Title

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Journal

Development and psychopathology, 29(4)

ISSN

0954-5794

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Publication Date

2017-10-01

DOI

10.1017/s0954579416001310

Peer reviewed

HHS Public Access

Author manuscript

Dev Psychopathol. Author manuscript; available in PMC 2017 October 01.

Published in final edited form as:

Dev Psychopathol. 2017 October ; 29(4): 1289–1304. doi:10.1017/S0954579416001310.

Parenting and adolescents' psychological adjustment: Longitudinal moderation by adolescents' genetic sensitivity

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Abstract

We examined whether adolescents' genetic sensitivity, measured by a polygenic index score, moderated the longitudinal associations between parenting and adolescents' internalizing and externalizing problems. The sample included 323 mothers, fathers, and adolescents (177 female, 146 male; Time 1 [T1] average age = 12.61 [*SD* = 0.54] years, Time 2 [T2] average age = 13.59 [*SD* = 0.59] years). Parents' warmth and hostility were rated by trained, independent observers using videotapes of family discussions. Adolescents reported their symptoms of anxiety, depressed mood, and hostility at T1 and T2. Results from autoregressive linear regression models showed that adolescents' genetic sensitivity moderated associations between observations of mothers' T1 parenting and adolescents' T2 symptoms of depression, anxiety, and hostility. For fathers, the same pattern was found for adolescents' anxiety and hostility, but not for depressed mood. Compared to adolescents with low genetic sensitivity, adolescents with high genetic sensitivity had worse adjustment outcomes when parenting was low on warmth and high on hostility. When parenting was characterized by high warmth and low hostility, adolescents with high genetic sensitivity had better adjustment outcomes than their counterparts with low genetic sensitivity. Results support the differential susceptibility model and highlight the complex ways that genes and environment interact to influence development.

Psychologists working from a variety of theoretical traditions concur that parenting quality influences children's psychological adjustment such that warm, supportive, and otherwise sensitive parenting behaviors promote child wellbeing; whereas hostile, angry, and coercive parenting behaviors appear to thwart it (e.g., Barber, Stolz & Olsen, 2005; Maccoby, 2000; Patterson, DeBaryshe, & Ramsey, 1989). Another body of research has demonstrated that certain genetic characteristics also influence children's psychological adjustment (see

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Plomin, DeFries, Knopf, & Neiderhiser, 2013 for a review). Recently, these perspectives have been brought together with the idea that genes moderate the influence of the environment on psychological adjustment (e.g., Caspi, Hariri, Holmes, Uher, & Moffit, 2010). In other words, both genes (G) and the quality of one's environment (E) are dynamically linked forces that interact to contribute to psychological wellbeing (G×E). Based on this proposition, in the current study we examine the degree to which adolescents' genetic sensitivity moderates the associations between earlier exposure to parental behaviors, ranging from high warmth and low hostility to low warmth and high hostility, and adolescents' later psychological adjustment including depressed mood, anxiety symptoms, and feelings of hostility (i.e., anger and irritability). To address these issues, we use prospective, longitudinal, and multi-method data from a community sample of young adolescents and both of their biological parents.

Adolescent Adjustment: Parenting (E) and Genetic (G) Influences

Rates of both internalizing (e.g. depressed mood and anxiety) and externalizing (e.g. hostility and delinquency) symptoms tend to increase across adolescence and may differ for males and females (Kessler, et al., 2005; Thapar, Collishaw, Pine, & Thapar, 2012). Regardless of whether these symptoms reach clinical levels, research has demonstrated that they have negative consequences for a number of important areas of adolescent functioning such as interpersonal relationships with friends and family, academic performance, and physical health (Thapar et al., 2012). Moreover, these symptoms are likely to interfere with normative developmental tasks, such as separating from parents, forming romantic relationships and launching careers, as individuals progress through their teen years and into emerging adulthood, when most major psychiatric disorders have their onset in the late teens to the early 20s (Paus, Keshavan & Giedd., 2008). Improved understanding of the genetic and environment factors that influence adolescents' internalizing and externalizing problems may have implications for theory development, research, and intervention.

Many years of research support the notion that parents play an important role in the psychosocial development of their children (Eisenberg & Valiente, 2002; Steinberg & Silk, 2002). For example, parental hostility, rejection and psychological control are associated with increases in children's and adolescent's internalizing and externalizing problems (Conger, Conger, & Scaramella, 1997; Luebbe, Bump, Fussner, & Rulon, 2014; Repetti, Taylor, & Seeman, 2002). On the other hand, numerous studies have identified parental support, affection, and acceptance as important protective factors against youth and adolescent risk for emotional and behavioral problems (for review, see Berg-Nielsen, Vikan, & Dahl, 2002).

Researchers also have found evidence for genetic influences for these adjustment outcomes (see Plomin et al., 2013). Using family, twin and adoption designs, behavioral geneticists have shown that genes (i.e., heritability) account for 40% to 60% of the variance in adolescents' depression (Levinson, 2006), 30% to 80% of the variance in anxiety (McLeod, Wood & Weisz., 2007), and 40% to 60% of the variance in externalizing problems (Hicks, Foster, Iacono, & McGue, 2013). Accordingly, it appears that both environmental and genetic influences directly contribute to rates of internalizing and externalizing symptoms.

What is less understood, however, is how genes and environment work together to predict psychological adjustment.

Adolescent Adjustment: G×E Research

In addition to the direct environmental and genetic influences discussed above, some research has shown that an individual's genetic makeup can moderate the effect of the environment on mental health (Caspi et. al., 2003, 2010). Originally, these findings were interpreted to support the diathesis-stress model, which hypothesizes that individuals carrying more "risk" alleles on certain "vulnerability" genes make them more susceptible to environmental stressors (e.g., more depressive symptoms; higher rates of antisocial behavior and so forth) compared to individuals without these genetic variants. More recently, this model has been refined and presented as a framework of differential susceptibility (Belsky & Pluess, 2009, 2013; Boyce & Ellis, 2005). The differential susceptibility framework hypothesizes that individuals carrying more risk or "plasticity" alleles on certain candidate genes are particularly sensitive to environmental influences regardless of valence such that they exhibit more positive outcomes in response to supportive environments and more negative outcomes in response to stressful environments. That is, according to the differential susceptibility hypothesis, risk alleles may be better characterized as plasticity or "sensitivity" alleles that moderate the effect of the environment on certain outcomes in a for-better *and* for-worse fashion (Belsky & Pluess, 2009).

Most of the existing G×E research involving adolescent adjustment has focused on genes from the dopaminergic system, involved in reward sensitivity and sensation seeking (e.g., Dreher, Kohn, Kolachana, Weinberger, & Berman, 2009; Stice, Yokum, Burger, Epstein, & Smolen, 2012) and the serotonergic system, linked to sensitivity to punishment and displeasure (e.g., Caspi et al., 2010). Neuropsychological research has shown that variants in dopamine and serotonin genes expressed in the limbic system, and in particular, the amygdala, were associated with increased emotional sensitivity to the environment. For instance, in a fMRI study, carriers of two short alleles (ss) in the linked polymorphism of the serotonin transporter gene (5-HTTLPR) had heighted amygdala reactivity to emotionally salient stimuli compare to individuals carrying a short and a long allele (sl) and two long alleles (ll) (Walsh et al., 2012).

Indeed, some research has shown that variants of 5-HTTLPR interact with environmental stressors to predict psychological adjustment in a manner consistent with the differential susceptibility model. For example, in a sample of young adults, ss individuals reported greater depressive symptoms if they experienced early family adversity, such as physical or verbal abuse, observed aggression between other family members, or recent adversity assessed by a checklist of stressful life events in the past six months (Taylor et al., 2006). Additionally, compared to those with sl or ll genotypes, ss individuals had significantly fewer depressive symptoms if they reported supportive early family environments (e.g. physical affection, feeling cared for, well-organized and well-managed households) or few recent stressful life events. In a study of adolescents, 5-HTTLPR moderated the link between family support (e.g. parental closeness, communication, feeling loved) and depressed mood and suicide ideation or attempts for boys, but not for girls. Specifically,

among boys with poor family support, youth with at least one short allele had more symptoms of depression and higher scores on suicide ideation or attempts relative to boys with two long alleles; however, in the presence of high family support, boys with ss alleles had the fewest depression symptoms relative to sl and ll carriers (Li, Berk, & Lee, 2013).

Although research on gene by environment interactions using single candidate genes has yielded useful information, results have been inconsistent and difficult to replicate (Duncan & Keller, 2011). This approach is giving way to a growing consensus that complex mental health outcomes have a significant polygenic component, in which genetic influences operate as a function of combined additive effects of a number of variants (Sullivan, Daly, & O'Donovan, 2012). Thus, some researchers are beginning to use additive scoring methods to account for cumulative genetic effects across a series of relevant candidate genes (see Belsky & Israel, 2014). This strategy operates similarly to other kinds of indices in which several risk or protective factors are combined to create a single score of overall risk or protection (e.g., Evans, Li, & Whipple, 2013). Moreover, this approach is consistent with the notion that individual candidate genes have small effects on behavior and that larger effects are more likely to be observed when considering a number of these small effects in combination.

Indeed, several recent studies have found support for the differential susceptibility hypothesis using cumulative genetic index scores, created by summing polymorphic variation across a set of candidate genes that, individually, have been shown to contribute small effects to outcomes of interest (e.g., 5-HTTLPR and depression: see Caspi et al., 2010). For example, Masarik and her colleagues (2014) found that a cumulative genetic index made up of variants on five dopaminergic and serotonergic genes moderated the link between earlier exposure to parenting behaviors and later behavior toward a romantic partner in adulthood. Moreover, these results were consistent with the differential susceptibility hypothesis because individuals who had higher scores on the cumulative genetic index were: (a) more likely to behave in a hostile fashion toward their romantic partner in adulthood if they were exposed to higher levels of parental hostility in adolescence and (b) more likely to behave in a positive, supportive, and engaging fashion toward their adult romantic partner if, during adolescence, they experienced similarly supportive behaviors from their parents. Similarly, Simons et al. (2012) found that a cumulative genetic index score comprised of variants on the dopamine receptor D4 (*DRD4*) and the *5-HTT* gene interacted with a composite measure of a hostile/demoralizing social environment (e.g., harsh parenting, caregiver substance use, racial discrimination, and community crime) to predict aggression and delinquency in African American adolescents. Consistent with the differential susceptibility hypothesis, when the social environment was adverse, genetically sensitive adolescents were more aggressive than adolescents with low scores on genetic sensitivity, yet when social adversity was low, they were less aggressive than adolescents who were low on genetic sensitivity. In another study, adolescents who had high scores on a genetic index of plasticity had more depressive symptoms when their parents had disrupted marriages than adolescents with low genetic plasticity scores. Consistent with the differential susceptibility hypothesis, these adolescents had fewer depressive symptoms when parents had consistently stable marriages than adolescents who had low genetic plasticity scores (Wickrama & O'Neal, 2013). In another study, a cumulative plasticity score made up of two candidate genes (BDNF Val66met, 5HHTLPR) interacted with family environmental quality

(combined score of marital, mother–child and father–child relationships) to predict adolescents' depressed mood at age 15 (but not at age 20 or 25), consistent with the differential susceptibility model (Dalton, Hammen, Naijman, & Brennan, 2014). These studies provide support for the differential susceptibility hypothesis using cumulative genetic index scores of sensitivity. To date, however, research has not examined the moderating role of adolescents' polygenic sensitivity separately for mothers' and fathers' behavior and for both internalizing and externalizing problems. The current study is uniquely positioned to extend our understanding in this area.

The Present Study

The goal of the present study is to contribute to the emerging literature on genetic moderation of the environment on adolescent adjustment in a number of ways. First, most previous G×E research has relied heavily on a diathesis-stress perspective such that one's diathesis (i.e., genetic risk) is hypothesized to interact with exposure to negative experiences or environments (i.e., stress) to predict a given outcome (e.g., depression). The current study, in contrast, draws upon the differential susceptibility framework (Belsky & Pluess, 2009, 2013) to test the proposition that adolescents' polygenic sensitivity would moderate the impact of both positive and negative parenting on adolescents' adjustment. In other words, we examined whether adolescents hypothesized to be more genetically sensitive would have worse psychological adjustment if exposed to hostile, angry, and controlling parenting behaviors, but better adjustment (i.e., less depression, anxiety, and hostility) if exposed to warm, supportive, and nurturing parenting behaviors. Second, rather than relying on one candidate gene, we add to a growing body of research that uses a cumulative genetic index score to represent the additive effect of variation in a set of candidate genes (see Belsky & Israel, 2014). Specifically, we examined genetic variation across five commonly studied dopaminergic and serotonergic candidate genes: serotonin transporter gene, 5-HTT; ankyrin repeat and kinase domain containing 1 gene/dopamine receptor D2 gene, *ANKK1/DRD2*; dopamine receptor D4 gene; dopamine active transporter gene *DAT*; and catechol-O-methyltransferase gene, *COMT*.

Third, most previous work on G×E interactions involving parenting and adolescent adjustment outcomes has been cross-sectional or has relied on retrospective reports of earlier parenting (see Duncan & Keller, 2011; Karg et al., 2011 for reviews); thus, leaving open the possibility of shared method variance and biased recall. In contrast, we use prospective, longitudinal data from multiple reporters. Fourth, given that rates of internalizing and externalizing problems typically differ by sex, we test whether adolescents' sex impacts the role of genetic sensitivity in moderating links between mothers' or fathers' parenting behaviors and adolescents' adjustment outcomes; results from prior research have been either mixed or absent on this issue (Dalton et al., 2014; Li et al., 2009). Finally, relatively little attention has been given to fathers' role in adolescent risk for emotional and behavioral problems (Phares, Fields, Kamboukos, & Lopez, 2005) in general, and we know of no other studies that have examined polygenic sensitivity as a moderator of the links between fathers' parenting and adolescents' adjustment specifically. To address this gap in the literature, the current study includes independent observer ratings of both mothers' and fathers' parenting behaviors, and we test all of our models separately for mothers and fathers.

In sum, using longitudinal, multi-method data from a community sample, the current study examines adolescent polygenic sensitivity as a moderator of the prospective association between mothers' and fathers' parenting behaviors and adolescent adjustment. Consistent with the differential susceptibility hypothesis, we expect that higher levels of adolescent polygenic sensitivity will be associated with: (a) more symptoms of adolescent depression, anxiety, and hostility when parenting behaviors are marked by high levels of hostility and low levels of warmth; and (b) fewer symptoms of adolescent depression, anxiety, and hostility when parenting behaviors are characterized by low levels of hostility and high levels of warmth.

Method

Participants

Data come from the first two waves of a prospective, longitudinal, and multi-informant study of family members living in the rural Midwest (see Conger & Conger, 2002). Starting in 1989, a 7th grade "target" adolescent, a close-aged sibling, and their biological parents were visited in their homes by trained interviewers. At study initiation, a total of 451 families were eligible to participate. In the present report, we focus on a sub-sample of target participants with complete data on measures of polygenic sensitivity, quality of parenting behaviors, and adolescent adjustment during the early adolescent years corresponding to the 1989 (T1) and 1990 (T2) assessments (N = 323: female n = 177; male n = 146). The average age of targets in this sub-sample was 12.61 (SD = 0.54) and 13.59 (SD = 0.59) at T1 and T2, respectively. The average age of mothers was 37.98 (SD = 4.13) and 38.94 (SD = 4.10) at T1 and T2, respectively, and the average age of fathers was 39.87 (SD = 5.00) and 40.89 (SD = 4.89) at T1 and T2, respectively. The ethnic/racial background is predominately European American reflecting the demographics of the region at study initiation.

Procedure

Target adolescents were initially recruited from 34 public and private schools from eight counties in central Iowa in 1989, when they were in the seventh grade. In brief, names and addresses of seventh-grade students and their parents were collected from schools in communities of 6,500 people or less. Letters were sent to families explaining the project and they were later contacted by telephone and asked to participate. Families without telephones were contacted in person. Seventy-eight percent of the families eligible for the study agreed to participate in 1989 (N = 451).

Trained interviewers visited each family at home at T1 and T2 and conducted the assessments, which lasted for approximately two hours on each of two occasions. During the first visit, each family member completed a set of questionnaires that focused on individual family member characteristics and experiences, the quality of family interactions, and family economic circumstances. During the second visit, which usually occurred within two weeks of the first visit, family members were videotaped as they participated in semi-structured interaction tasks designed to stimulate family interaction and elicit information about social skills and emotional responses. We assessed the quality of parenting behaviors (toward the target adolescent) from the 30-minute family discussion task (Task 1), a task designed to

provide family members with the opportunity to express a range of emotions including both negative and positive sentiment (see Melby & Conger, 2001 for more details).

During the family discussion task, trained interviewers videotaped family members as they were given a set of cards, instructed to read questions aloud, and then discuss their answers to the questions. These cards contained general questions about family life such as important family events, approaches to parenting, and household chores. Approximately 20% of the videotaped interaction tasks were randomly assigned for rating by a second, independent observer. The primary and secondary ratings were then used to generate estimates of inter-observer reliability using Intraclass Correlation Coefficient (ICC) procedures (see Choukalas, Melby, & Lorenz, 2000).

Measures

Parenting quality—At T1, parenting quality was assessed via observer ratings of the videotaped family discussion interaction task (Task 1). Observers rated verbal and nonverbal behavior by the mother and father to the target adolescent using the Iowa Family Interaction Rating Scales (IFIRS: Melby & Conger, 2001). Before rating any of the videotaped interactions, however, observers received 200 hours of training and passed extensive written and viewing reliability tests. Once reliability was established, all observers attended at least two training sessions each week to ensure continued reliability. The IFIRS has been utilized in a variety of cross-sectional and longitudinal studies examining diverse topics such as economic stress, parenting, adolescent development, and romantic relationships, and has acceptable reliability and validity (Melby & Conger, 2001).

Several behavioral codes were used to measure the quality of mothers' and fathers' parenting behavior toward the target adolescent at T1. Each behavior was rated on a scale from 1 (*the behavior is not at all characteristic*) to 5 (*the behavior is highly characteristic*). Mother and father *Hostility*, *Angry Coercion*, and *Antisocial Behavior* were left in their original scoring format whereas *Warmth/Support*, *Listener Responsiveness*, *Positive Assertiveness*, *Positive Communication*, and *Prosocial Behavior* were reverse scored. Thus, high scores on our measure of parenting quality represent more hostility and less warmth by parents toward their adolescent child; likewise, low scores on our measure of parenting quality represent less hostility and more warmth by parents toward their adolescent child. These eight behavioral codes were averaged together separately for mothers (Cronbach's α = .86; inter-observer ICC = .92) and fathers (Cronbach's α = .86; inter-observer ICC = .93). As shown in Table 1, the average parenting quality score for mothers was 3.25 (*SD* = 1.40) and 3.63 (*SD* = 1.19) for fathers.

Adolescent adjustment—Symptoms of adolescent depression, anxiety, and hostility were assessed using the self-reported Symptom Checklist-90-Revised (*SCL-90-R*) subscales, which have demonstrated reliability and validity (Derogatis, 1983). At T1 and T2, adolescents indicated the degree of discomfort regarding adjustment problems on a scale of 0 (*not at all*) to 4 (*extremely*) during the past week. The 13-item *Depression* subscale had adequate reliability (α = .87 at T1; α = .85 at T2), as did the 10-item *Anxiety* subscale (α = .82 at T1; α = .83 at T2), and the 6-item *Hostility* subscale (α = .82 at T1; α = .77 at T2).

Example items include: “feeling blue” and “low in energy or slowed down (depression); “nervousness or shakiness inside” and “feeling tense or keyed up” (anxiety); and “temper outbursts you cannot control” and “having urges to beat, injure, or harm someone” (hostility). Items corresponding to each subscale were averaged together to reflect symptoms of depression, anxiety, and hostility at T1 and T2 (see Table 1 for descriptive statistics).

Polygenic sensitivity—The polygenic sensitivity index is based on genotyping of saliva samples which were obtained from target participants in later waves of assessment (2007–2010) with Oragene™ (DNA Genotek, Ontario, Canada) collection kits. DNA was isolated with Agencourt DNAdvance™ DNA Isolation Kits (Beckman Coulter, Brea, CA) using a Beckman-Coulter Biomek® FX workstation according to company protocols. Methods for genotyping the *DAT* and *DRD4* VNTRs are detailed in Anchordoquy, McGeary, Liu, Krauter, and Smolen (2003) and the method for 5-HTTLPR is in Whisman, Richardson, and Smolen (2011). Genotyping of the Taq1A polymorphism and Val158Met polymorphism in *COMT* are outlined in Haberstick and Smolen (2004). The Taq1A polymorphism has previously been studied in association with *DRD2* but it has been suggested that *ANKK1* (downstream from *DRD2*) may be responsible for some of the effects attributed to *DRD2* (see Neville, Johnstone, & Walton, 2004); thus, we refer to this genotype as *ANKK1*/*DRD2*.

Based on past research (e.g., Belsky & Pluess, 2009), we consider the following alleles to confer sensitivity: short (s) allele of 5-HTTLPR in *5-HTT* (accounting for SNP rs25531); A1 allele of the Taq1A polymorphism in *ANKK1*/*DRD2*; 7R allele of exon-3 VNTR in *DRD4*; 10R allele of the 5’ VNTR in *DAT*; and the Met allele of the Val158Met polymorphism in *COMT*. Polymorphisms received a score of ‘0’ if none of these alleles were observed, a score of ‘1’ if one of these alleles was observed, and ‘2’ if two of these alleles were observed. Finally, these scores were summed to create an index of polygenic sensitivity. Although index scores could theoretically range from 0–10, the observed range was 1–8 indicating that all participants had at least one of the hypothesized sensitivity alleles (M = 4.41, SD = 1.36). Based on examination of duplicate controls and Mendelian inconsistencies among family members, genotype error rates were less than 1% for all five polymorphisms; and allele and expected genotype distributions were in Hardy-Weinberg equilibrium. Moreover, the allele frequencies were consistent with other Caucasian populations (see http://alfred.med.yale.edu; Rajeevan, Soundararajan, Kidd, Pakstis, & Kidd, 2012).

Control variables—Mothers’ and fathers’ education, as well as family income-to-needs were included as controls in our tests of study hypotheses because both of these variables have been shown to correlate with parenting quality and adolescent adjustment (for a review, see Conger, Conger, & Martin, 2010). Mothers’ and fathers’ *education* at T1 was measured with dummy variables that ranged from 0–11 (highest grade completed) to 20 (PhD or other professional degree). *Income-to-needs* was created using guidelines from the U. S. Department of Health and Human Services (DHHS) and indicates family income relative to the poverty line for a family of a particular size. For example, a score of 1.0 indicates the family is at the poverty line, a score of 2.0 indicates the family income is two times higher than the poverty line, and so forth. At Time 1, total family income including all wages, salaries, and other sources of income (e.g., self-employment income, farm net income, and

supplemental security income) was divided by the DHHS poverty guideline (for 1989) for a family of a given size to create the income-to-needs ratio.

Statistical Analyses

Following preliminary descriptive and correlational analyses, predictors of adolescent adjustment outcomes (*SCL-90-R* Depression, Anxiety, and Hostility scales) were examined using linear regression models in IBM SPSS Statistics Software 22 (Chicago, IL., USA). The main and interactive effects of parenting quality and polygenic sensitivity in predicting adolescent outcomes were run separately for mothers and fathers. To account for the temporal order of causality, we used an autoregressive approach (see Cohen, Cohen, West, & Aiken, 2003) to model change in adolescent depressive, anxiety, and hostility symptoms from T1 to T2. In addition to baseline adolescent symptoms, all regression analyses controlled for sociodemographic variables including adolescent sex, parent educational attainment, and family income-to-needs ratio.

A moderated multiple regression framework (Aiken & West, 1991) was used to model the multiplicative interactions between parenting quality and adolescent cumulative genetic sensitivity as predictors of adolescent adjustment over time. In our statistical models ($y_i = \beta_0 + \beta_1 X_{1i} + \beta_2 X_{2i} + \beta_3 X_{3i} + \varepsilon_i$), the outcome variable y_i (T2 adolescent outcome) was examined as a function of independent variables in the model (X_1 = parenting quality; X_2 = adolescent polygenic sensitivity), and the moderating effects indicated by the interaction ($X_3 = X_1 \times X_2$). To assist in the interpretation of moderation effects and reduce multicollinearity between product terms, all continuous independent variables were grand mean centered prior to conducting moderation analyses. Models were estimated by entering the main effects of all study variables simultaneously in the first step and adding the two-way gene by environment interaction between parenting quality and genetic sensitivity in the second step. The R^2 was examined in each step and tests of $R^2\Delta$ were used to assess the significance of moderation effects (Cohen et al., 2003).

The interpretation and post-hoc testing of significant interaction effects followed methods outlined by Holmbeck (2002), in which significant moderating effects were examined by graphically plotting and calculating the simple slopes of parenting at high (one *SD* above the mean) and low (one *SD* below the mean) levels of cumulative genetic sensitivity. In cases where a significant interaction was found but simple slopes were not significant at one *SD* above or below the mean, we probed the simple effects at +2 *SD* / −2 *SD*. We also examined whether the moderating effect of genetic sensitivity was specific to adolescent girls or boys (i.e., the three-way interaction between parenting quality, adolescent genotype, and adolescent sex). In these models, all possible two-way interactions (Parenting Quality × Adolescent Polygenic Sensitivity, Parenting Quality × Adolescent Sex, and Adolescent Polygenic Sensitivity × Adolescent Sex) were entered prior to the second-order (i.e., 3-way) interaction.

Results

Preliminary Analyses

Descriptive statistics and bivariate correlations among study variables are presented in Table 1. In accordance with guidelines for testing gene–environment interactions (Belsky, Bakermans-Kranenburg, & van Ijzendoorn, 2007), correlational analyses revealed no significant bivariate associations between adolescent polygenic sensitivity scores and parenting quality for mothers ($r = .01$, $p = .83$) or fathers ($r = .01$, $p = .92$), suggesting that evocative effects of genetic sensitivity on parenting did not account for the observed findings.

Predicting Adolescent Adjustment

Depressive symptoms—Results from linear regression analyses predicting adolescent outcomes from maternal and paternal parenting quality are shown in Tables 2 and 3, respectively. The main effect regression model predicting adolescent depressive symptoms was significant for mothers, $F(6, 316) = 22.19$, $p < .001$, and fathers, $F(6, 316) = 21.97$, $p < .001$. Consistent with the existing literature on gender differences in the prevalence of depression (Nolen-Hoeksema, 2009), the main effect of adolescent sex was statistically significant in both the mother and father models, indicating higher levels of depressive symptoms among females. In addition, adolescents' baseline depression was a strong predictor of subsequent depressive symptoms. Parenting quality and adolescent polygenic sensitivity were not significant independent predictors of youth depression, although the maternal parenting by adolescent polygenic sensitivity two-way interaction was significant. The effect of fathers' parenting on adolescent depressive symptoms did not vary as a function of adolescent polygenic sensitivity.

Post-hoc simple slope analyses revealed that the association between maternal parenting and adolescent depressive symptoms was significant among adolescents with high (+1 *SD*), but not low (−1 *SD*), polygenic sensitivity scores (see Figure 1). Adolescents with higher scores on the polygenic sensitivity index reported more depressive symptoms one year later if they were exposed to maternal parenting behaviors marked by high levels of hostility and low levels of warmth; yet, in the presence of high warmth and low hostility maternal parenting, adolescents with higher scores on the index reported fewer depressive symptoms one year later, consistent with differential susceptibility. Adolescents in the low sensitivity group were essentially unaffected by maternal parenting quality.

Anxiety symptoms—The main effect model predicting adolescent anxiety symptoms was significant for the mother model, $F(6, 316) = 14.17$, $p < .001$, as well as the father model, $F(6, 316) = 13.22$, $p < .001$. Baseline anxiety symptoms were significantly associated with T2 anxiety symptoms in both models. The main effects of parenting quality and adolescent polygenic sensitivity were not statistically significant, although the two-way interactions between parenting quality and adolescent polygenic sensitivity were significant for both mothers and fathers.

As shown in Figure 2, post-hoc analyses indicated that adolescents with high polygenic sensitivity (+1 *SD*) reported the highest levels of anxiety one year later when exposed to high levels of maternal hostility and low levels of maternal warmth and the lowest levels of anxiety in the context of high maternal warmth and low maternal hostility. When probing the significant interaction between fathers' parenting quality and adolescent polygenic sensitivity, the simple slope of parenting quality predicting to adolescent anxiety was not significant at one *SD* above or below the mean of adolescent polygenic sensitivity; therefore, we probed the interaction effect for the father model at two *SDs* above and below the mean. Figure 4 demonstrates that adolescents with high polygenic sensitivity (+2 *SD*) reported the highest levels of anxiety when exposed to more hostile (and less warm) paternal behaviors and the lowest levels of anxiety in the context of more warm (and less hostile) parental behaviors. There was no significant association between parenting and anxiety among the low sensitivity (−2 *SD*) group.

Hostility symptoms—The main effect regression model explained a significant portion of the variance in adolescent hostility symptoms for both the mother, $F(6, 316) = 4.37$, $p < .001$, and father model, $F(6, 316) = 4.22$, $p < .001$. Adolescents' hostility at T1 was a significant predictor of later hostility in both models. The independent effects of maternal and paternal parenting quality and adolescent polygenic sensitivity were not statistically significant, although the two-way interaction between parenting and adolescent polygenic sensitivity was statistically significant for both mothers and fathers.

Results from simple slope analyses for maternal parenting predicting adolescent hostility are presented in Figure 3. Adolescents high in polygenic sensitivity (+1 *SD*) reported more symptoms of hostility if exposed to more hostile and less warm maternal parenting behaviors one year prior, but reported fewer symptoms of hostility if exposed to more warm and less hostile maternal parenting behaviors. Again, when probing the significant interaction between paternal parenting quality and adolescent polygenic sensitivity, the simple slopes for fathers' parenting behaviors predicting to adolescent hostility were not significant at one *SD* above or below the mean of adolescent polygenic sensitivity. When testing the simple slopes at two *SD* above and below the mean, however, findings indicated that adolescents who scored higher on the polygenic sensitivity index (+ 2 *SD*) reported higher levels of hostility in the context of hostile parenting quality, but fewer symptoms of hostility in the context of warm parenting quality (see Figure 5). Fathers' parenting did not have significant effects on adolescent hostility symptoms among the low polygenic sensitivity (−2 *SD*) group.

Sex differences in G×E interactions—To examine whether the moderating effect of adolescent polygenic sensitivity might operate differently for adolescent boys and girls, we tested a series of models with three-way interaction terms between parenting quality, adolescent polygenic sensitivity, and adolescent sex for each outcome, controlling for symptoms at T1, parent education, and family income-to-needs ratio. No second-order interactions were significant; therefore, adolescent sex was included only as a covariate. For the sake of brevity, nonsignificant interaction models are omitted from the results presented here. In sum, the pattern of G×E results was consistent for both adolescent girls and boys.

Discussion

Guided by the differential susceptibility framework (Belsky & Pluess, 2009, 2013), we investigated whether adolescents' genetic sensitivity moderated longitudinal associations between mothers' and fathers' parenting behaviors toward their adolescent children and adolescents' internalizing and externalizing problems one year later. Results showed that adolescents' genetic sensitivity, assessed by a composite polygenic score of five dopaminergic and serotonergic genes (*5-HTT*, *ANKK1*/*DRD2*, *DRD4*, *DAT*, and *COMT*), significantly moderated the associations between observational measures of mothers' parenting and adolescents' depressed mood, anxiety symptoms and hostility one year later, and between observations of fathers' parenting and adolescents' later anxiety and hostility (but not depressive symptoms). Compared to adolescents who had low scores on polygenic sensitivity, adolescents with high polygenic sensitivity scores were more depressed, more anxious, and more hostile when they experienced high levels of negative (i.e., the combination of high hostility and low warmth) maternal parenting; yet, were less depressed, less anxious, and less hostile when they experienced high levels of positive maternal parenting (i.e., high warmth and low hostility). Similarly, adolescents with high polygenic sensitivity scores were more anxious and more hostile when they experienced high levels of fathers' negative parenting yet were less anxious and hostile when they experienced high levels of fathers' positive parenting compared to adolescents who had low scores on polygenic sensitivity.

These results are consistent with the differential susceptibility model (Belsky & Pluess, 2009, 2013) and indicate that adolescents' polygenic sensitivity moderated the associations between both mothers' and fathers' T1 parenting and adolescents' T2 adjustment outcomes at 14 years of age. These effects held even after controlling for adolescents' baseline levels of adjustment at 13 years of age. Adolescents who scored high on polygenic sensitivity were more affected in terms of their psychological adjustment by both positive (i.e., "for better) and negative aspects (i.e., "for worse") of parenting than were adolescents who had lower scores on polygenic sensitivity. It is important to note that we found support for the differential susceptibility hypothesis for both positive (warmth, support, positive communication) as well as negative (hostility, angry-coercion, and antisocial behavior) parental behaviors; thus, our measure of parenting ranged from low levels of warmth with a combination of high hostility (i.e., negative valence of parenting) to low levels of hostility with a combination of high warmth (i.e., positive valence of parenting). Much of the previous G×E research has tended to focus solely on negative aspects of parenting or other measures of environmental adversity or has assumed that the absence of parental hostility is equivalent to the presence of parental warmth (see Caspi et al., 2010; Duncan & Keller, 2011 for reviews). In short, consistent with past research, we found that mothers' and fathers' parenting had longitudinal influences on adolescents' adjustment (see Barber, et al., 2005; Maccoby, 2000 for reviews). Our novel contribution to this literature was that these associations were moderated by adolescents' polygenic sensitivity across a set of serotonergic and dopaminergic genes.

The mechanisms by which adolescents' genetic sensitivity moderates the association between parenting and adolescents' psychological adjustment have not been definitively

identified in the literature. However, by examining the neuropsychological functioning of the serotonergic and dopaminergic systems, we can propose some plausible hypotheses. The serotonergic system has been linked to punishment and displeasure (e.g., Caspi et al., 2010), and the dopaminergic system has been associated with reward sensitivity and sensation seeking (e.g., Dreher et al., 2009; Stice et al., 2012). As noted by Belsky and Pluess (2009), variants in genes from these systems expressed in the limbic system, and in particular, the amygdala, have been associated with increased emotional sensitivity to the environment). Thus, adolescents who—for reasons having to do with genetics—are particularly sensitive to reward (e.g., parental warmth and support), as well as punishment (e.g., parental hostility and angry-coercion) may be more affected in terms of their psychological adjustment compared to adolescents with less genetic sensitivity. Additional neuropsychological research is needed to more fully understand how genetic characteristics are linked to sensitivity to the environment and, in turn, moderate (i.e., interact with) environmental influences.

In the current study, we used polygenic sensitivity scores to move beyond methodological and conceptual problems of testing single candidate genes (see Duncan & Keller, 2011 for a review). We created scores by adding variants of five genes from the serotonergic and dopaminergic systems. This strategy was predicated on the notion that complex psychological constructs are influenced by small effects of a number of genetic variants rather than by a single candidate gene variant (Evans et al., 2013; Sullivan, et al., 2012). Our significant results add to those from several other researchers showing that the role of genetic sensitivity, assessed by polygenic index scores, moderates the associations between the environment and later adjustment and behavior in romantic relationships (Dalton et al., 2014; Masarik et al., 2014; Simons et al., 2012; Wickrama & O'Neal, 2013).

We found that adolescents' genetic sensitivity moderated the links between mothers' and fathers' parenting and all the measures of adolescent adjustment (depression, anxiety, and hostility), with one exception: there was no genetic moderation for the association between fathers' parenting and adolescents' depressive symptoms. Relatively little research has examined whether associations between parenting quality and adolescent depression vary for mothers and fathers (Lewis & Lamb, 2003). However, our results are consistent with those from a recent study that found longitudinal associations between maternal, but not paternal, hostility and adolescent depressive symptoms (Lewis, Collishaw, Thapar, & Harold, 2014). Furthermore, when we probed and plotted the significant parenting by genetic sensitivity interactions, we needed to use a 2 *SD* cut-off for low and high levels of adolescent polygenic sensitivity involving fathers' parenting and only a 1 *SD* cut-off for low and high levels of adolescent polygenic sensitivity involving mothers' parenting. Thus, the regions of significance for the observed G×E interactions were slightly different for mother versus father parenting behaviors, perhaps indicating stronger G×E effects for mothers' parenting. Our findings are some of the first that include fathers' parenting and support the notion that further research is needed concerning potential G×E differences between mothers' and fathers' parenting as well as their independent influence on adolescent adjustment.

Our final set of analyses showed that the moderating effect of adolescent genetic sensitivity did not differ by adolescent sex in either the mother or father parenting models. In other

words, there was no evidence to suggest that parenting was more impactful for: (a) father–son versus father–daughter dyads; or for (b) mother–son versus mother–daughter dyads. Some previous research has found higher rates of G×E interaction for parenting and adjustment for boys (Li et al., 2009) and others for girls (Dalton et al., 2014), while most research has not considered sex differences (see Duncan & Keller, 2011; Karg et al., 2011 for reviews). Further research is needed on possible differences in these processes for male and female adolescents.

In addition to considering sex differences, behavioral geneticists have pointed out the importance of ruling out GE correlations (i.e., *r*GE) when interpreting G×E interactions (Caspi & Moffit, 2006; Jaffee & Price, 2007). Our analyses showed that there was little evidence to suggest an evocative genetic effect on the part of the adolescent since adolescents' genetic sensitivity was not significantly associated with the type of behavior they received from mothers or fathers. In other words, adolescents who were high on polygenic sensitivity did not elicit different levels of maternal or paternal warmth or hostility compared to adolescents who were low on polygenic sensitivity. Instead, adolescents' genetic sensitivity moderated the effect that parenting behaviors had on their adjustment.

To summarize the strengths of this study, we found support for the differential susceptibility hypothesis over time using prospective, longitudinal data; whereas most previous G×E research has used retrospective reports of parenting or has been cross-sectional (see Duncan & Keller, 2011; Karg et al., 2011 for reviews). We also controlled for the level of adolescents' internalizing and externalizing behaviors at Time 1; thus, our significant G×E results indicate that adolescent polygenic sensitivity moderated the link between parents' behavior and rank-order change in adolescents' adjustment. Moreover, we assessed both positive and negative dimensions of parenting for both mothers and fathers whereas previous research has primarily focused on mothers' parenting behaviors only and/or has tended to assess only negative aspects of parenting behaviors (or other aspects of early family adversity). Another strength is that our data consisted of independent measures of parenting behavior (trained observer report) and adolescent adjustment (self-report). Hence, the results are unlikely to be explained by shared method variance. In addition, we demonstrated that the results were not explained by GE correlations. In other words, it was not the case that genetically sensitive adolescents elicited particular types of behavior from their parents. Finally, much of the previous research in this area has focused on single candidate genes (Caspi et al., 2010; Duncan & Keller, 2011; Karg et al., 2011). We used polygenic sensitivity scores that take into account that most genetic influence on complex psychological variables operates by additive effects of a number of genetic variants, each with a small effect (Sullivan et al., 2012).

Despite these strengths, there are several limitations to this study. Our sample was predominantly Caucasian and from rural America. This relatively homogeneous sample is advantageous for genetic analyses because it avoids problems of population stratification and spurious associations due to ethnic group differences (Cardon & Palmer, 2003). Nevertheless, further research is needed on samples with different ethnic backgrounds and from different geographic regions to ensure generalizability of these results. In addition, we

used a community sample, and it is possible that genetic sensitivity would operate differently in extreme levels of family adversity or for adolescents' with clinical diagnoses.

In conclusion, our findings indicate that adolescents' genetic sensitivity moderated the links between both mothers' and fathers' parenting and adolescents' internalizing and externalizing problems; these findings further support the idea that there are variations in how individuals respond to their environments for reasons having to do with genetics. One implication of this is that intervention programs might need to be tailored to address the potentially different learning styles and reward systems for those children and adolescents who are high on genetic sensitivity and for those who are low on genetic sensitivity (van Ijzendoorn & Bakersman-Kranenburg, 2014). Future research on the practical implications of differential genetic sensitivity is needed. Our results highlight the importance of assessing adolescents' genetic characteristics when investigating associations between parenting and adolescents' psychological adjustment and demonstrate one of the complex ways that nature and nurture work together to influence development.

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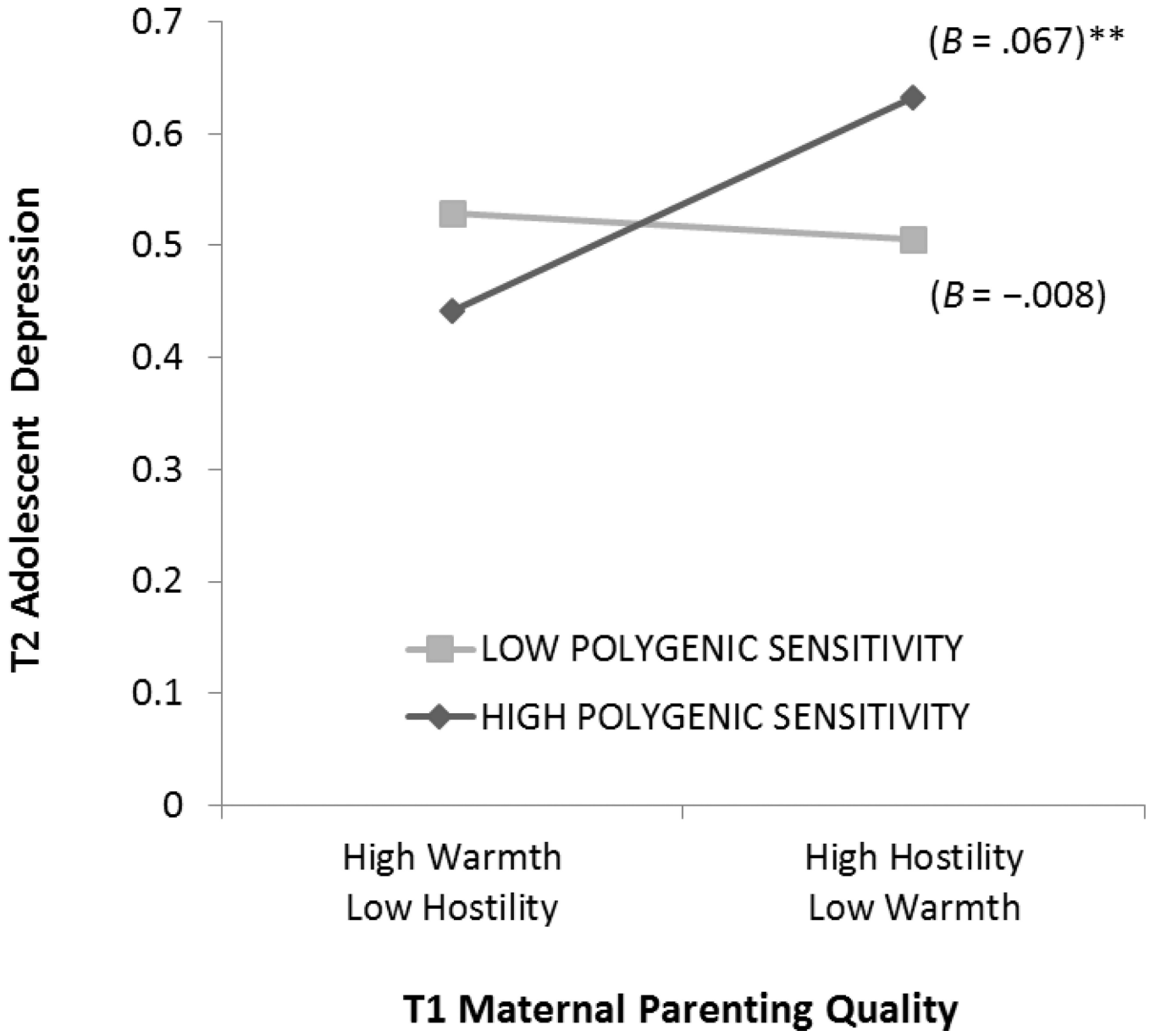

Figure 1.

The prospective association between observed maternal parenting quality and adolescent *SCL-90-R* Depression at high (+1 *SD*) and low (−1 *SD*) levels of adolescent polygenic sensitivity. *B* = unstandardized regression coefficient.

**$p < 01$.

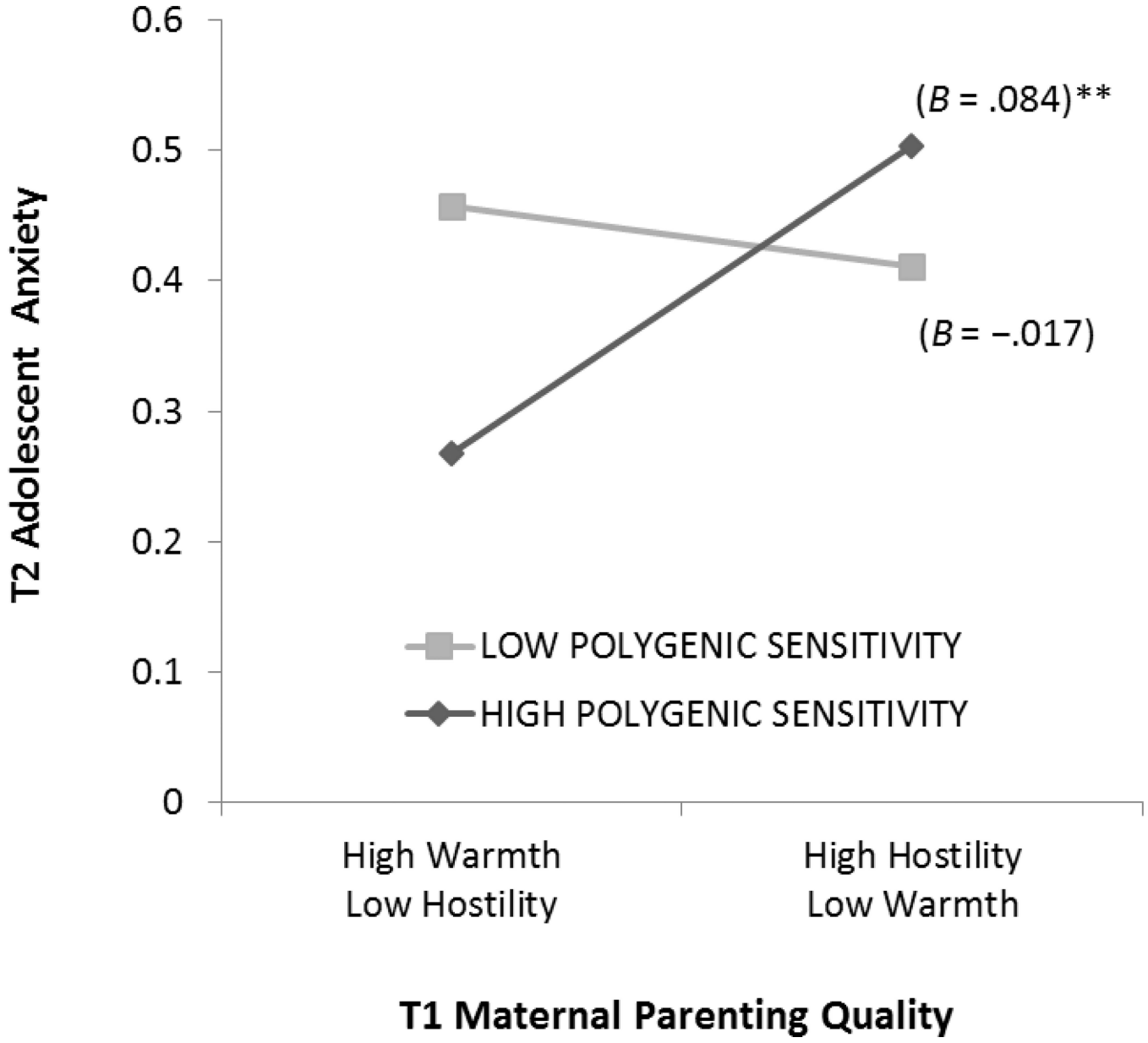

Figure 2.

The prospective association between observed maternal parenting quality and adolescent *SCL-90-R* Anxiety at high (+1 *SD*) and low (−1 *SD*) levels of adolescent polygenic sensitivity. *B* = unstandardized regression coefficient.

**$p < .01$.

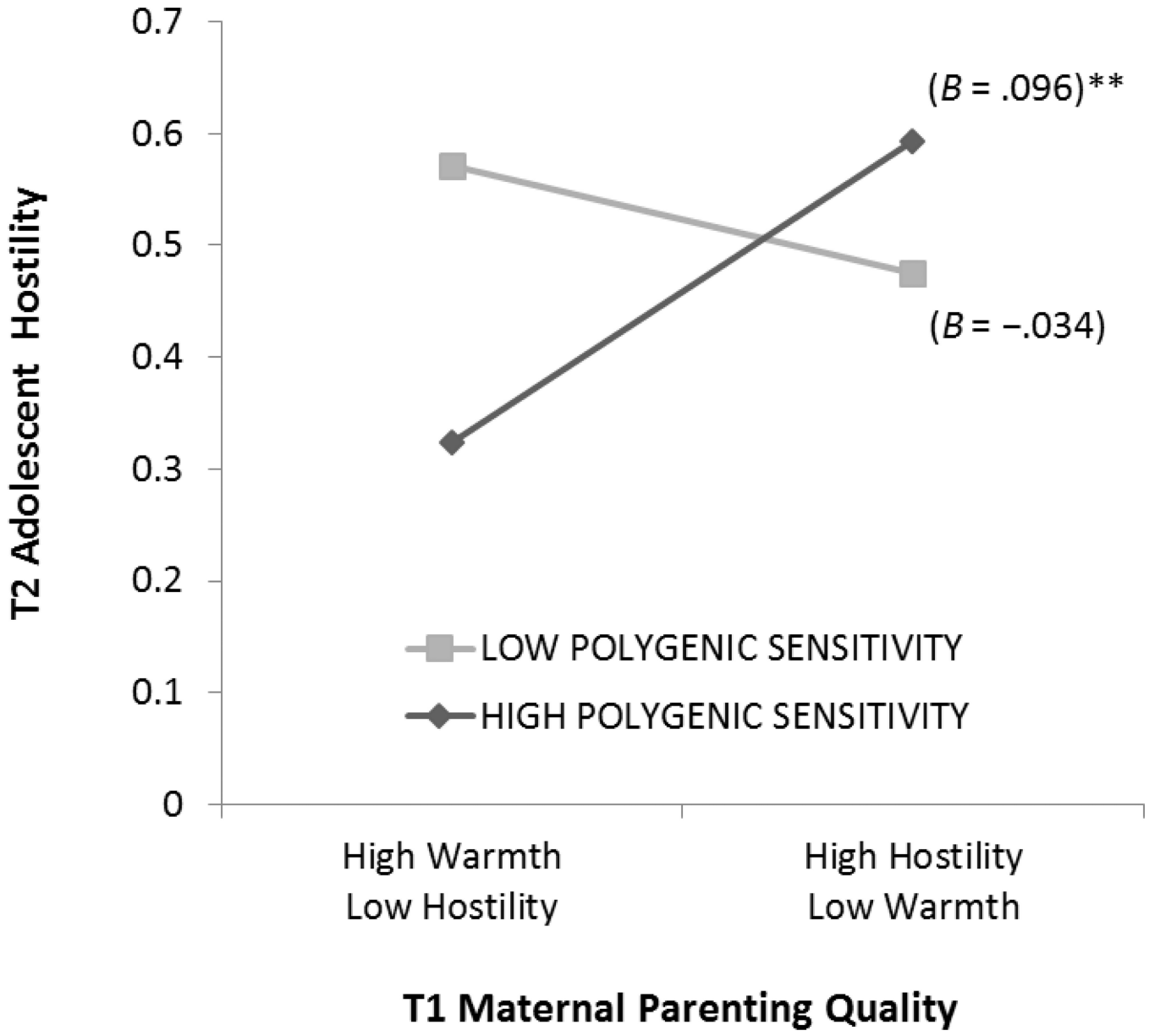

Figure 3.

The prospective association between observed maternal parenting quality and adolescent *SCL-90-R* Hostility at high (+1 *SD*) and low (−1 *SD*) levels of adolescent polygenic sensitivity. *B* = unstandardized regression coefficient.

**$p < .01$.

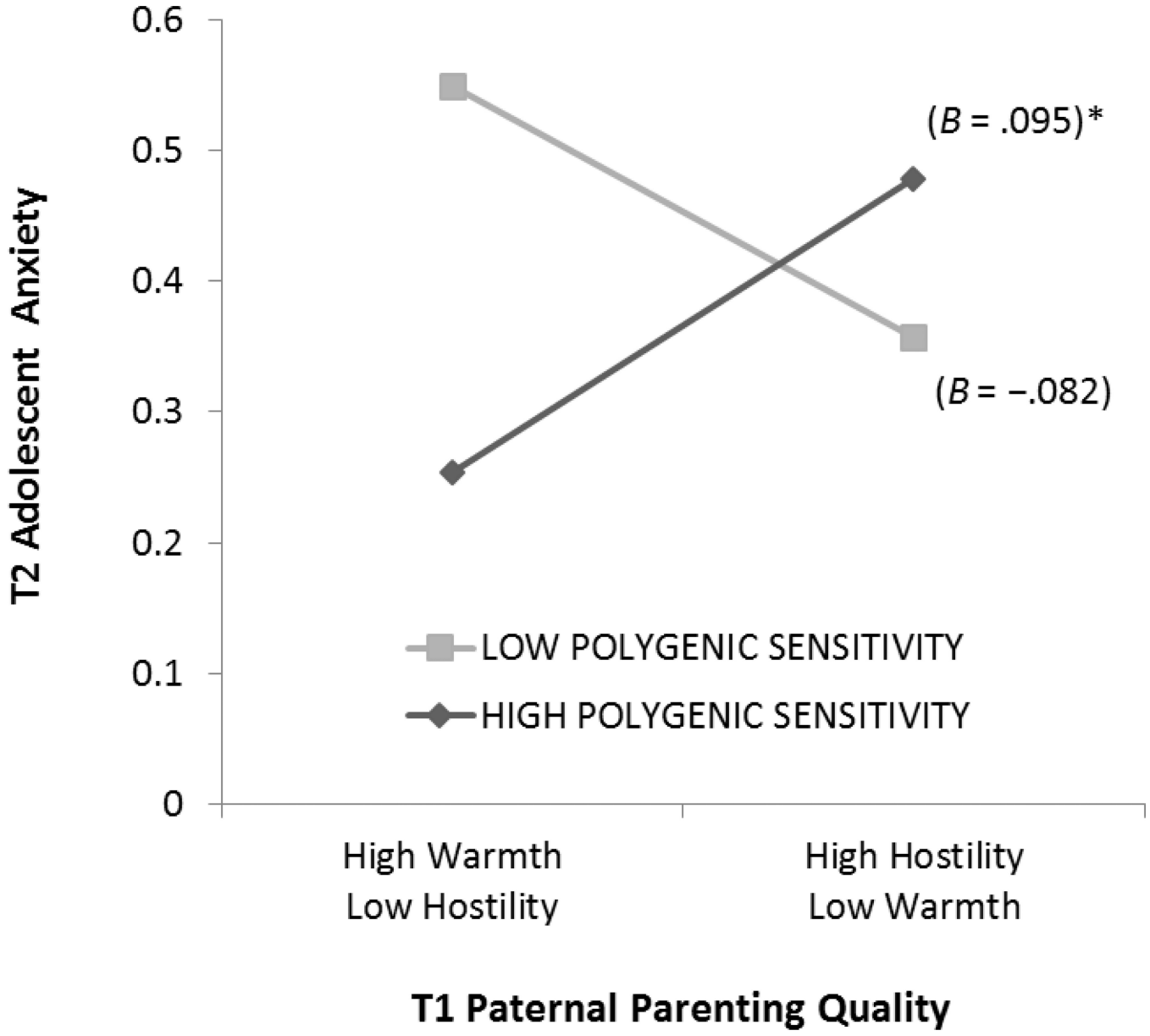

Figure 4.

The prospective association between observed paternal parenting quality and adolescent *SCL-90-R* Anxiety at high (+2 *SD*) and low (−2 *SD*) levels of adolescent polygenic sensitivity. *B* = unstandardized regression coefficient.

**p* < .05.

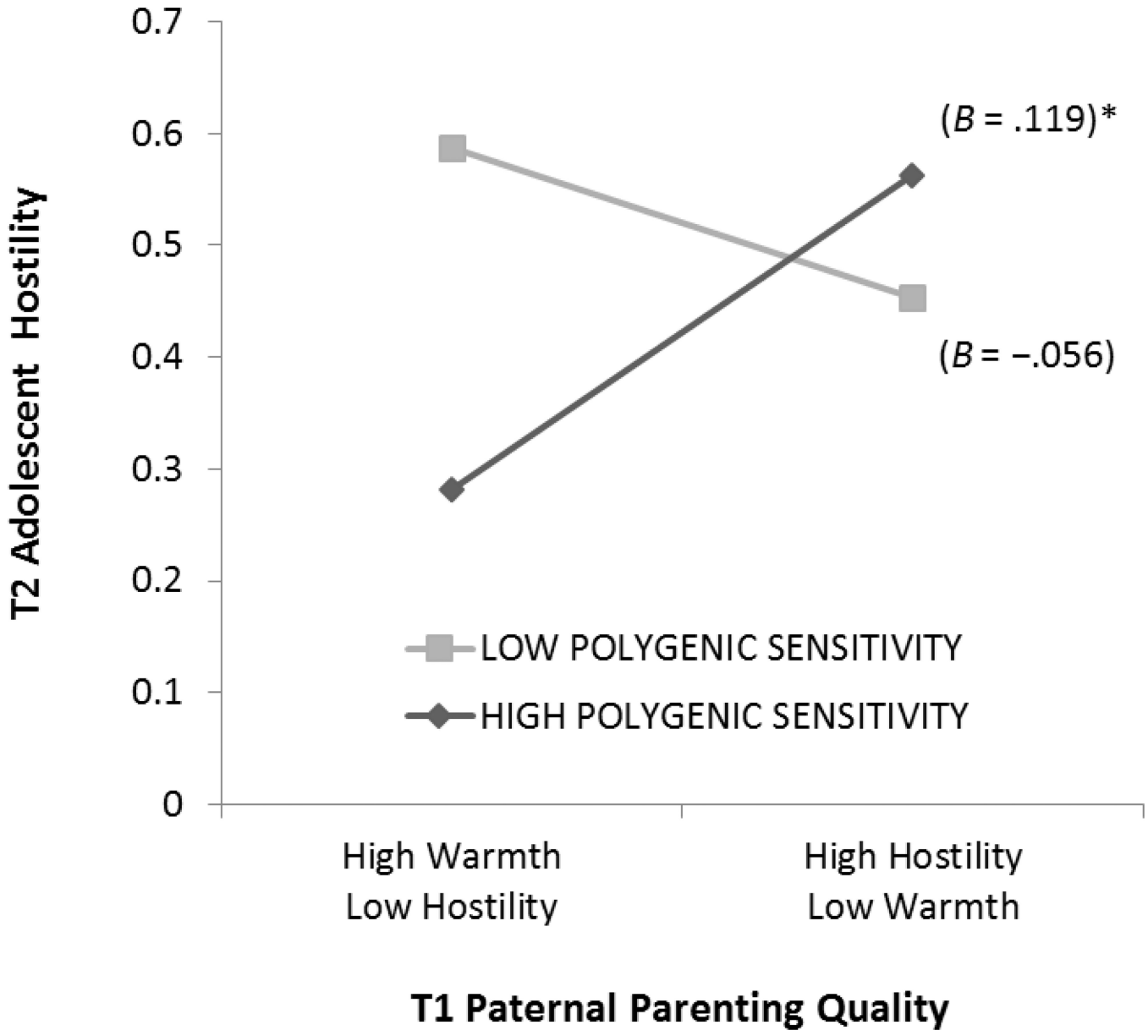

Figure 5.

The prospective association between observed paternal parenting quality and adolescent *SCL-90-R* Hostility at high (+2 *SD*) and low (−2 *SD*) levels of adolescent polygenic sensitivity. *B* = unstandardized regression coefficient.

**p* < .05.

Table 1

Descriptive Statistics and Intercorrelations Among Study Variables

	M or %	SD	1	2	3	4	5	6	7	8	9	10	11	12
Time 1: Predictors														
1. Adolescent depressive symptoms	.63	.61	—											
2. Adolescent anxiety symptoms	.51	.53	.78***	—										
3. Adolescent hostility symptoms	.61	.68	.67***	.69***	—									
4. Maternal parenting quality	3.25	1.40	.07	.10†	.13*	—								
5. Paternal parenting quality	3.63	1.19	.08	.10†	.15**	.47***	—							
6. Adolescent polygenic sensitivity	4.41	1.36	−.02	−.01	−.02	.01	.01	—						
7. Adolescent sex (male)	45%	—	−.13*	.02	.07	.01	−.01	.02	—					
Time 1: Family SES														
8. Maternal education	13.27	1.63	−.04	−.03	−.08	−.15**	−.19**	.03	.04	—				
9. Paternal education	13.62	2.24	−.11†	.13*	−.08	−.09†	−.25***	.06	−.05	.04	—			
10. Family income-to-needs ratio	2.93	2.18	.03	.13*	−.03	−.14*	−.15**	−.06	−.01	.08	.25***	—		
Time 2 Outcomes														
11. Adolescent depressive symptoms	.47	.48	.53***	.45***	.36***	.11†	.05	.02	−.18**	−.02	.04	.02	—	
12. Adolescent anxiety symptoms	.39	.48	.42***	.44***	.37***	.13*	.07	−.05	−.04	−.10†	−.08	−.03	.70***	—
13. Adolescent hostility symptoms	.48	.55	.38***	.44***	.51***	.13*	.10†	−.05	.02	.03	−.01	.02	.62***	.64***

Note. (N = 323). Psychiatric symptoms assessed using the *SCL-90-R*.

† $p < 10$,

* $p < .05$,

** $p < .01$,

*** $p < .001$ (2-tailed tests).

Table 2

Gene by Environment Interactions Between Adolescent Cumulative Polygenic Sensitivity and Maternal Parenting Quality Predicting Change in Adolescent Adjustment

	Depression				Anxiety				Hostility			
Predictors	***B***	***SE B***	**β**	**ΔR^2**	***B***	***SE B***	**β**	**ΔR^2**	***B***	***SE B***	**β**	**ΔR^2**
Main Effects												
Adolescent sex[a]	−.12	.05	−.12*		−.04	.05	−.05		−.02	.05	−.02	
Previous adolescent symptoms	.40	.04	.51***		.39	.05	.43***		.41	.04	.51***	
Maternal parenting quality	.03	.02	.07		.03	.02	.08		.03	.02	.08	
Adolescent polygenic sensitivity	.01	.02	.03		−.01	.02	−.04		−.02	.02	−.05	
R^2		.296***				.212***				.274***		
Interaction Effects												
Maternal Parenting × Polygenic Sensitivity	.03	.01	.11*	.011*	.04	.01	.15**	.021**	.05	.01	.17**	.027**

Notes. (N = 323). Predictors were measured at Time 1. Psychiatric symptoms assessed using the *SCL-90-R*. All main effect predictor variables were entered simultaneously in Step 1. Socioeconomic indicators including parent education and family income-to-needs ratio were included as statistical controls; however, none were statistically significant and are not presented here due to space considerations.

[a](0 = *female*, 1 = *male*).

*$p < .05$,

**$p < .01$,

***$p < .001$ (2-tailed tests).

Table 3

Gene by Environment Interactions Between Adolescent Cumulative Polygenic Sensitivity and Paternal Parenting Quality Predicting Change in Adolescent Adjustment

	Depression				Anxiety				Hostility			
Predictors	***B***	***SE B***	**β**	**ΔR^2**	***B***	***SE B***	**β**	**ΔR^2**	***B***	***SE B***	**β**	**ΔR^2**
Main Effects												
Adolescent sex[a]	−.11	.05	−.12*		−.05	.05	−.05		−.01	.05	−.01	
Previous adolescent symptoms	.40	.04	.51***		.39	.05	.44***		.41	.04	.51***	
Paternal parenting quality	.01	.02	.02		.01	.02	.02		.02	.02	.03	
Adolescent polygenic sensitivity	.01	.02	.03		−.02	.02	−.04		−.02	.02	−.04	
R^2		.294***				.201***				.265***		
Interaction Effects												
Paternal Parenting × Polygenic Sensitivity	.02	.01	.06	.004	.03	.02	.11*	.012*	.04	.02	.10*	.011*

Notes. (*N* = 323). Predictors were measured at Time 1. Psychiatric symptoms assessed using the *SCL-90-R*.All main effect predictor variables were entered simultaneously in Step 1. Socioeconomic indicators including parent education and family income-to-needs ratio were included as statistical controls; however, none were statistically significant and are not presented here due to space considerations.

[a](0 = *female* , 1 = *male*).

* $p < .05$,

** $p < .01$,

*** $p < .001$ (2-tailed tests).