11. <i>DRD4</i> : Youth	.11*	–.01	.02	.03	–.06	–.09	–.09	.07	.06	.42**	–

*
 $p < .05$.**
 $p < .01$.

Table 2
Conditional indirect effects on youth risk behavior in a condition of parent and youth DRD4-l status

Predictors	Mediator(s)	Outcomes	Indirect Effect	Effect Size	95% CI
Community disadvantage	Protective parenting	Planful future orientation	-.03	.56	[-.060, -.008]
Protective parenting	Planful future orientation	Risky behavior	-.03	.32	[-.063, -.007]
Community disadvantage	Protective parenting	Planful future orientation	.01	.21	[.003, .015]