Development and Psychopathology **29** (2017), 791–803

doi:10.1017/S095457941600047X

Youth temperament, harsh parenting, and variation in the oxytocin receptor gene forecast allostatic load during emerging adulthood

GENE H. BRODY,[a] TIANYI YU,[a] ALLEN W. BARTON,[a] GREGORY E. MILLER,[b] AND EDITH CHEN[b]
[a]*University of Georgia; and* [b]*Northwestern University*

Abstract

An association has been found between receipt of harsh parenting in childhood and adult health problems. However, this research has been principally retrospective, has treated children as passive recipients of parental behavior, and has overlooked individual differences in youth responsivity to harsh parenting. In a 10-year multiple-wave prospective study of African American families, we addressed these issues by focusing on the influence of polymorphisms in the oxytocin receptor gene (*OXTR*), variants of which appear to buffer or amplify responses to environmental stress. The participants were 303 youths, with a mean age of 11.2 at the first assessment, and their parents, all of whom were genotyped for variations in the rs53576 (A/G) polymorphism. Teachers rated preadolescent (ages 11 to 13) emotionally intense and distractible temperaments, and adolescents (ages 15 and 16) reported receipt of harsh parenting. Allostatic load was assessed during young adulthood (ages 20 and 21). Difficult preadolescent temperament forecast elevated receipt of harsh parenting in adolescence, and adolescents who experienced harsh parenting evinced high allostatic load during young adulthood. However, these associations emerged only among children and parents who carried A alleles of the *OXTR* genotype. The results suggest the oxytocin system operates along with temperament and parenting to forecast young adults' allostatic load.

Receipt during childhood and adolescence of parenting characterized by frequent striking and shouting (which we term harsh parenting here in this article) has been associated consistently with learning difficulties, anxiety, depression, and aggression (Cicchetti & Toth, 2005). Recent research also indicates that harsh parenting exerts less visible adverse effects on youths' vulnerability to chronic diseases of aging, particularly those in the cardiometabolic domain, such as diabetes, heart disease, and stroke (Miller, Chen, & Parker, 2011). For example, the Adverse Childhood Experiences Study assessed the medical histories of more than 17,000 adults and found that the rates of cardiovascular disease, autoimmune disorders, and premature death were 1.5 to 2.0 times higher among respondents who were exposed to family violence than among those who were not exposed (Dube et al., 2009). Other studies reveal that adults reared in harsher home environments evince higher blood pressure, poorer metabolic profiles, greater inflammatory activity, and higher levels of depressive symptoms than do adults reared in less harsh households (Miller et al., 2011; Repetti, Taylor, & Seeman, 2002).

Using a 10-year multiple-wave, multiple-informant research design, in the present study we sought to advance understanding of the association between harsh parenting practices and health status by testing hypotheses involving prospective pathways among child temperament, harsh parenting, and health outcomes with a representative sample of rural African American adolescents. Specifically, the study was designed to clarify several conceptual and empirical issues in the emerging literature on harsh parenting practices and children's later health outcomes. First, past research addressing links between exposure to harsh parenting and indicators of health has depicted children as passive recipients of parental behavior. Children, however, are part of a dynamic system in which their behavioral styles and temperaments contribute to the rearing practices they receive (Lengua & Kovacs, 2005). Second, with one exception (Danese et al., 2009), existing research has relied primarily on retrospective reports of receipt of harsh parenting. This design precludes investigation into processes of change and has the potential to confound harsh parenting with family conflict, family violence, and neighborhood violence. Third, research has not considered the possibility that children's physiological responses to harsh parenting can differ depending on their genetic makeup. Previous research has revealed genetic moderation effects on the association between parental maltreatment and children's mental and behavioral health (Belsky & Pluess, 2009; Cicchetti & Rogosch, 2012; Kim-Cohen et al., 2006). To circumvent these limitations, this study used a longitudinal research design to examine questions concerning temporal relations among child temperament, harsh parenting, and allostatic load (AL), and the moderation of these relations by a variant in the oxytocin receptor gene (*OXTR* rs53576).

The research reported in this article was supported by Grant P30 DA027827 from the National Institute on Drug Abuse and Grant R01 HD030588 from the National Institute of Child Health and Human Development.

Address correspondence and reprint requests to: Gene H. Brody, University of Georgia, Center for Family Research, 1095 College Station Road, Athens, GA 30602-4527; E-mail: gbrody@uga.edu.

The study outcome, AL, is the toll that stress exacts on the body by changing multiple, interconnected systems. AL is often operationalized as a composite reflecting various mediators and outcomes of the stress response, including the sympathetic–adrenomedullary system, the hypothalamus–pituitary–adrenal axis, lipid metabolism, fat deposition, indices of inflammation, and immune functioning (McEwen, 2000). AL composites have been shown to predict the onset of cardiovascular disease and all-case mortality later in life (Karlamangla, Singer, & Seeman, 2006). We hypothesized that emotionally intense and distractible temperaments, to which researchers often refer as "difficult," during preadolescence would forecast elevated levels of AL in young adulthood, with this effect mediated by increased exposure to harsh parenting during adolescence. In the following sections, we discuss the hypothesized prospective associations among child temperament, harsh parenting, and poor health, along with the moderating effect of a variant in *OXTR*.

Child Temperament, Harsh Parenting, and Health

To address the first purpose of this study, we investigated prospective relations among child temperament in preadolescence, changes in harsh parenting during adolescence, and cardiovascular health risk in late adolescence as measured by an AL index. Most research conducted with adolescents has focused on parents' influence on youths, whereas youths' influence on parents has been understudied (Laursen & Collins, 2009). This stands in contrast to an established body of research that has highlighted reciprocity in the parent–child relationship and children's contributions to the rearing practices they receive (Lengua & Kovacs, 2005). For example, child temperament has been shown to have an evocative effect on parenting. The literature on determinants of parenting indicates that rearing a child with a difficult temperament, which includes characteristics such as low levels of positivity, highly intense reactions, and distractibility (Laukkanen, Ojansuu, Tolvanen, Alatupa, & Aunola, 2014), can tax caregivers, leading even the most capable parents to use harsh parenting practices (Sanson & Rothbart, 1995).

Temperament refers to biologically rooted and relatively stable individual differences in emotional, physiological, and attentional reactivity and regulation (Posner & Rothbart, 2007). Childhood temperament is widely understood to be a multifaceted construct, involving dimensions related to areas such as negative affectivity, effortful control, and surgency (Else-Quest, Hyde, Goldsmith, & Van Hulle, 2006). The current study included two dimensions of temperament, negative affectivity and distractibility. Negative affectivity describes general tendencies to express negative emotions, including distress, anger, or fear (Rothbart & Bates, 1998). Distractibility describes the inability to focus attention; it is a behavioral indicator of the broad temperament domain of effortful control (Else-Quest et al., 2006). Both negative emotionality and distractibility persist as distinct characteristics across childhood, adolescence, and adulthood (Putnam, Ellis, & Rothbart, 2001). Further, children and adolescents displaying such temperaments often receive elevated levels of negative parenting, as documented in both observational (Davenport, Yap, Simmons, Sheeber, & Allen, 2011; Kim, Conger, Lorenz, & Elder, 2001) and self-report (Laukkanen et al., 2014) studies. This association between children's negative emotionality and unsupportive parenting appears to be stronger in low socioeconomic status (SES) families and among ethnic minorities (Paulussen-Hoogeboom, Stams, Hermanns, & Peetsma, 2007), such as the families in the current sample.

In addition to influencing parenting practices, emerging research also suggests childhood temperament may be associated with physical health into adulthood. The findings from the Cardiovascular Risk in Young Finns Study (a population-based study in Finland spanning more than 20 years) document the ways in which aspects of youth temperament prospectively predict elevated body mass index (Pulkki-Råback, Elovainio, Kivimäki, Raitakari, & Keltikangas-Järvinen, 2005); low parasympathetic activity (Puttonen et al., 2008), high systolic blood pressure; and, in women only, intima media thickness (a risk factor for atherosclerosis; Keltikangas-Järvinen, Pulkki-Råback, Puttonen, Viikari, & Raitakari, 2006). These effects of child temperament on young adult health appeared independent of childhood and adulthood risk factors for adult obesity. Beyond direct effects, however, few investigations have examined pathways that account for this effect, including the quality of the parenting that difficult temperament elicits.

OXTR as a Moderator

Regarding the second purpose of this study, we investigated the reasons why many caregivers, despite rearing a child with a difficult temperament, do not use harsh parenting practices and why many youths, despite exposure to harsh parenting, do not show elevated levels of AL. The current study specifically considered whether, for genetic reasons, parents and children differ in the extent to which they are affected by aspects of their environment. During the past decade, research investigated the hypothesis that particular genetic polymorphisms amplify individuals' reactions to stressful conditions in their environment, thereby enhancing the probability of compromised behavioral, mental, or physical health functioning (Way & Taylor, 2010). Some of this research has investigated the hypothesis that oxytocin has anxiolytic or calming effects. Oxytocin moderates neural and behavioral responses to aversive stimuli and attenuates cardiovascular and neuroendocrine reactivity to laboratory stressors (Campbell, 2010). Some of the individual differences in social interaction reactivity as a function of oxytocin are conferred by polymorphisms in the gene that codes for *OXTR*. One of the most studied polymorphisms is rs53576, a single nucleotide variant involving a silent G to A change in the third intron of *OXTR* (Klahr, Klump, & Burt, 2015).

Two bodies of research support the proposition that *OXTR* genotype will moderate the associations among difficult tem-

perament, harsh parenting, and AL. The first was generated by scientists who sought to determine whether polymorphisms in *OXTR* affected social behavior. The results from this line of research indicated that, compared to carriers of the GG genotype, persons with the A allele (the A+ genotype) exhibited diminished positive affect (Lucht et al., 2009) and prosocial behavior (Kogan et al., 2011), along with low maternal warmth (Klahr et al., 2015). Additional research suggests A+ allele carriers experience heightened depressive symptomology, with this effect largely mediated by the influence of *OXTR* on individuals' lack of psychological resources such as optimism, mastery, and self-esteem (Saphire-Bernstein, Way, Kim, Shermna, & Taylor, 2011). Findings on the effects of *OXTR* on social temperament and social relationships have been replicated in studies with individuals of European and African ancestry (Creswell et al., 2015). However, a study by Michalska et al. (2014) did not replicate this pattern; rather, they found higher levels of positive parenting among carriers of the A+ genotype than among GG carriers. These main effects of *OXTR* genotype should be interpreted with caution (Bakermans-Kranenburg & van IJzendoorn, 2014), but such divergent findings should not rule out the possibility that parents and their offspring who carry the A+ genotype are more reactive to difficult temperament and harsh parenting, respectively, than are carriers of the GG genotype.

The second body of research was conducted by scientists testing hypotheses involving *OXTR* and exposure to stressful life events. These studies described the ways in which genetic variability at *OXTR* alters individuals' reactivity to stressful life conditions. To date, evidence is somewhat mixed regarding the nature of the polymorphisms at *OXTR* rs53576 that confer heightened susceptibility. One body of research has found that adults carrying the G allele at rs53576, relative to those who carry the A allele, are more susceptible to both supportive (Chen et al., 2011) and harsh (Bradley et al., 2011) social interactions. In the one *OXTR* moderation study we identified with an exclusively African American sample, carriers of the GG genotype exhibited greater emotional dysregulation and disorganized attachment as a result of childhood maltreatment than did A+ carriers (Bradley et al., 2011). Conversely, a second body of research suggests that individuals carrying the A allele at rs53576 are more responsive to contextual stressors. These studies suggest that carriers of the A+ genotype display more behavioral, neural, and affective reactivity to interpersonal stressors than do persons with the GG genotype (Poulin, Holman, & Buffone, 2012; Rodrigues, Saslow, Garcia, John, & Keltner, 2009; Thompson et al., 2014; Tost et al., 2010).[1] While the literature is not consistent, we resonated to the results of the aforementioned second body of research and translated those findings into the study hypotheses. Specifically, we hypothesized that (a) parents who carry the A+ *OXTR* genotype would increase their use of harsh parenting over time, more than will carriers of the GG *OXTR* genotype, when their child was noted as having a difficult temperament; and (b) youth who carry the A+ *OXTR* genotype will show higher AL levels at ages 20 and 21, relative to carriers of the GG *OXTR* genotype, when they receive higher levels of harsh parenting.

We also considered in the present study whether carriers of the A+ genotype would respond to environmental conditions in a manner consistent with differential susceptibility theory (Belsky, 1997; Belsky & Pluess, 2009). Differential susceptibility theory posits that many putative sources of vulnerability, including genetic polymorphisms, are more accurately conceptualized as plasticity factors that not only amplify risk for maladaptation in poor environments but also increase the probability of positive adaptation in favorable environments (Roisman et al., 2012). Various genetic polymorphisms have been noted as functioning consistently with differential susceptibility tenets; to date, such polymorphisms have primarily related to genes associated with serotonergic (e.g., serotonin transporter linked polymorphic region [5-HTTLPR]) and dopaminergic (e.g., dopamine receptor D4 [DRD4]) systems (see Belsky & Pluess, 2009). In the present study, we examined the possibility that single nucleotide polymorphisms (SNPs) associated with the oxytonergic system may also conform to a differential susceptibility pattern, with carriers of the A+ genotype being both more vulnerable to negative (high levels of harsh parenting) and more responsive to positive (low levels of harsh parenting) environmental influences.

Summary of the Study Hypotheses and Research Design

We conducted this study with rural African American youths and their primary caregivers using procedures that have been shown in developmental psychopathology research to yield reliable data. These procedures include computer-based interviewing, matching of interviewers and participants by ethnicity, and extensive reassurances concerning confidentiality of the data (Brody et al., 2004; Patrick et al., 1994). We obtained genetic data from youths and parents using procedures developed in partnership with rural African American community members.

We predicted that teacher assessments of preadolescent temperament as emotionally intense and distractible would forecast increases in harsh parenting from preadolescence to adolescence. Receipt of harsh parenting, in turn, was hypothesized to forecast heightened levels of AL during young adulthood. Consistent with a differential susceptibility framework, parents' and youths' genetic statuses were hypothesized to moderate these associations (see Figure 1 for a conceptual model). For genetic moderation, we evaluated three specific prospective hypotheses. First, we expected difficult preadolescent temperament to presage the use of harsh parenting more strongly among parents with the A+ genotype than the GG genotype. Second, we expected to find a stronger

1. These discrepancies in plasticity alleles may be partially attributable to A and G alleles responding differently to different environmental conditions and in different populations. Given the few studies with racially homogenous minority samples, however, additional research is needed to confirm or refute this conjecture.

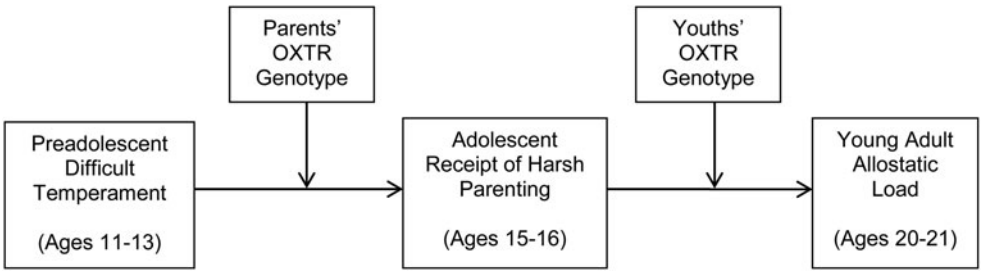

Figure 1. Conceptual model of study hypotheses.

association between receipt of harsh parenting and AL among youths with the A+ than the GG genotype. Third, we predicted a moderated-mediational scenario, wherein difficult temperament leads to harsh parenting, which in turns forecasts greater AL for families in which both the parent and adolescent carry the A+ genotype of *OXTR*.

A 10-year prospective design for testing the aforementioned hypotheses included 303 participants. The data gathered comprised teacher-rated youth temperament during preadolescence (ages 11 to 13), adolescents' self-reports of receipt of harsh parenting (at ages 11 to 13 and ages 15 and 16), genotyping of parents and adolescents for *OXTR* rs53576 polymorphisms, and a composite indicator of AL at ages 20 and 21. Although underpowered by current standards for molecular genetic studies, the present study represents one of the largest longitudinal molecular genetic studies in the literature that involves parents and youths. The composite reflects mediators and outcomes of activation of the stress response system, including the sympathetic–adrenomedullary system, the hypothalamus–pituitary–adrenal axis, and fat deposition as measured by body mass index. Composites of these indicators, which contribute to AL, predict the onset of hypertension, cardiac disease, diabetes, and all-cause mortality (Seeman, Singer, Ryff, Dienberg Love, & Levy-Storms, 2002).

Method

Participants

The data for this study were drawn from the Strong African American Families Healthy Adult Panel study (Brody et al., 2013). The Institutional Review Board at the University of Georgia approved all procedures. A target youth from each family and the parent who was identified as the youth's primary caregiver participated in annual data collections. Youths' mean age was 11.2 years ($SD = 0.34$) at the first assessment and 21.1 years ($SD = 0.71$) at the last assessment. Of the youths in the sample, 53% were female. At the first assessment, 78% of the caregivers had completed high school or earned a General Equivalency Diploma. The families resided in nine rural counties in Georgia, in small towns and communities in which poverty rates are among the highest in the nation and unemployment rates are above the national average (Proctor & Dalaker, 2003). Although the parents in the sample worked an average of 39.4 hours per week ($SD = 11.51$) at the first assessment, 46.3% lived below federal poverty standards with a median monthly family income of $1,655; at the last assessment, the proportion was 48.5% with a median monthly income of $1,914. Overall, the families can be described as working poor.

At the first assessment, 667 families were selected randomly from lists of fifth-grade students that schools provided. From a sample of 561 at the age 18 data collection (retention rate of 84%), 500 families were selected randomly to take part in an assessment of AL at ages 20 and 21. The selection of a random subsample was necessary because of financial constraints associated with the costs of assaying catecholamines and cortisol from urine samples. Of this subsample, 491 agreed to provide AL data at age 20, age 21, or both (479 provided data at age 20, 453 provided data at age 21). The subsample that provided AL data was comparable to the full age 18 sample on difficult temperament and family SES risk during preadolescence. The 491 families with AL data reported higher levels of harsh parenting during adolescence ($M = 5.59$, $SD = 1.29$) than did those who did not provide these data ($M = 5.31$, $SD = 0.95$), t (590) $= 2.54$, $p = .012$. The participating families, therefore, should be a higher risk sample than the larger sample from which they were drawn.

Of the 491 families for whom youths' AL data had been collected, 350 had provided, at the age 16 assessment, DNA samples both from the youth and one of the parents, which were successfully genotyped at *OXTR* rs53576. Parents in 303 of these 350 families were the youths' biological parents. These 303 families constituted the sample for the present study (295 biological mothers, 8 biological fathers). Comparisons on the demographic and study variables, using independent t tests and chi-square tests, between the 303 families who were included and the 188 who were not included in the analyses revealed two differences. On average, the families who were included in the analyses reported higher levels of harsh parenting ($M = 5.71$, $SD = 1.42$) and higher levels of parental depressive symptoms ($M = 10.35$, $SD = 8.35$) than did those who were not included in the analyses ($M = 5.38$, $SD = 1.02$), t (477) $= 2.65$, $p = .008$, for harsh parenting ($M = 8.71$, $SD = 7.91$), t (478) $= 2.11$, $p = .035$, for parent depressive symptoms. Again, these findings suggest that the analytic sample here is at higher risk than is the broader study population from which they were drawn.

Procedure

All data were collected in participants' homes using a standardized protocol. At each wave of data collection, two African American field researchers conducted one home visit that lasted approximately 2 hr. Interviews were conducted privately, with no other family members present or able to overhear the conversation. Informed consent was obtained at each data collection wave. Participants were told that the purpose of the study was to identify the predictors of health and well-being among rural African American adolescents. They were compensated $100 at each wave of data collection. Primary caregivers consented to minor youths' participation in the study, and youths assented or consented to their own participation.

Measures

Preadolescent difficult temperament. Each youth's English or social studies teacher assessed temperament at each of the three waves of preadolescent data collection (ages 11, 12, and 13). Difficult temperament was assessed using the seven-item irritability subscale and the six-item distractibility subscale of the Early Adolescent Temperament Scale (Capaldi & Rothbart, 1992). Each item was rated on a Likert scale ranging from 0 (*very false*) to 5 (*very true*). Irritability entails unpleasant affect in response to stimulation; a sample item is "This child hates it when people do not agree with her/him." The distractibility subscale assessed the ability to focus and shift attention; a sample item is "This child often is in the middle of doing one thing, and then goes off to do something else, without finishing it." Both the irritability and the distractibility subscales load on a difficult temperament factor (Capaldi & Rothbart, 1992). They have been shown to predict harsh parenting behaviors (Davenport et al., 2011). Difficult temperament was operationalized as the average of the teachers' ratings across the three assessments ($\alpha = 0.92$).

Harsh parenting in preadolescence and adolescence. Youths assessed receipt of harsh parenting during preadolescence and adolescence. Four items that index harsh parenting, the Harsh/Inconsistent Parenting Scale (Brody et al., 2001), assessed parents' use of striking and shouting to discipline the youths. Youths rated each item on a scale of 1 (*never*) to 4 (*always*) during preadolescence (ages 11 to 13) and adolescence (ages 15 and 16). Harsh parenting was operationalized as the average of the youths' ratings across the preadolescent ($\alpha = 0.74$) and adolescent ($\alpha = 0.71$) assessments.

Young adult AL. The protocol for measuring AL when youths were 20 and 21 years of age was based on procedures developed for field studies involving children and adolescents (Evans, 2003). Resting blood pressure was monitored with a Critikon Dinamap Pro 100 (Critikon; Tampa, FL) while the youth sat reading quietly. Three readings were taken every 2 min, and the average of the last two systolic readings and last two diastolic readings were used as resting blood pressure indices. This procedure yields highly reliable indices of chronic resting blood pressure (Kamarck et al., 1992). Overnight urinary catecholamines and cortisol were assayed. Beginning on the evening of data collection, all urine that the young adult voided from 8 p.m. to 8 a.m. was stored on ice in a container with metabisulfite as a preservative. Urine was delivered to the Emory University Hospital medical laboratory in Atlanta, Georgia, for assaying. Total unbound cortisol was assessed with a radioimmune assay (Contreras, Hane, & Tyrrell, 1986). Epinephrine and norepinephrine were assayed with high-pressure liquid chromatography with electrochemical detection (Riggin & Kissinger, 1977). Creatinine was assayed to control for differences in body size and incomplete urine voiding. Technicians blind to the study assayed the samples.

The AL composite was calculated by summing the standardized scores of six indicators: overnight cortisol, epinephrine, and norepinephrine; resting diastolic blood pressure and systolic blood pressure; and body mass index (weight in kilograms divided by the square of height in meters). Prior studies in adults (Seeman et al., 2002) and in children (Evans, 2003) used similar metrics, combining multiple physiological indicators of risk into a composite. Scores at ages 20 and 21 were highly correlated ($r = .51$, $p < .001$) and were averaged to form the young adulthood AL composite.

Genotyping. DNA was obtained from youths and parents using Oragene DNA kits (DNA Genotek, Kanata, ON, Canada). Participants 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 *OXTR* SNP rs53576 was determined for each sample using TaqMan SNP Genotyping technology (Life Technologies, Grand Island, NY). Detailed information about extraction and genotyping procedures is available from the authors. Of the youths' samples, 5.6% ($n = 17$) were homozygous for the A allele, 33.3% ($n = 101$) were heterozygous, and 61.1% ($n = 185$) were homozygous for the G allele. Of the parents' samples, 6.9% ($n = 21$) were homozygous for the A allele, 31.4% ($n = 95$) were heterozygous, and 61.7% ($n = 187$) were homozygous for the G allele. Genotype frequencies were checked for Hardy–Weinberg equilibrium ($\chi^2 = 0.42$, $p = .51$ for youths' sample; $\chi^2 = 3.28$, $p = .07$ for parents' sample). No gender differences could be detected ($\chi^2 = 2.50$, $df = 2$, $p = .29$ for youths; $\chi^2 = 0.51$, $df = 2$, $p = .78$ for parents). For tests of the Gene × Environment (G × E) hypotheses, *OXTR* rs53576 was coded as GG (1) vs. A+ (0) to ensure sufficient power for the analyses. A significant χ^2 indicated that parents' and youths' genotypes were associated, χ^2 (1) = 52.256, $p < .001$. Of the 303 families, in 144 (47.5%) both youths and one of their parents were homozygous for the G allele, whereas 75 (24.8%) youth–parent pairs both carried the A+ genotype. In 43 families (14.2%), youths were homozygous for the G allele and one of their parents carried the A+ genotype, whereas 41

(13.5%) youths who carried the A+ genotype had a parent who was homozygous for the G allele.

Control variables. Youth gender and family cumulative socioeconomic risk during preadolescence were controlled in all analyses. Cumulative risk was defined as the mean of the sums of six socioeconomic risk factors measured during each annual preadolescent assessment. This yielded a cumulative risk index that ranged from 0 to 6 ($M = 2.37$, $SD = 1.31$). The six risk indicators were family poverty as assessed using United States government criteria (income to needs ratio ≤ 1.5), primary caregiver noncompletion of high school or an equivalent, primary caregiver unemployment, single-parent family structure, family receipt of Temporary Assistance for Needy Families, and income rated by the primary caregiver as inadequate to meet all needs. Gender was dummy coded, with male youths coded 1 and female youths coded 0.

Given previous literature in this area (Miller et al., 2011), we also considered the possibility that the predicted associations would be confounded by depressive symptoms and health practices. Accordingly, adolescents' depressive symptoms were measured by using the Children's Depression Inventory (Kovacs, 1979), a 27-item self-report assessing depressive symptoms experienced in the past 2 weeks. The Children's Depression Inventory is a widely used self-report measure for children and youth 7 to 17 years of age ($\alpha = 0.85$); it was included in the analysis of predictors of harsh parenting. Parents' depressive symptoms during the youths' adolescence, measured by self-report on the Center for Epidemiologic Studies Depression Scale (Radloff, 1977), was also controlled in the analysis of predictors of harsh parenting. Parents rated each of 20 symptoms on a scale of 0 (*rarely or none of the time*), 1 (*some or a little of the time*), 2 (*occasionally or a moderate amount of time*), or 3 (*most or all of the time*) during the past week. The alpha value was 0.87. Youths' alcohol use, smoking, and depressive symptoms at ages 20 and 21 were also controlled in the analyses of AL. Youths were asked how much they had engaged in each form of substance use. A 7-point response set ranging from *not at all* to *about two packs a day* was used for cigarette smoking; a 6-point scale ranging from *none* to *20 or more days* was used for alcohol use (Brody et al., 2012). Because the distributions of both smoking and alcohol use were skewed, we applied a log transformation to normalize the ratings. Young adults' depressive symptoms were measured via self-report on the Center for Epidemiologic Studies Depression Scale. The alpha value was 0.85.

Results

Plan of analysis

Bivariate correlations and descriptive statistics for the study variables are presented in Table 1. Linear regression analyses were executed to test the study hypotheses. All interaction analyses were executed according to prescribed conventions whereby difficult temperament and harsh parenting indicators are standardized before the interaction terms are calculated (Aiken & West, 1991). Benefits of standardized weights in the interaction models include making coefficients easier to interpret, reducing multicollinearity, and making the simple slope easier to test (Aiken & West, 1991). The conceptual model presented earlier in Figure 1 illustrates the study hypotheses. We hypothesized that the link between difficult temperament and increases in harsh parenting would be moderated by parents' *OXTR* genotypes, whereas the link between harsh parenting and young adults' AL would be moderated by youths' *OXTR* genotypes. The size of the indirect effect of difficult temperament on youths' AL through harsh parenting, therefore, depends on both parents' and youths' genotypes. We calculated the conditional indirect effects (moderated mediation) of difficult temperament on AL through harsh parenting (Preacher, Rucker, & Hayes, 2007). Regression coefficients were obtained for the path between difficult temperament and harsh parenting (a_1) and the path between Difficult Temperament × Parents' Genotype and harsh parenting (a_2). The regression coefficients (simple slopes) were calculated for the association between difficult temperament and harsh parenting for each parental genotype using the formula, simple slope $a = (a_1 + a_2) \times$ parental genotype. Regression coefficients then were obtained for the path between harsh parenting and AL (b_1) and the path between Harsh Parenting × Youths' Genotype and AL (b_2). The regression coefficients (simple slopes) were calculated for the association between harsh parenting and AL for each youth genotype using the formula, simple slope $b = (b_1 + b_2) \times$ youth genotype. Finally, the conditional indirect effect in which harsh parenting serves as a link connecting preadolescent temperament to AL was quantified as the product of the two simple slopes: indirect effect = (simple slope a) × (simple slope b). In addition, nonparametric bootstrapping, which has been found to be sensitive in mediational analyses (Preacher et al., 2007), was used to obtain the bias-corrected and accelerated confidence intervals of the parameter estimates for significance testing. The parameter estimate was calculated 1,000 times using random sampling with replacement to build a sampling distribution.

Several authors (Belsky & Pluess, 2009; Roisman et al., 2012) have outlined recommendations for documenting differential susceptibility and, in particular, distinguishing it from other models of risk and developmental adaptation (e.g., diathesis–stress; Monroe & Simons, 1991). Establishing differential susceptibility involves probing the interaction and statistically testing for the presence of a crossover (or *disordinal*) interaction. Methodology pertaining to a proportion of the interaction (PoI) index (Roisman et al., 2012) offers a technique for testing explicitly whether a Gene × Environment moderation effect is consistent with the type of disordinal interaction that characterizes differential susceptibility. Because differential sensitivity predicts that individuals carrying "plasticity" agents will exhibit worse outcomes in difficult environments and better outcomes in supportive environments, the PoI quantifies the equality of the regions on the left (i.e., worse outcomes) and right (i.e., better outcomes) sides of the crossover point. An in-

Table 1. *Descriptive statistics and correlations among study variables (N = 303)*

Variables	1	2	3	4	5	6	7	8	9	10	11	12	13
1. Gender, male	—												
Age 11–13													
2. SES-related risk	.072	—											
3. Difficult temperament	.277***	.214***	—										
4. Harsh parenting	.016	.003	.161**	—									
Age 15–16													
5. Youth depression	−.074	.097	.202***	.144*	—								
6. Parent depression	−.074	.447***	.131*	.103	.213***	—							
7. Harsh parenting	−.067	.013	.188**	.476***	.309***	.155**	—						
Age 20–21													
8. Allostatic load	.168**	.166**	.149**	.043	−.033	.019	.067	—					
9. Alcohol use	.115*	−.123*	−.025	.110	.114*	−.011	.130*	.006	—				
10. Smoking	.358***	.049	.275***	.032	.147*	.070	.098	.024	.362***	—			
11. Youth depression	−.122*	.056	.146*	.068	.491***	.129*	.221***	−.020	.176**	.202***	—		
12. Parent rs53576 (GG)	−.019	.016	−.020	.012	−.092	.024	−.082	−.083	−.026	−.101	−.100	—	
13. Youth rs53576 (GG)	.037	.047	−.071	−.009	−.056	.069	.012	−.017	.022	−.039	−.075	.415***	—
Mean	0.45	2.30	5.55	7.08	7.24	10.35	5.71	−0.13	0.22	0.13	12.91	0.61	0.62
SD	0.50	1.25	1.16	1.70	5.44	8.35	1.42	2.76	0.18	0.22	7.75	0.49	0.49

Note: SES, Socioeconomic status.
*$p < .05$. **$p < .01$. ***$p < .001$.

teraction model consistent with differential susceptibility theory produces relatively equal regions of significance on both sides of the graph. Values approximating 0.50 offer strong support for differential susceptibility, whereas values under 0.16 favor a diathesis–stress model (for more details, see Roisman et al., 2012). In the present study, PoI values supporting tenets of differential susceptibility would indicate that the A+ genotype of *OXTR* renders parents more vulnerable to rearing a child with a challenging temperament and render youths more vulnerable to the receipt of harsh parenting.

Difficult temperament at ages 11 to 13, parents' genotype, and harsh parenting at ages 15 and 16

The first model, presented in Table 2, was designed to determine whether preadolescent temperament interacts with variations in parents' *OXTR* SNP rs53576 to forecast increases in harsh parenting during adolescence. This analysis did not reveal a significant main effect of difficult temperament during preadolescence on receipt of harsh parenting during adolescence after controlling for youths' gender, family SES-related risk, preadolescent receipt of harsh parenting, and depression in parents and adolescents. There was, however, a significant interaction between difficult temperament and parents' rs53576 genotype, $b = –0.196$, 95% confidence interval = (–0.41, –0.01), $p < .05$. To interpret this interaction, we followed previous guidelines (Aiken & West, 1991) to plot graphically and to calculate the simple slope of difficult temperament on harsh parenting by each parental genotype group (A+ vs. GG).

As shown in Figure 2, parents' rs53576 genotype moderated the association of preadolescent difficult temperament with increases in harsh parenting. Difficult temperament at ages 11 to 13 was significantly associated with increased harsh parenting at ages 15 and 16 among youths whose parents carried the A+ genotype at rs53576 (simple slope = 0.227, SE = 0.083, $p = .007$). Preadolescent difficult temperament was not associated with increases in receipt of harsh parenting during adolescence among youths whose parents carried GG alleles at rs53576 (simple slope = 0.030, $SE = 0.064$, $p = .473$). An examination of Figure 2 suggested that the interaction obtained for parents carrying the A+ genotype may have conformed to a differential susceptibility pattern (Belsky & Pluess, 2009). We explored that pattern to see if it characterized carriers of the A+ genotype. To determine whether the effect of the Child Temperament × Parent Genotype interaction on harsh parenting assumed a form that differential susceptibility theory predicted, we calculated the PoI index to test for the equality of the regions on the left and right sides of the crossover point. The value was 0.18, suggesting a differential susceptibility pattern with the A allele as a plasticity gene.

Harsh parenting at ages 15 and 16, youths' genotypes, and AL at ages 20 and 21

The second model, presented in Table 3, did not detect a significant main effect of harsh parenting on AL. A significant interaction emerged between receipt of harsh parenting and youths' rs53576 genotype, $b = –0.965$, 95% confidence interval = (–1.64, –0.11), $p < .05$. To interpret this interaction, we plotted estimated levels of AL at low versus high levels of harsh parenting ranging from –1 to +1 *SD* from the mean for each genotype group (see Figure 3). The results of the analysis were not plotted from –2 to +2 *SD* from the mean of harsh parenting because the range of adolescent receipt of harsh parenting ranged from –1.2 to +5.3 *SD* from the mean. As hypothesized, youths' rs53576 genotype interacted with receipt of harsh parenting to forecast AL. Receipt of harsh parenting at ages 15 and 16 was significantly associated with greater AL at ages 20 and 21 among youths who carried the A+ genotype at rs53576 (simple slope = 0.861, $SE = 0.297$, $p = .004$). Receipt of harsh parenting was not associated with AL among youths carrying GG alleles at rs53576 (simple slope = –0.004, $SE = 0.186$, $p = .98$). Again, we examined the A allele's function as a plasticity gene inducing adolescents' differential susceptibility to harsh parenting. The PoI test was conducted once more to determine directly whether the data conformed to a differential susceptibility pattern.

Table 2. *Difficult temperament and parents' rs53576 status as predictors of increases in harsh parenting (N = 303)*

Predictors	Harsh Parenting (Ages 15–16)					
	B	95% CI	β	*B*	95% CI	β
1. Gender, male	−0.159	(–0.39, 0.03)	−0.079	−0.157	(–0.38, 0.03)	−0.078
2. SES-related risk	−0.045	(–0.12, 0.03)	−0.056	−0.042	(–0.12, 0.03)	−0.052
3. Harsh parenting (ages 11–13)	0.425	(0.32, 0.55)	0.425***	0.420	(0.32, 0.54)	0.420***
4. Youth depressive symptoms[a]	0.038	(0.02, 0.06)	0.205***	0.037	(0.02, 0.06)	0.203***
5. Parent depressive symptoms[a]	0.009	(–0.01, 0.03)	0.076	0.009	(–0.01, 0.02)	0.072
6. Difficult temperament (ages 11–13)	0.101	(–0.01, 0.22)	0.101	0.227	(0.06, 0.44)	0.227**
7. Parent rs53576 (GG)	−0.142	(–0.34, 0.07)	−0.069	−0.140	(–0.35, 0.08)	−0.068
8. Temperament × Parent Gene	—	—	—	−0.196	(–0.41, –0.01)	−0.157*

Note: SES, Socioeconomic status.
[a]Assessed when youths were ages 15–16.
*$p \leq .05$. **$p \leq .01$. ***$p \leq .001$.

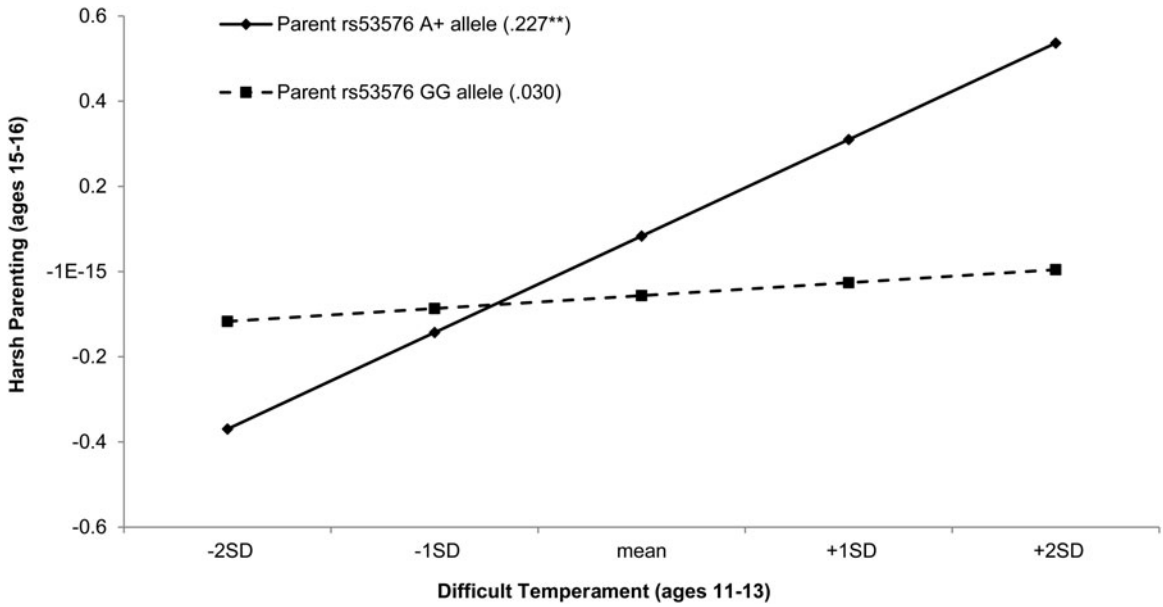

Figure 2. The effect of difficult temperament on harsh parenting by parent rs53576 genotype. The numbers in parentheses refer to slopes for each genotype group. $^{**}p < .01$.

The PoI index of 0.38 for the moderating role of youths' genotype in the link between receipt of harsh parenting and AL was within the range of values supporting differential susceptibility theory, demonstrating that the A allele functioned as a plasticity gene in separate analyses involving parents and adolescents. Finally, analyses were conducted to determine whether participant gender conditioned any of these findings. No moderating gender effects were detected.

Indirect effects analyses linking difficult temperament, harsh parenting, and AL

Alternative potential interactions of Difficult Temperament × Youths' Genotype, Harsh Parenting × Parents' Genotype, Difficult Temperament × Youths' Genotype × Parents' Genotype, and Harsh Parenting × Parents' Genotype × Youths' Genotype were tested. None of these interaction terms was significant. The conditional indirect effects were calculated for each Parent × Youth Genotype group (see Table 4). A significant indirect effect linking difficult temperament during preadolescence to AL during young adulthood via increases in harsh parenting during adolescence only emerged when both the parent and youth carried the A+ genotype at rs53576. No indirect effects emerged for other genotype combinations. This analysis supported a moderated mediation pathway linking preadolescent temperament to AL via increases in harsh parenting when both parents and adolescents carried the A+ genotype at rs53576.

Discussion

We used a 10-year multiple-wave, multiple-informant design to investigate the operation of childhood temperament, harsh

Table 3. *Harsh parenting and youths' rs53576 as predictors of allostatic load (N = 303)*

	Allostatic Load (Ages 20–21)					
Predictors	*B*	95% CI	β	*B*	95% CI	β
1. Gender, male	1.003	(0.32, 1.65)	0.181**	1.062	(0.38, 1.74)	0.192**
2. SES-related risk (ages 11–13)	0.355	(0.11, 0.59)	0.160**	0.349	(0.10, 0.59)	0.157**
3. Alcohol use (ages 20–21)	0.301	(–1.46, 2.11)	0.020	0.488	(–1.21, 2.30)	0.033
4. Smoking (ages 20–21)	−0.763	(–2.15, 0.80)	−0.062	−0.869	(–2.23, 0.71)	−0.071
5. Youth depressive symptoms (ages 20–21)	−0.007	(–0.06, 0.04)	−0.019	−0.007	(–0.06, 0.03)	−0.021
6. Harsh parenting (ages 15–16)	0.235	(–0.14, 0.61)	0.085	0.861	(0.36, 1.45)	0.312**
7. Youth rs53576 (GG)	−0.204	(–0.77, 0.38)	−0.036	−0.217	(–0.74, 0.38)	−0.038
8. Harsh Parenting × Youth Gene	—	—	—	−0.865	(–1.64, –0.11)	−0.266*

Note: SES, Socioeconomic status.
$^{*}p \leq .05$. $^{**}p \leq .01$.

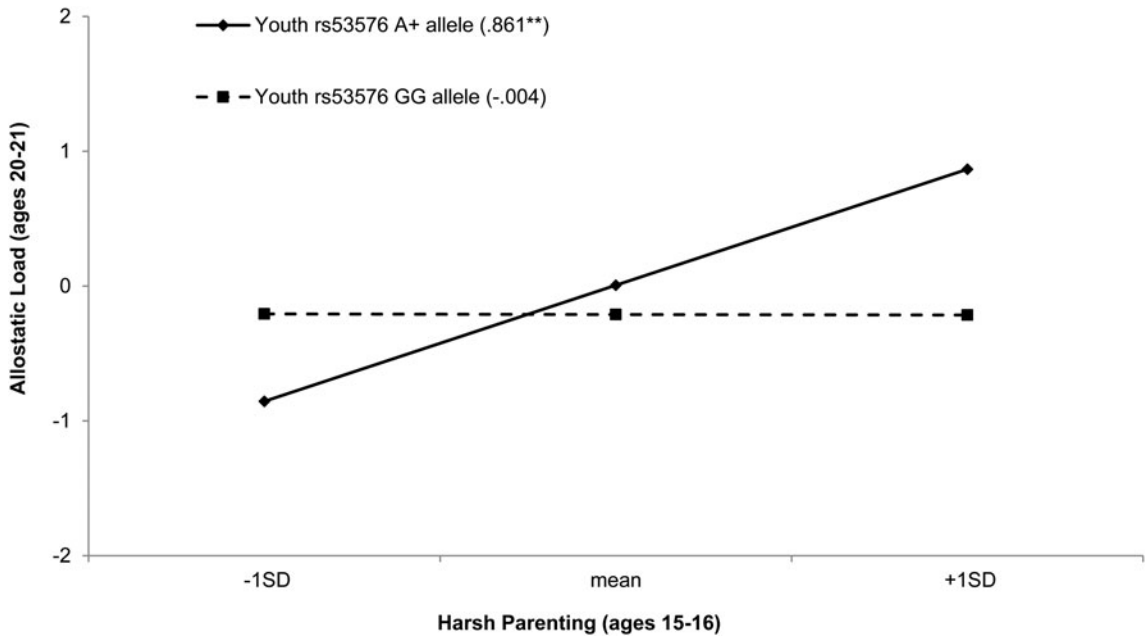

Figure 3. The effect of harsh parenting on cardiometabolic risk by youth rs53575 genotype. The numbers in parentheses refer to slopes for each genotype group. $^{**}p < .01$.

parenting, and *OXTR* gene polymorphisms in affecting rural African American youths' AL. The results indicated that difficult temperament predicted increases in harsh parenting and forecasted greater AL, but only when both parents and youths carried the A+ genotype at *OXTR* rs53576. In addition to replicating findings documented previously relating child temperament to parenting practices (Lengua & Kovacs, 2005) and harsh parenting to offspring physical health (Repetti et al., 2002), these results also extend the current literature by identifying genetic polymorphisms that explain why some caregivers' parenting is more or less affected by children's difficult temperaments and, similarly, why some youths' physical health is more or less affected by harsh parenting.

These results converge with a growing amount of evidence on the stress-buffering and stress-amplifying effects of *OXTR* allelic variants (Chen et al., 2011; Poulin et al., 2012; Rodrigues et al., 2009; Tost et al., 2010). The study findings are consistent with a central hypothesis about the functions of oxytocin. It induces physiological anxiolytic effects for individuals homogeneous for the G allele by decreasing cortisol levels, inhibiting physiological responses to stress, and attenuating amygdala responsivity to emotional stimuli (Campbell, 2010). These findings have important implications for understanding how naturally occurring variations in the oxytocin system affect both parent–child relationships and offspring health.

The results are also consistent with an emerging literature that addresses the possibility that individual differences in parenting may be partially a function of genetic differences. Genes that influence the oxytocin system recently have attracted empirical attention. Several studies have examined associations between *OXTR* rs53576 genotype and parental behavior. The A allele has been found to be associated with reduced positive affect (Lucht et al., 2009), diminished prosocial behavior (Israel et al., 2009), attachment insecurity

Table 4. *Conditional indirect effects (moderated mediation effects) for parent and youth OXTR rs53576 genotype groups*

Genotypes		Simple Slopes		Indirect Effect	
Parents	Youths	Path a	Path b	Estimates	95% CI
A+	A+	0.227	0.861	0.195	(0.04, 0.51)
GG	A+	0.030	0.861	0.026	(–0.08, 0.14)
A+	GG	0.227	−0.004	−0.001	(–0.11, 0.18)
GG	GG	0.030	−0.004	0	(–0.04, 0.04)

Note: Path a, Temperament to harsh parenting; Path b, harsh parenting to allostatic load; Estimates, Path a × Path b; 95% CI, 95% confidence interval with 1,000 bootstraps.

(Costa et al., 2009), and low empathy (Rodrigues et al., 2009), phenotypes that detract from warm and sensitive parental behavior. In most studies, the *OXTR* rs53576 A allele's association with this phenotype has been confirmed for parents with toddlers (Bakermans-Kranenburg & van IJzendoorn, 2008) and school-age children (Klahr et al., 2015). These findings suggest that the stronger association found in this study between difficult temperament and subsequent increases in the use of harsh parenting among carriers of A+ alleles may have been due to (a) a lower tolerance for difficult child behavior (anxiolytic effects), (b) a propensity for disinterested parenting, or (c) a combination of both. Future research is needed to examine these potential explanations.

The disparate patterns by genotype are striking and support differential susceptibility theory (Belsky & Pluess, 2009). The rs53576 A allele seemed to function as a marker of plasticity; it not only appeared to render parents and adolescents more susceptible to temperament difficulty and harsh parenting but also provided benefits under conditions of easy temperament and good parenting. These results raise the possibility that the A+ polymorphism is not invariably detrimental, but only in conjunction with certain behavioral characteristics and rearing practices. Accordingly, results from the study are consistent with other recent findings showing differential susceptibility effects for genes associated with the oxytonergic systems (e.g., Sturge-Apple, Cicchetti, Davies, & Suor, 2012; Hammen, Bower, & Cole, 2015); furthermore, differential susceptibility effects involving *OXTR* rs53576 were evinced in two G×E interactions: one involving African American adult caregivers in relation to child temperament and the second involving African American adolescents in relation to harsh parenting.

The results from the current study add to the growing literature supporting the proposition that poor health in adulthood is tied to experiences earlier in life, particularly for persons reared in harsh family environments. This body of research has documented the effects of harsh parenting on a range of health outcomes, including inflammatory activity (Miller & Cole, 2012), telomere length (Beach, Lei, Brody, Yu, & Philibert, 2014), AL (Danese & McEwen, 2012), and, as identified in the current study, AL. As an important qualification, results from the current study indicated that these parenting effects on AL were only evident for youth with a particular genetic status. Consistent with our expectations, individuals' *OXTR* genotype explained why some youth, despite exposure to harsh parenting, do not present compromised physical health biomarkers. In addition to informing the literature on factors that set boundary conditions determining when particular family environments do (and do not) affect offspring physical health, these genetic moderation findings also inform research on youth resilience. To date, the locus of resilience effects has been situated in multilevel contextual processes (e.g., family, peer, school, or neighborhood) that promote positive development in the midst of adverse conditions. As others have suggested (Caspi, Hariri, Holmes, Uher, & Moffitt, 2010; Rutter, 2012), the present results indicate that innate biological characteristics of the individual also contribute to youth resilience, at least with respect to physical health outcomes.

The limitations of this study should be noted. Further replications with hard end points such as diabetes, metabolic syndrome, and asthma are indicated. Only one genetic polymorphism was examined; this does not represent all of the variation that could place individuals at greater susceptibility to influences from their environment. Many genetic variants may heighten risk (or conversely, promote positive adaptation), the expression of which may emerge only under particular contextual conditions. It also is not known whether the results generalize to Caucasian or Latino families living in rural or urban communities. The findings' applicability with ethnically, socioeconomically, and residentially diverse participants must be established empirically. Caution is also warranted in interpreting and generalizing the plasticity effects of the *OXTR* genotype to all rural African American emerging adults. Parent and youth genetic status may confer differential susceptibility to environmental conditions in some outcomes of interest (i.e., parenting and physical health, respectively), but be less sensitive in predicting other outcomes, such as aspects of vocational/academic achievement and risk behaviors. Although genetically influenced difficult youth temperament can be confounded with symptoms of attention-deficit/hyperactivity disorder, we did not collect clinical data on diagnosable behavior disorders. The *OXTR* genotype was not associated with environmental conditions in the present study, ruling out gene–environment correlation as an alternative explanation for the results. Given previous findings linking *OXTR* to observed parenting behavior (Bakermans-Kranenburg & van IJzendoorn, 2008), however, future studies in this area that explore G×E hypotheses should continue to consider potential gene–environment correlation confounds. Finally, body mass index was used as the indicator for adiposity; future research should consider more direct assessments of adiposity such as fasting leptin and insulin levels or dual-energy X-ray absorptiometry.

The strengths of the study included a 10-year prospective research design with multiple waves of data on temperament, harsh parenting, and AL, as well as *OXTR* genotypes for parents and children. Assessments were collected from multiple reporters (i.e., teachers, parents, and youths), reducing concerns about common method variance. Implications for prevention should also be considered. The present results suggest that parents who have a sensitivity gene or other factors that predispose them to be particularly reactive to their environment who also are rearing a child with a difficult temperament are at high risk for maladaptive parenting processes. Similarly, youths with such sensitivities to environmental conditions who receive harsh parenting appear to be at heightened risk for compromised physical health. Research on the design of preventive intervention for these youths and parents may yield approaches that are effective in promoting positive parenting processes and overall health within the family.

References

Aiken, L. S., & West, S. G. (1991). *Multiple regression: Testing and interpreting interactions*. Thousand Oaks, CA: Sage.

Bakermans-Kranenburg, M. J., & van IJzendoorn, M. H. (2008). Oxytocin receptor (*OXTR*) and serotonin transporter (*5-HTT*) genes associated with observed parenting. *Social Cognitive and Affective Neuroscience*, *3*, 128–134.

Bakermans-Kranenburg, M. J., & van IJzendoorn, M. H. (2014). A sociability gene? Meta-analysis of oxytocin receptor genotype effects in humans. *Psychiatric Genetics*, *24*, 45–51.

Beach, S. R. H., Lei, M. K., Brody, G. H., Yu, T., & Philibert, R. A. (2014). Nonsupportive parenting affects telomere length in young adulthood among African Americans: Mediation through substance use. *Journal of Family Psychology*, *28*, 967–972.

Belsky, J. (1997). Variation in susceptibility to environmental influence: An evolutionary argument. *Psychological Inquiry*, *8*, 182–186.

Belsky, J., & Pluess, M. (2009). Beyond diathesis stress: Differential susceptibility to environmental influences. *Psychological Bulletin*, *135*, 885–908.

Bradley, B., Westen, D., Mercer, K. B., Binder, E. B., Jovanovic, T., Crain, D., et al. (2011). Association between childhood maltreatment and adult emotional dysregulation in a low-income, urban, African American sample: Moderation by oxytocin receptor gene. *Development and Psychopathology*, *23*, 439–452.

Brody, G. H., Chen, Y.-F., Kogan, S. M., Yu, T., Molgaard, V. K., DiClemente, R. J., et al. (2012). Family-centered program to prevent substance use, conduct problems, and depressive symptoms in Black adolescents. *Pediatrics*, *129*, 108–115.

Brody, G. H., Ge, X., Conger, R. D., Gibbons, F. X., Murry, V. M., Gerrard, M., et al. (2001). The influence of neighborhood disadvantage, collective socialization, and parenting on African American children's affiliation with deviant peers. *Child Development*, *72*, 1231–1246.

Brody, G. H., Murry, V. M., Gerrard, M., Gibbons, F. X., Molgaard, V., McNair, L., et al. (2004). The Strong African American Families program: Translating research into prevention programming. *Child Development*, *75*, 900–917.

Brody, G. H., Yu, T., Chen, Y.-F., Kogan, S. M., Evans, G. W., Beach, S. R. H., et al. (2013). Cumulative socioeconomic status risk, allostatic load, and adjustment: A prospective latent profile analysis with contextual and genetic protective factors. *Developmental Psychology*, *49*, 913–927.

Campbell, A. (2010). Oxytocin and human social behavior. *Personality and Social Psychology Review*, *14*, 281–295.

Capaldi, D. M., & Rothbart, M. K. (1992). Development and validation of an early adolescent temperament measure. *Journal of Early Adolescence*, *12*, 153–173.

Caspi, A., Hariri, A. R., Holmes, A., Uher, R., & Moffitt, T. E. (2010). Genetic sensitivity to the environment: The case of the serotonin transporter gene and its implications for studying complex diseases and traits. *FOCUS*, *8*, 398–416.

Chen, F. S., Kumsta, R., von Dawans, B., Monakhov, M., Ebstein, R. P., & Heinrichs, M. (2011). Common oxytocin receptor gene (*OXTR*) polymorphism and social support interact to reduce stress in humans. *Proceedings of the National Academy of Sciences*, *108*, 19937–19942.

Cicchetti, D., & Rogosch, F. A. (2012). Gene × Environment interaction and resilience: Effects of child maltreatment and serotonin, corticotropin releasing hormone, dopamine, and oxytocin genes. *Development and Psychopathology*, *24*, 411–427.

Cicchetti, D., & Toth, S. L. (2005). Child maltreatment. *Annual Review of Clinical Psychology*, *1*, 409–438.

Contreras, L. N., Hane, S., & Tyrrell, J. B. (1986). Urinary cortisol in the assessment of pituitary-adrenal function: Utility of 24-hour and spot determinations. *Journal of Clinical Endocrinology and Metabolism*, *62*, 965–969.

Costa, B., Pini, S., Gabelloni, P., Abelli, M., Lari, L., Cardini, A., et al. (2009). Oxytocin receptor polymorphisms and adult attachment style in patients with depression. *Psychoneuroendocrinology*, *34*, 1506–1514.

Creswell, K. G., Wright, A. C., Troxel, W. M., Ferrell, R. E., Flory, J. D., & Manuck, S. B. (2015). *OXTR* polymorphism predicts social relationships through its effects on social temperament. *Social Cognitive and Affective Neuroscience*, *10*, 869–876.

Danese, A., & McEwen, B. S. (2012). Adverse childhood experiences, allostasis, allostatic load, and age-related disease. *Physiology & Behavior*, *106*, 29–39.

Danese, A., Moffitt, T. E., Harrington, H., Milne, B. J., Polanczyk, G., Pariante, C. M., et al. (2009). Adverse childhood experiences and adult risk factors for age-related disease: Depression, inflammation, and clustering of metabolic risk markers. *Archives of Pediatrics and Adolescent Medicine*, *163*, 1135–1143.

Davenport, E., Yap, M. B. H., Simmons, J. G., Sheeber, L. B., & Allen, N. B. (2011). Maternal and adolescent temperament as predictors of maternal affective behavior during mother-adolescent interactions. *Journal of Adolescence*, *34*, 829–839.

Dube, S. R., Fairweather, D., Pearson, W. S., Felitti, V. J., Anda, R. F., & Croft, J. B. (2009). Cumulative childhood stress and autoimmune diseases in adults. *Psychosomatic Medicine*, *71*, 243–250.

Else-Quest, N. M., Hyde, J. S., Goldsmith, H. H., & Van Hulle, C. A. (2006). Gender differences in temperament: A meta-analysis. *Psychological Bulletin*, *132*, 33–72.

Evans, G. W. (2003). A multimethodological analysis of cumulative risk and allostatic load among rural children. *Developmental Psychology*, *39*, 924–933.

Hammen, C., Bower, J. E., & Cole, S. W. (2015). Oxytocin receptor gene variation and differential susceptibility to family environment in predicting youth borderline symptoms. *Journal of Personality Disorders*, *29*, 177–192.

Israel, S., Lerer, E., Shalev, I., Uzefovsky, F., Riebold, M., Laiba, E., et al. (2009). The oxytocin receptor (OXTR) contributes to prosocial fund allocations in the Dictator Game and the Social Value Orientations task. *PLOS ONE*, *4*, e5535.

Kamarck, T. W., Jennings, J. R., Debski, T. T., Glickman-Weiss, E., Johnson, P. S., Eddy, M. J., et al. (1992). Reliable measures of behaviorally-evoked cardiovascular reactivity from a PC-based test battery: Results from student and community samples. *Psychophysiology*, *29*, 17–28.

Karlamangla, A. S., Singer, B. H., & Seeman, T. E. (2006). Reduction in allostatic load in older adults is associated with lower all-cause mortality risk: MacArthur studies of successful aging. *Psychosomatic Medicine*, *68*, 500–507.

Keltikangas-Järvinen, L., Pulkki-Råback, L., Puttonen, S., Viikari, J., & Raitakari, O. T. (2006). Childhood hyperactivity as a predictor of carotid artery intima media thickness over a period of 21 years: The Cardiovascular Risk in Young Finns Study. *Psychosomatic Medicine*, *68*, 509–516.

Kim, K. J., Conger, R. D., Lorenz, F. O., & Elder, G. H., Jr. (2001). Parent-adolescent reciprocity in negative affect and its relation to early adult social development. *Developmental Psychology*, *37*, 775–790.

Kim-Cohen, J., Caspi, A., Taylor, A., Williams, B., Newcombe, R., Craig, I. W., et al. (2006). MAOA, maltreatment, and gene-environment interaction predicting children's mental health: New evidence and a meta-analysis. *Molecular Psychiatry*, *11*, 903–913.

Klahr, A. M., Klump, K., & Burt, S. A. (2015). A constructive replication of the association between the oxytocin receptor genotype and parenting. *Journal of Family Psychology*, *29*, 91–99.

Kogan, A., Saslow, L. R., Impett, E. A., Oveis, C., Keltner, D., & Rodrigues Saturn, S. (2011). Thin-slicing study of the oxytocin receptor (OXTR) gene and the evaluation and expression of the prosocial disposition. *Proceedings of the National Academy of Sciences*, *108*, 19189–19192.

Kovacs, M. (1979). Treating depressive disorders: The efficacy of behavior and cognitive therapies. *Behavior Modification*, *3*, 496–517.

Laukkanen, J., Ojansuu, U., Tolvanen, A., Alatupa, S., & Aunola, K. (2014). Child's difficult temperament and mothers' parenting styles. *Journal of Child and Family Studies*, *23*, 312–323.

Laursen, B., & Collins, W. A. (2009). Parent-child relationships during adolescence. In R. M. Lerner & L. Steinberg (Eds.), *Handbook of adolescent psychology* (3rd ed., Vol. 2, pp. 3–42). Hoboken, NJ: Wiley.

Lengua, L. J., & Kovacs, E. A. (2005). Bidirectional associations between temperament and parenting and the prediction of adjustment problems in middle childhood. *Journal of Applied Developmental Psychology*, *26*, 21–38.

Lucht, M. J., Barnow, S., Sonnenfeld, C., Rosenberger, A., Grabe, H. J., Schroeder, W., et al. (2009). Associations between the oxytocin receptor gene (OXTR) and affect, loneliness and intelligence in normal subjects. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, *35*, 860–866.

McEwen, B. S. (2000). Allostasis and allostatic load: Implications for neuropsychopharmacology. *Neuropsychopharmacology*, *22*, 108–124.

Michalska, K. J., Decety, J., Liu, C., Chen, Q., Martz, M. E., Jacob, S., et al. (2014). Genetic imaging of the association of oxytocin receptor gene (OXTR) polymorphisms with positive maternal parenting. *Frontiers in Behavioral Neuroscience*, *8*, 21.

Miller, G. E., Chen, E., & Parker, K. J. (2011). Psychological stress in childhood and susceptibility to the chronic diseases of aging: Moving toward a

model of behavioral and biological mechanisms. *Psychological Bulletin*, *137*, 959–997.
Miller, G. E., & Cole, S. W. (2012). Clustering of depression and inflammation in adolescents previously exposed to childhood adversity. *Biological Psychiatry*, *72*, 34–40.
Monroe, S. M., & Simons, A. D. (1991). Diathesis-stress theories in the context of life stress research: Implications for the depressive disorders. *Psychological Bulletin*, *110*, 406–425.
Patrick, D. L., Cheadle, A., Thompson, D. C., Diehr, P., Koepsell, T., & Kinne, S. (1994). The validity of self-reported smoking: A review and meta-analysis. *American Journal of Public Health*, *84*, 1086–1093.
Paulussen-Hoogeboom, M. C., Stams, G. J. J. M., Hermanns, J. M. A., & Peetsma, T. T. D. (2007). Child negative emotionality and parenting from infancy to preschool: A meta-analytic review. *Developmental Psychology*, *43*, 438–453.
Posner, M. I., & Rothbart, M. K. (2007). *Educating the human brain*. Washington, DC: American Psychological Association.
Poulin, M. J., Holman, E. A., & Buffone, A. (2012). The neurogenetics of nice: Receptor genes for oxytocin and vasopressin interact with threat to predict prosocial behavior. *Psychological Science*, *23*, 446–452.
Preacher, K. J., Rucker, D. D., & Hayes, A. F. (2007). Addressing moderated mediation hypotheses: Theory, methods, and prescriptions. *Multivariate Behavioral Research*, *42*, 185–227.
Proctor, B. D., & Dalaker, J. (2003). *Poverty in the United States: 2002* (Current Population Reports, P60-222). Washington, DC: US Census Bureau.
Pulkki-Råback, L., Elovainio, M., Kivimäki, M., Raitakari, O. T., & Keltikangas-Järvinen, L. (2005). Temperament in childhood predicts body mass in adulthood: The Cardiovascular Risk in Young Finns Study. *Health Psychology*, *24*, 307–315.
Putnam, S. P., Ellis, L. K., & Rothbart, M. K. (2001). The structure of temperament from infancy through adolescence. In A. Eliasz & A. Angleitner (Eds.), *Advances in research on temperament* (pp. 165–182). Lengerich, Germany: Pabst Science.
Puttonen, S., Elovainio, M., Kivimäki, M., Koskinen, T., Pulkki-Råback, L., Viikari, J. S. A., et al. (2008). Temperament, health-related behaviors, and autonomic cardiac regulation: The Cardiovascular Risk in Young Finns Study. *Biological Psychology*, *78*, 204–210.
Radloff, L. S. (1977). The CES-D Scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement*, *1*, 385–401.
Repetti, R. L., Taylor, S. E., & Seeman, T. E. (2002). Risky families: Family social environments and the mental and physical health of offspring. *Psychological Bulletin*, *128*, 330–366.
Riggin, R. M., & Kissinger, P. T. (1977). Determination of catecholamines in urine by reverse-phase liquid chromatography with electrochemical detection. *Analytical Chemistry*, *49*, 2109–2111.
Rodrigues, S. M., Saslow, L. R., Garcia, N., John, O. P., & Keltner, D. (2009). Oxytocin receptor genetic variation relates to empathy and stress reactivity in humans. *Proceedings of the National Academy of Sciences*, *106*, 21437–21441.
Roisman, G. I., Newman, D. A., Fraley, R. C., Haltigan, J. D., Groh, A. M., & Haydon, K. C. (2012). Distinguishing differential susceptibility from diathesis–stress: Recommendations for evaluating interaction effects. *Development and Psychopathology*, *24*, 389–409.
Rothbart, M. K., & Bates, J. E. (1998). Temperament. In W. Damon (Ed.), *Handbook of child psychology: Vol. 3. Social, emotional and personality development* (5th ed., pp. 105–176). New York: Wiley.
Rutter, M. L. (2012). Resilience as a dynamic concept. *Development and Psychopathology*, *24*, 335–344.
Sanson, A. V., & Rothbart, M. K. (1995). Child temperament and parenting. In M. H. Bornstein (Ed.), *Handbook of parenting: Vol. 4. Applied and practical parenting* (pp. 299–321). Hillsdale, NJ: Erlbaum.
Saphire-Bernstein, S., Way, B. M., Kim, H. S., Sherman, D. K., & Taylor, S. E. (2011). Oxytocin receptor gene (*OXTR*) is related to psychological resources. *Proceedings of the National Academy of Sciences*, *108*, 15118–15122.
Seeman, T. E., Singer, B. H., Ryff, C. D., Dienberg Love, G., & Levy-Storms, L. (2002). Social relationships, gender, and allostatic load across two age cohorts. *Psychosomatic Medicine*, *64*, 395–406.
Sturge-Apple, M. L., Cicchetti, D., Davies, P. T., & Suor, J. H. (2012). Differential susceptibility in spillover between interparental conflict and maternal parenting practices: Evidence for OXTR and 5-HTT genes. *Journal of Family Psychology*, *26*, 431–442.
Thompson, S. M., Hammen, C., Starr, L. R., & Najman, J. M. (2014). Oxytocin receptor gene polymorphism (rs53576) moderates the intergenerational transmission of depression. *Psychoneuroendocrinology*, *43*, 11–19.
Tost, H., Kolachana, B. S., Hakimi, S., Lemaitre, H., Verchinski, B. A., Mattay, V. S., et al. (2010). A common allele in the oxytocin receptor gene (*OXTR*) impacts prosocial temperament and human hypothalamic-limbic structure and function. *Proceedings of the National Academy of Sciences*, *107*, 13936–13941.
Way, B. M., & Taylor, S. E. (2010). The serotonin transporter promoter polymorphism is associated with cortisol response to psychosocial stress. *Biological Psychiatry*, *67*, 487–492.