Positive Maternal Parenting and Adolescent Prosocial Behavior: The Mediating Role of Empathy and the Moderating Role of the OXTR Gene

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Abstract

Numerous studies have demonstrated that maternal positive parenting can facilitate the development of adolescent prosocial behavior; however, the underlying mechanisms remain unclear to date. Based on the "gene-environment-endophenotype-behavior" model, this study employed questionnaire methods and DNA genotyping technology to conduct a two-year longitudinal investigation of 1082 adolescents (initial mean age = 12.32 ± 0.48 years, 50.3% female) and their mothers, examining the mediating role of empathy between maternal positive parenting and adolescent prosocial behavior, as well as the moderating effect of OXTR gene rs53576 polymorphism on this mediating mechanism. The results revealed: (1) Adolescents' cognitive empathy (perspective-taking) mediated the relationship between maternal positive parenting and prosocial behavior, whereas the mediating effect of emotional empathy (empathic concern) was not significant; (2) The moderating effect of OXTR gene on the direct path between positive parenting and prosocial behavior was not significant; (3) OXTR gene could moderate the first half of the "maternal positive parenting–cognitive empathy–prosocial behavior" mediating mechanism, demonstrating a superdominant genetic effect. Specifically, among adolescents carrying GG and AA genotypes, maternal positive parenting significantly positively predicted cognitive empathy, which in turn increased their prosocial behavior, whereas this mediating effect was not significant among those carrying the AG heterozygous genotype. These findings contribute to elucidating the mechanisms and individual differences in adolescent prosocial behavior from the perspectives of oxytocin receptor gene polymorphism, empathy capacity, and family parenting.

Full Text

Maternal Positive Parenting and Adolescent Prosocial Behavior: The Mediating Role of Empathy and the Moderating Role of the OXTR Gene

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Abstract

Numerous studies have demonstrated that maternal positive parenting promotes the development of adolescent prosocial behavior, yet the underlying mechanisms remain unclear. Based on the "Gene-Environment-Endophenotype-Behavior" model, this two-year longitudinal study employed questionnaire methods and DNA genotyping technology to examine 1082 adolescents (mean age at baseline = 12.32 ± 0.48 years, 50.3% female) and their mothers. We investigated the mediating role of empathy in the association between maternal positive parenting and adolescent prosocial behavior, as well as the moderating effect of OXTR gene rs53576 polymorphism on this mediating mechanism. The findings revealed: (1) Adolescents' cognitive empathy (perspective-taking) significantly mediated the relationship between maternal positive parenting and prosocial behavior, whereas the mediating effect of emotional empathy (empathic concern) was not significant; (2) The OXTR gene did not significantly moderate the direct path between positive parenting and prosocial behavior; (3) The OXTR gene moderated the first half of the "maternal positive parenting–cognitive empathy –prosocial behavior" mediation pathway, demonstrating a pattern of overdominance. Among adolescents carrying GG and AA genotypes, maternal positive parenting significantly and positively predicted cognitive empathy, which in turn increased prosocial behavior; however, this mediating effect was not significant among adolescents carrying the AG heterozygous genotype. These results contribute to elucidating the mechanisms and individual differences in adolescent prosocial behavior from the perspectives of oxytocin receptor gene polymorphisms, empathic capacity, and family parenting.

Keywords: prosocial behavior, maternal positive parenting, OXTR gene, cognitive empathy, emotional empathy

1. Introduction

Prosocial behavior refers to actions intended to benefit others (Eisenberg et al., 2015) and is closely associated with positive interpersonal relationships, academic achievement, and psychosocial adjustment in children and adolescents (e.g., Carlo et al., 2017). The phylogenetic evolution and ontogenetic development of human prosocial behavior represent a major scientific question that has attracted considerable attention from the scientific community (Kennedy &

Norman, 2005). Researchers have long been committed to uncovering the origins and developmental mechanisms of human prosocial behavior from multiple perspectives, including evolutionary, sociocultural, physiological, and cognitive levels (e.g., Hackel et al., 2017). In recent years, a growing body of prosocial research has consistently indicated that physiological factors, temperamental characteristics, socialization factors, and social cognition interact to jointly influence prosocial behavior (Knafo-Noam et al., 2018). Current studies examining "Gene × Environment → Prosocial Behavior/Empathy" (e.g., Fortuna & Knafo, 2014; Knafo et al., 2011; Knafo-Noam et al., 2018) and "Parenting → Empathy → Prosocial Behavior" (e.g., Padilla-Walker & Christensen, 2011) have helped researchers understand the mechanisms and individual differences underlying prosocial behavior from different angles. However, how to integrate influences across molecular, cognitive/emotional, and behavioral levels and construct theoretical models remains an unresolved issue in current research. Based on the theoretical framework of "Gene-Environment-Endophenotype-Behavior" (Caspi & Moffitt, 2006), this study focuses on susceptibility factors at the molecular biological level (genetic factors), endophenotypic level (cognitive and emotional empathy), and environmental level (maternal parenting behavior) to examine the multi-level mechanisms of prosocial behavior. This approach not only helps identify the conditions and individual differences in the emergence of prosocial behavior but also illuminates the "black box" between genes, environment, and prosocial behavior. Therefore, this study adopts a molecular genetics research paradigm to examine the relationships among maternal positive parenting, empathy, and adolescent prosocial behavior, and tests the moderating effect of the oxytocin receptor (OXTR) gene to enrich our understanding of the mechanisms and individual differences in prosocial behavior.

The family serves as a crucial context for the socialization of children and adolescents, and parent-child interaction experiences in the family environment exert a sustained direct influence on the development of prosocial behavior (Eisenberg et al., 2015). Socialization theories posit that children and adolescents' prosocial behavior originates from positive experiences in close family relationships (Hastings et al., 2015). Relevant empirical studies have provided abundant evidence for the relationship between positive parenting and prosocial behavior in children and adolescents, revealing that positive parenting can promote the development of prosocial behavior through multiple pathways (e.g., Eisenberg et al., 2015; Hastings et al., 2015). On one hand, positive parenting behaviors such as warmth and guidance provide observational learning models for children' s caring and comforting behaviors, thereby facilitating the acquisition of prosocial behavior (Augustine & Stifter, 2015). On the other hand, parental warmth and guidance provide children with a sense of security, trust, and protection, enhance their connection with others and sense of belonging, and simultaneously reduce self-focused concern, thereby promoting prosocial behavior (Hoffman, 2001). Moreover, intimate and warm parent-child relationships are more conducive to promoting children' s internalization of parental values concerning care and respect for others (Grusec & Goodnow, 1994), which in turn increases

prosocial behavior.

Positive parenting not only directly influences prosocial behavior but also affects offspring prosocial behavior through mediating processes involving certain social-cognitive capacities. Hoffman's theory of moral internalization posits that positive parenting behaviors (such as guidance) can direct children' s attention to the negative consequences of misbehavior through explanation of behavioral rules, promote children' s capacity to experience others' negative emotions, and generate guilt upon recognizing others' suffering (Hoffman, 1970, 1983). Additionally, according to Batson' s empathy-altruism hypothesis (Batson et al., 2007) and Hoffman' s triarchic model of empathy, moral principles, and prosocial behavior (Hoffman, 2001), empathy as a motivational factor can directly elicit prosocial behavior. Based on these theoretical models, empathy—defined as the ability to understand and share others' emotional experiences (Decety et al., 2015)—plays an important mediating role in the process through which parenting influences prosocial behavior (Eisenberg et al., 2015; Padilla-Walker et al., 2016). Empirical studies have also found that maternal positive parenting in early adolescence positively predicts empathy levels, which further predict prosocial behavior toward friends and strangers (Padilla-Walker & Christensen, 2011). This may be because mothers with higher levels of warmth and guidance are more sensitive to children' s needs, can provide timely emotional and instrumental support, guide children to perceive others' emotions, and facilitate the development of emotional understanding and empathy in children and adolescents (Kiang et al., 2004), which in turn promotes the development of prosocial behavior (Lim & DeSteno, 2016).

It should be noted that empathy is not a unidimensional construct; it comprises two components—cognitive empathy and emotional empathy—that exhibit distinct developmental patterns and mechanisms (Singer, 2006; Huang & Su, 2012). Emotional empathy refers to emotional reactions or experiences generated through feeling others'emotional states, whereas cognitive empathy involves understanding others' emotions and feelings, primarily related to inferring others'perspectives (de Waal & Preston, 2017). The dual-process model of empathy and meta-analytic research indicate that cognitive and emotional empathy follow "inverted U-shaped"and "U-shaped"developmental trajectories, respectively, with adolescents at the peak where the difference between cognitive and emotional empathy is greatest, showing significantly lower emotional empathy than cognitive empathy (Huang & Su, 2012; Yan & Su, 2021). Relevant research has shown that cognitive and emotional empathy not only differ in psychological components and developmental trajectories but also in the magnitude of their influence on prosocial behavior and their underlying mechanisms. For instance, some studies have demonstrated that cognitive empathy is a stronger predictor of prosocial behavior than emotional empathy (Kim et al., 2019), while others have shown that although both cognitive and emotional empathy mediate the relationship between parental positive parenting and prosocial behavior in adolescents, the patterns of effect differ (e.g., Davis & Carlo, 2018). In summary, differentiating the components of empathy is crucial for more clearly revealing

the internal mechanisms underlying prosocial behavior. Given that the difference between cognitive and emotional empathy capacities further expands during adolescence, this study hypothesized that both cognitive and emotional empathy would mediate the relationship between positive parenting and prosocial behavior, but that cognitive empathy would demonstrate stronger predictive power.

The development of adolescent prosocial behavior and empathy is influenced not only by positive parenting environments but also has important genetic underpinnings. Domestic and international research consistently shows that the OXTR gene is a significant candidate gene for prosocial behavior and empathy (Gong et al., 2017; Wu & Su, 2015). Located in the p25 region of chromosome 3, this gene encodes oxytocin receptors that are widely distributed in brain regions such as the limbic system and prefrontal cortex, with receptor density and activity influencing individuals' social behavior (Tost et al., 2010). Among the various OXTR gene polymorphisms, the rs53576 polymorphism is the most extensively studied functional polymorphic site, featuring A and G alleles. This polymorphism has been found to be closely associated with individual differences in prosocial behavior (e.g., Wu & Su, 2015) and empathy (e.g., Uzefovsky et al., 2015). However, there remains disagreement regarding which genotype is associated with higher levels of prosocial behavior or empathy. Most studies have shown that the G allele of OXTR gene rs53576 polymorphism is associated with higher levels of helping and comforting behaviors (e.g., Wu & Su, 2015) and greater empathy capacity (e.g., Gong et al., 2017). Nevertheless, other studies have failed to find positive effects of the G allele (Bakermans-Kranenburg & van IJzendoorn, 2014), and some have even found that the A allele has a protective effect (e.g., Costa et al., 2009).

The social salience hypothesis may provide insight into these divergent findings. This hypothesis proposes that oxytocin increases individuals' sensitivity and responsiveness to social environments rather than directly influencing prosocial behavior (Bartz et al., 2011). Shamay-Tsoory and Abu-Akel (2016) further elaborated on the neurophysiological mechanisms through which oxytocin influences social salience, suggesting that the oxytocinergic system and dopaminergic system interact to regulate individuals' environmental sensitivity. Although the OXTR gene does not directly affect oxytocin levels, it can influence the oxytocinergic system by regulating the quantity, organization, and function of oxytocin receptors (Yamasue, 2013), thereby modulating individuals' sensitivity to environmental factors. fMRI research has also shown that the OXTR gene can influence social emotions and behavior by modulating the functional coupling between the hypothalamus and amygdala, thereby regulating individuals' sensitivity to environmental factors (Tost et al., 2010). Based on the social salience hypothesis and fMRI evidence, this study hypothesizes that whether the OXTR gene exhibits protective or risk effects depends on the individual' s social environment, suggesting a gene-environment interaction.

Existing research has provided abundant evidence for gene-environment interac-

tions involving the OXTR gene. On one hand, the OXTR gene can moderate the direct effects of environmental factors on prosocial behavior. Poulin et al. (2012) found that OXTR gene rs53576 polymorphism interacted with real-world fear events to influence individuals' prosocial behavior. Compared to GG carriers, individuals carrying the A allele participated in fewer charitable activities when perceiving high fear but more when perceiving low fear. On the other hand, the OXTR gene can moderate the effects of environmental factors on empathy. Flasbeck et al. (2018) showed that early childhood trauma and OXTR gene rs53576 polymorphism interacted to affect women' s empathy for others' pain. Specifically, for women carrying the A allele, childhood abuse experiences positively predicted empathy levels, whereas this predictive effect was not significant for GG carriers. Mcdonald et al. (2016) found that for infants with the GG genotype, positive parent-child emotional interactions significantly predicted empathy levels, but this predictive effect was not significant for A allele carriers. A recent EEG study found that the OXTR gene interacted with intergroup relations to influence individuals' empathy-related neural activity when facing others' pain; in the ingroup context, GG carriers showed higher empathic reactivity than AA carriers (Luo et al., 2019). These findings indicate that the OXTR gene not only moderates the direct path through which environmental factors influence prosocial behavior but may also moderate the mediating pathways.

Although increasing research has found that the OXTR gene is sensitive to environmental influences, disagreement remains regarding which allele demonstrates greater environmental sensitivity. Most studies have shown that G allele carriers are more likely to attend to social environmental cues (Hostinar et al., 2014; Luo et al., 2019; McQuaid et al., 2013), while a minority of studies have found that AA carriers show higher sensitivity to negative environments than G allele carriers (Poulin et al., 2012; van Roekel et al., 2013). This divergence in findings may be related to different genotype coding approaches (Aliev et al., 2014). Indeed, existing research also shows disagreement regarding how to group heterozygous AG carriers (e.g., Smearman et al., 2015), and different coding approaches may lead to biased results. Some studies have even analyzed only AA and GG genotypes (e.g., Luo et al., 2019), potentially overlooking the effect of heterozygotes. Since the physiological function of OXTR gene rs53576 polymorphism has not been definitively established, this study, based on findings from the majority of research, hypothesized that the G allele is the environment-sensitive allele. Simultaneously, to avoid result biases caused by genotype coding approaches, we employed dummy coding, additive coding, dominant coding, and recessive coding to test the moderating effect of the OXTR gene, ensuring the accuracy and stability of our results.

In summary, this study aims to investigate the relationships and mechanisms among maternal positive parenting, empathy, OXTR gene rs53576 polymorphism, and adolescent prosocial behavior. By constructing a moderated mediation model, we separately examined the mediating roles of adolescent cognitive empathy (perspective-taking) and emotional empathy (empathic concern) in

the relationship between maternal positive parenting and prosocial behavior, as well as the moderating effects of OXTR gene rs53576 polymorphism on the associations between maternal positive parenting and prosocial behavior/empathy capacity. This approach seeks to reveal the internal mechanisms through which parenting influences adolescent prosocial behavior. The conceptual model is presented in Figure 1 [Figure 1: see original paper].

2. Method

2.1 Participants

The data for this study were derived from a large-scale longitudinal project. At Time 1 (T1), when participants were in sixth grade, we measured adolescents' prosocial behavior, maternal positive parenting, and family socioeconomic status. At Time 2 (T2), when participants were in eighth grade, we collected adolescent genetic data, empathy measures, and reassessed prosocial behavior. The effect size for gene-environment interaction is typically 0.01 (e.g., Starr et al., 2014). Power analysis using G*Power 3.1.9.2 indicated that approximately 787 participants were needed to achieve statistical power greater than 80% (α = 0.05). Based on this, we randomly selected 1082 participants at T2 for OXTR genotyping, which satisfied the statistical power requirements. The sample consisted of 538 males (49.7%) and 544 females (50.3%), with a mean age of 14.32 $\pm$ 0.48 years at T2. Participants with genetic data (N = 1082) and those without genetic data (N = 1094) did not differ significantly on family socioeconomic status (t = -0.71, p = 0.48), maternal positive parenting (t = -1.53, p = 0.13), cognitive empathy (t = -0.60, p = 0.55), emotional empathy (t = 1.07, p = 0.29), or T1 prosocial behavior (t = 0.90, p = 0.37). However, individuals with genetic data had higher scores on T2 prosocial behavior (t(1080) = -7.14, p < 0.001). Regarding parental education, 34.2% of mothers and 44.7% of fathers had a bachelor' s degree or higher; 53.3% of mothers and 45.3% of fathers had education between high school and bachelor' s degree; and 11.4% of mothers and 8.1% of fathers had education below high school. In terms of family monthly income, 1.9% of families earned less than 1000 RMB, 20.7% earned between 1000-3000 RMB, 47.0% earned between 3000-6000 RMB, and 28.4% earned more than 6000 RMB.

2.2.1 Maternal Positive Parenting

Maternal positive parenting was assessed using the Chinese version of the Child-Rearing Practices Report (CRPR; Chen et al., 2010), which has been widely used in research on Chinese children and adolescents and has demonstrated good reliability and validity (e.g., Cao et al., 2018; Zhang et al., 2017). In this study, we used eight items from the maternal report on warmth and guidance as indicators of positive parenting. The questionnaire employed a 5-point scale ranging from 0 (completely uncharacteristic) to 4 (completely characteristic), with higher scores indicating more frequent maternal positive parenting behav-

iors. The Cronbach' s α coefficient for positive parenting in this study was 0.83.

2.2.2 Empathy

Adolescents' empathy was measured using the Interpersonal Reactivity Index (IRI; Davis, 1980). The scale consists of 28 items rated on a 5-point scale from 0 (completely uncharacteristic) to 4 (completely characteristic), comprising four dimensions: perspective-taking, empathic concern, fantasy, and personal distress. Perspective-taking and empathic concern measure the cognitive and emotional components of empathy, respectively (Zhang et al., 2010), and existing research indicates that these two dimensions best represent empathy capacity (Siu & Shek, 2005). Therefore, this study used the perspective-taking and empathic concern subscales to assess cognitive and emotional empathy, respectively. Perspective-taking (e.g., "Before criticizing somebody, I try to imagine how I would feel if I were in their place") and empathic concern (e.g., "When I see someone being taken advantage of, I feel kind of protective toward them") each contained seven items, though one item from the empathic concern subscale ("When I see someone who is being treated unfairly, I sometimes don' t feel very much pity for them") was removed due to factor loading below 0.3. The Cronbach' s α coefficients for cognitive empathy and emotional empathy in this study were 0.80 and 0.68, respectively.

2.2.3 Adolescent Prosocial Behavior

The adolescent prosocial behavior questionnaire was adapted from the Children' s Social Behavior Rating Scale (Wang et al., 2011) and measured using peer nominations. Since participants were from a longitudinal project and target students were distributed across different classes due to school transitions (each class included both target and non-target students), we invited all non-target students in each class to rate each same-gender target student on the behavioral descriptions in the questionnaire, considering both familiarity among raters and rating bias. Because class sizes varied, the number of peer raters per target student ranged from 8 to 19 at T1 ($M = 12.77 \pm 2.23$) and from 4 to 21 at T2 ($M = 10.62 \pm 2.97$). The prosocial behavior measure included nine items (e.g., "Helps others when they have difficulty completing a task or activity") rated on a 4-point scale from 0 (never) to 3 (always). For each target student, we calculated the mean score across multiple same-gender peer raters for each item, which served as the target student' s score on that item. We calculated the intra-class correlation coefficient (ICC) for each item separately by class, with all items showing ICCs exceeding 0.65, indicating acceptable inter-rater reliability (Chen et al., 2019). Additionally, our analyses revealed that less than 0.1 of the variance in prosocial behavior was at the class level (T1: ICC = 0.079; T2: ICC = 0.061); therefore, we did not control for class-level covariates in subsequent analyses (Field, 2005). The Cronbach' s α coefficients for prosocial behavior at T1 and T2 were 0.97 and 0.96, respectively.

2.2.4 Family Socioeconomic Status

Family socioeconomic status (SES) was computed as a composite of parental education, parental occupation, and family income. Parental occupation was categorized into three levels based on professional/technical skill requirements: "farmer or unemployed" (1), "blue-collar worker" (2), and "professional or semi-professional worker"(3). Parental education included six categories: "elementary school or below" (1), "middle school (including incomplete middle school)" (2), "high school or technical school (including incomplete high school)" (3), "junior college (including night school or TV university)" (4), "bachelor' s degree" (5), and "graduate degree (master' s or doctoral)" (6). Family monthly income was divided into nine categories from "below 1000 RMB" (1) to "above 8000 RMB" (9) in increments of 1000 RMB. Following previous research (Fan et al., 2012), we used factor analysis to create a composite SES indicator, with higher scores representing higher family socioeconomic status. This composite SES score was used as a control variable in this study.

2.3.1 Data Collection Procedure

The data for this study were derived from a large-scale longitudinal study that began when children were 9 years old (third grade) and conducted annual assessments. The initial design of this longitudinal study aimed to examine the developmental characteristics and influencing factors of problem behaviors in children and adolescents, with empathy added as a new variable when participants reached eighth grade (T2). The early waves of the project used the CRPR to measure maternal positive parenting, but when participants entered middle school, the measure was changed to the Parenting Style Index (PSI; Steinberg et al., 1992), which assesses parenting styles rather than positive parenting behaviors. Therefore, based on our research objectives and the actual data collection situation, we conducted a limited research design within the available data, employing a two-year interval to examine the associations among T1 maternal positive parenting, T2 empathy, and T2 prosocial behavior.

This study was approved by the Ethics Committee of Shandong Normal University. Before data collection, we informed the adolescents' schools, guardians, and the adolescents themselves about the questionnaire administration, saliva collection, and DNA genotyping procedures, and obtained informed consent from all three parties before proceeding. We collected saliva samples from adolescents by class and performed genotyping for OXTR gene rs53576 polymorphism, while using questionnaires to assess maternal positive parenting, adolescent prosocial behavior, and empathy. All sampling and testing procedures were conducted by rigorously trained psychology graduate students.

2.3.2 DNA Sample Collection, Extraction, and Genotyping

With the consent of adolescents, their guardians, and cooperating schools, we collected saliva samples from student participants by class, with 2-5 ml collected

from each participant. Saliva sample collection strictly followed standardized protocols: participants were required to refrain from eating, drinking, chewing gum, or smoking for 30 minutes before sampling, and those with high fever above 38°C were not sampled. Sample quality was checked individually on-site after collection, and participants with substandard samples were re-sampled later. DNA samples were extracted from saliva using standard procedures. OXTR gene rs53576 polymorphism was genotyped using the Sequenom (San Diego, CA, USA) chip-based matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry platform. The primers for this polymorphism were forward: 5' -GGGCCGAGCTTGTGCACTCT-3' and reverse: 5' -TGAGCTTCCCAGCCCCTCCC-3' . PCR conditions were: 94°C for 15 min; 45 cycles of 94°C for 20 s, 56°C for 30 s, and 72°C for 1 min; and a final extension at 72°C for 3 min. This was followed by a single-base extension reaction, with genotyping analysis completed by the MassARRAY Typer software system (version 3.4). The detection platform and technology used in this study demonstrated high reliability (genotyping success rate $> 97\%$).

In this study, the genotype distribution for OXTR gene rs53576 polymorphism was as follows: AA = 48.9% (529 individuals), AG = 41.6% (450 individuals), and GG = 9.5% (103 individuals). Hardy-Weinberg equilibrium tests indicated that the observed genotype frequencies (AA, AG, and GG) matched expected values well, conforming to Hardy-Weinberg equilibrium ($^2 = 0.26$, df = 1, p = 0.61).

2.4 Data Processing and Analysis

Data analysis was conducted using SPSS 21.0, the SPSS macro PROCESS (Hayes, 2013), Mplus 6.0, MATLAB R2013b, and CMA 3.0. First, we used Pearson correlation analysis to calculate correlation coefficients among all study variables. Second, we used PROCESS macro Model 4 (mediation) and latent variable structural equation modeling to independently test the mediating effects of cognitive empathy and emotional empathy. Third, we used PROCESS macro Model 8 (moderated mediation) to test the moderating effect of the OXTR gene. Fourth, we conducted sensitivity analyses to ensure the reliability of our findings: (1) we randomly divided the sample into two subsamples for internal validation and meta-analysis; (2) to avoid potential effects of genotype frequency distribution, we randomly selected equal numbers of AG and AA carriers based on the number of GG carriers (N = 103) and repeated the analyses; (3) we performed k-fold cross-validation using MATLAB R2013b' s regress and crossvalind functions to test the generalizability and predictive validity of the OXTR gene moderation effect; and (4) we conducted a meta-analysis of effect sizes from existing OXTR gene-environment interaction studies to further examine the reliability of our results. For the meta-analysis, we searched NCBI, Web of Science, CNKI, and Google Scholar using keywords including "OXTR gene rs53576 polymorphism," "OXTR gene*environment interaction,*" "*OXTR gene,*" *and* "*OXTR gene-environment,*" *and identified 41 relevant studies. We*

contacted corresponding authors to request environment-phenotype association effect size data for each genotype (AA/AG/GG). Due to extremely low response rates, only three studies (Flasbeck et al., 2018; Yu et al., 2020; Zheng et al., 2020; studies marked with in the reference list) provided data, and we conducted a meta-analysis based on these three studies plus our own results.

Mediation and moderated mediation analyses controlled for gender and SES, with 5000 bootstrap samples drawn to obtain robust standard errors and bootstrap confidence intervals. Results were considered significant if the confidence interval did not contain zero. To further verify the stability of our results, we conducted supplementary analyses controlling for T1 prosocial behavior. In the moderated mediation model, we employed four coding schemes for the OXTR gene: dummy coding (with AA genotype as reference), additive coding (AA = 0, AG = 1, GG = 2), dominant coding (AA = 0, AG/GG = 1), and recessive coding (AA/AG = 0, GG = 1), to determine the impact of different coding approaches on results and ensure reliability (Chen et al., 2018).

3. Results

3.1 Descriptive Statistics and Correlation Analysis

Means, standard deviations, and correlation coefficients for all variables are presented in Table 1 . OXTR gene rs53576 polymorphism genotypes did not differ on positive parenting ($F = 0.37$, $df = 1070$, $p = 0.69$), ruling out gene-environment correlation (rGE). Positive parenting was significantly positively correlated with adolescent cognitive empathy, emotional empathy, and prosocial behavior at both time points. Cognitive empathy and emotional empathy were significantly positively correlated. Both cognitive and emotional empathy were significantly positively correlated with prosocial behavior at both time points. Additionally, prosocial behavior at the two time points was significantly positively correlated, indicating stability in adolescent prosocial behavior.

Table 1 Correlation coefficients among study variables

3.2 Testing the Mediating Role of Adolescent Empathy

Following the methods of Hayes (2013) and Wen and Ye (2014), we first used SPSS macro PROCESS Model 4 to separately test the mediating effects of adolescent cognitive empathy and emotional empathy in the relationship between maternal positive parenting and prosocial behavior. Analysis of the mediating effect of cognitive empathy showed that, after controlling for gender and SES, maternal positive parenting significantly positively predicted adolescent cognitive empathy ($a = 0.11$, $SE = 0.03$, $p < 0.001$), and adolescent cognitive empathy significantly positively predicted prosocial behavior ($b = 0.06$, $SE = 0.01$, $p < 0.001$). The direct effect of maternal positive parenting on prosocial behavior was significant ($c' = 0.03$, $SE = 0.01$, $p = 0.03$). Bootstrap results indicated that the mediating effect of cognitive empathy between positive parenting and

prosocial behavior was significant (ab = 0.006, Boot SE = 0.002), with a 95% confidence interval of [0.002, 0.011]. The mediating effect accounted for 16.7% of the total effect (ab/(ab+c')).

Analysis of the mediating effect of emotional empathy showed that, after controlling for gender and SES, maternal positive parenting significantly predicted adolescent emotional empathy (a = 0.06, SE = 0.03, p = 0.04), and adolescent emotional empathy significantly predicted prosocial behavior (b = 0.05, SE = 0.01, p < 0.001). The direct effect of maternal positive parenting on prosocial behavior was significant (c' = 0.03, SE = 0.01, p = 0.02). However, bootstrap results indicated that the mediating effect of emotional empathy between positive parenting and prosocial behavior was not significant (ab = 0.003, Boot SE = 0.002), with a 95% confidence interval of [0.000, 0.007]. The mediating effect accounted for 9.1% of the total effect (ab/(ab+c')).

To verify the reliability of these results, we conducted two additional analyses. First, because T1 and T2 prosocial behavior were highly stable (r = 0.53, p < 0.001), most of the variance in T2 prosocial behavior may have originated from T1 prosocial behavior. Therefore, we tested the mediation model controlling for T1 prosocial behavior. Consistent with previous results, the mediating effect of cognitive empathy (ab = 0.003, Boot SE = 0.002, 95% CI [0.001, 0.007]) but not emotional empathy (ab = 0.001, Boot SE = 0.001, 95% CI [-0.0004, 0.003]) was significant. Specifically, maternal positive parenting significantly positively predicted adolescent cognitive empathy (a = 0.09, SE = 0.03, p = 0.003), and adolescent cognitive empathy significantly predicted prosocial behavior (b = 0.04, SE = 0.01, p < 0.001), but the predictive effect of positive parenting on prosocial behavior was not significant (c' = 0.01, SE = 0.01, p = 0.26). Second, we tested the mediating effect using latent variable structural equation modeling, which yielded results consistent with the regression analyses (see Table 2), confirming the stability of our findings.

Table 2 Fit indices for mediation models of empathy between positive parenting and prosocial behavior

3.3 The Relationship Between Maternal Positive Parenting and Adolescent Prosocial Behavior: Testing the Moderated Mediation Model

The preceding mediation analyses showed that the mediating effect of emotional empathy did not reach significance; therefore, this study only tested the moderating effect of the OXTR gene on the mediating pathway from maternal positive parenting to prosocial behavior via cognitive empathy. We used four genotype coding schemes to verify the moderated mediation model, with detailed results presented in Table 3 .

In the dummy coding model, the moderated mediation model was supported, with a significant difference in mediating effects only between AA and AG genotypes (AG vs. AA: 95% CI [-0.01, -0.002]; GG vs. AA: 95% CI [-0.01, 0.01]). Specifically, the mediating effect of cognitive empathy was significant for both

AA and GG carriers (AA: 95% CI [0.04, 0.02]; GG: 95% CI [0.003, 0.02]) but not significant for AG carriers (AG: 95% CI [-0.01, 0.01]). After FDR correction, the positive parenting × AG/AA interaction remained significant (corrected p = 0.04). Based on this result, we re-ran the dummy coding moderated mediation model with AG heterozygotes as the reference group, which revealed a significant difference in mediating effects between GG and AG genotypes as well (AG vs. GG: 95% CI [0.002, 0.03]).

In the dominant coding model, the moderated mediation model was supported (95% CI [-0.02, -0.001]). Further analysis showed that the mediating effect of cognitive empathy was significant for AA carriers (95% CI [0.004, 0.02]) but not significant for G allele carriers (95% CI [-0.003, 0.01]). However, after FDR correction, the positive parenting × OXTR interaction was marginally significant (corrected p = 0.075). In both the additive and recessive coding models, the moderated mediation model was not supported (additive model: 95% CI [-0.01, 0.001]; recessive model: 95% CI [-0.003, 0.02]).

Taken together, the results from the four coding schemes suggest that the OXTR gene effect in this study follows an overdominance pattern (Aliev et al., 2014), which reflects heterozygote advantage—heterozygotes show higher fitness and are less susceptible to environmental changes than homozygotes. Clearly, additive, recessive, and dominant coding approaches cannot accurately describe the gene-environment interaction pattern and may confound heterozygote effects. Based on the dummy coding results, we conducted simple slope analyses of the OXTR gene-environment interaction, which revealed that compared to AG heterozygote carriers (simple slope = 0.002, t = 0.08, p = 0.94), positive parenting significantly and positively predicted cognitive empathy in both AA carriers (simple slope = 0.11, t = 4.01, p < 0.001) and GG carriers (simple slope = 0.14, t = 2.16, p = 0.03) (see Figure 2 [Figure 2: see original paper] and Figure 3a [Figure 3: see original paper]).

Furthermore, after simultaneously controlling for gender, SES, and T1 prosocial behavior, the dummy coding approach still supported the moderated mediation model, with a significant difference in mediating effects only between AA and AG genotypes (AG vs. AA: 95% CI [-0.01, -0.001]; GG vs. AA: 95% CI [-0.005, 0.01]). Specifically, the mediating effect of cognitive empathy was significant for both AA and GG carriers (AA: 95% CI [0.001, 0.01]; GG: 95% CI [0.001, 0.02]) but not significant for AG carriers (AG: 95% CI [-0.005, 0.003]).

3.4 Sensitivity Analysis: Internal Validation, k-Fold Cross-Validation, and Meta-Analysis

To verify the reliability of our findings, we conducted a series of analyses. First, we randomly divided the sample into two subsamples. Subsample 1 (N = 510) and Subsample 2 (N = 572) did not differ significantly on any study variables (gender: $^2(1) = 0.01$, p = 0.94; genotype: $^2(2) = 0.68$, p = 0.71; positive parenting: t = 0.17, p = 0.86; T1 prosocial behavior: t = -1.62, p = 0.11;

T2 prosocial behavior: t = -0.83, p = 0.41; cognitive empathy: t = -0.05, p = 0.96; emotional empathy: t = 0.64, p = 0.55; SES: t = 0.62, p = 0.54). We tested the moderated mediation model in both subsamples (see Table 4). In Subsample 1, the difference in mediating effects between AA and AG genotypes was marginally significant, with significant mediation effects in both AA and GG carriers. Positive parenting (b = 0.13, t = 2.14, p = 0.03) and the positive parenting × AG/AA interaction term (b = -0.18, t = -1.98, p = 0.048) significantly predicted cognitive empathy, which in turn significantly predicted prosocial behavior (b = 0.05, t = 2.45, p = 0.01). In Subsample 2, the difference in mediating effects between AA and AG genotypes was significant, with a significant mediation effect only in AA carriers, though the difference between GG and AA genotypes was not significant. Positive parenting (b = 0.23, t = 3.51, p < 0.001) and the positive parenting × AG/AA interaction term (b = -0.18, t = -1.91, p = 0.057) significantly predicted cognitive empathy, which in turn significantly predicted prosocial behavior (b = 0.06, t = 3.44, p < 0.001). The interaction patterns in the gene-environment plots for the two subsamples (Figures 3b and 3c) were generally consistent with the full sample.

Second, to verify the reliability of the OXTR gene-environment interaction, we conducted a meta-analysis of the combined effect sizes of positive parenting on cognitive empathy across genotypes, following previous research (Cao et al., 2019). The results showed that the effect size of positive parenting on cognitive empathy was r = 0.17 (p < 0.001, 95% CI [0.09, 0.26]) in the AA genotype, r = 0.01 (p = 0.89, 95% CI [-0.09, 0.10]) in the AG genotype, and r = 0.25 (p = 0.01, 95% CI [0.05, 0.43]) in the GG genotype. The differences among the three genotypes were significant (Qcontrast = 7.15, p = 0.03), with a significant difference between AA and AG genotypes (Qcontrast = 5.87, p = 0.02), a non-significant difference between AA and GG genotypes (Qcontrast = 0.36, p = 0.55), and a marginally significant difference between GG and AG genotypes (Qcontrast = 3.16, p = 0.08). Overall, our main findings were largely supported by internal validation.

Third, although the genotype frequency distribution in this study was similar to that of East Asian samples in the NCBI database and other Chinese samples (e.g., Luo et al., 2015), we could not rule out the possibility that our results were false positives due to genotype distribution differences. Therefore, based on the number of GG carriers (the least frequent genotype, N = 103), we randomly selected equal numbers of AG and AA carriers and repeated the statistical analyses. The results were largely consistent with the full sample. Mediation analysis showed that, after controlling for gender and SES, cognitive empathy (ab = 0.006, Boot SE = 0.005, 95% CI [0.0003, 0.0198]) but not emotional empathy (ab = 0.004, Boot SE = 0.004, 95% CI [-0.0006, 0.0152]) significantly mediated the relationship between maternal positive parenting and adolescent prosocial behavior. We further tested the moderated mediation model using dummy, additive, dominant, and recessive coding. In the dummy coding model, the difference in mediating effects between AA and AG genotypes was marginally significant (95% CI [-0.015, 0.000]). The mediating effect of cognitive empathy

was significant in both AA and GG carriers (AA: 95% CI [0.0004, 0.05]; GG: 95% CI [0.003, 0.02]) but not in AG carriers (AG: 95% CI [-0.02, 0.01]). Positive parenting (b = 0.14, t = 2.42, p = 0.02) and the positive parenting × AG/AA interaction term (b = -0.17, t = -2.02, p = 0.04) significantly predicted cognitive empathy, while cognitive empathy marginally predicted prosocial behavior (b = 0.04, t = 1.84, p = 0.06). In the additive, dominant, and recessive coding models, the moderated mediation model was not supported (additive model: 95% CI [-0.008, 0.006]; dominant model: 95% CI [-0.025, 0.003]; recessive model: 95% CI [-0.004, 0.019]). These results are consistent with our overall findings.

Fourth, to further verify the generalizability and predictive validity of the OXTR gene moderation model, we performed k-fold cross-validation (k = 10) using MATLAB R2013b' s regress and crossvalind functions, with nine groups as the training set and one group as the test set. The regression model was: y = c + $ $1*parenting* + $ $2AA/AG + $ $3*GG/AG* + $ $4AA/AG*parenting + $ 5 ∗ *GG/AG* ∗ *parenting* + *e.Theresultsshowedthatthemodel−predictedcognitiveempathyscoresweresignificantlycorrelatedwithactuala* 0.12, $p = 10^{-5}$ to 10^{-4}). To test the stability of this result, we repeated this process 10 times, with r values and p values remaining stably significant (r = 0.11 to 0.12, p = 7.37$×10^{-5}$ to 9.18$×10^{-4}$). *Totestwhetherthiscorrelationwassignificant, weperformedapermutationtestw* 4}$, indicating that the moderation model had good fit and stable results.

Finally, the meta-analysis of effect sizes from existing OXTR gene-environment interaction studies showed that the effect size of environment on outcome variables was r = -0.17 (p < 0.001, 95% CI [-0.24, -0.10]) in the AA genotype, with significant heterogeneity across studies (Q = 21.33, p < 0.001, I^2 = 85.94); r = -0.08 (p = 0.01, 95% CI [-0.15, -0.02]) in the AG genotype, with significant heterogeneity (Q = 12.78, p = 0.01, I^2 = 76.52); and r = -0.11 (p = 0.05, 95% CI [-0.210, -0.002]) in the GG genotype, with non-significant heterogeneity (Q = 6.67, p = 0.08, I^2 = 55.00). The differences among the three genotypes were not significant (Qcontrast = 1.69, p = 0.43), and pairwise comparisons between genotypes were all non-significant (AA vs. AG: Qcontrast = 1.55, p = 0.21; AA vs. GG: Qcontrast = 1.27, p = 0.26; AG vs. GG: Qcontrast = 0.01, p = 0.92). This meta-analysis indicated that OXTR gene-environment interactions were not significant.

Table 4 Bootstrap analysis of moderated mediation effects

4. Discussion

The development of prosocial behavior is influenced by multi-level factors including biological, cognitive, emotional, and environmental factors. This study, for the first time based on the "Gene-Environment-Endophenotype-Behavior" model, examined the mediating roles of cognitive empathy (perspective-taking) and emotional empathy (empathic concern) in the relationship between maternal positive parenting and adolescent prosocial behavior, as well as the moderating mechanism of the OXTR gene on this mediation. The findings revealed

that maternal positive parenting indirectly influences prosocial behavior through cognitive empathy, and that the OXTR gene moderates this mediating process, specifically the first half of the "maternal positive parenting–cognitive empathy –prosocial behavior" pathway. For adolescents carrying GG and AA genotypes, maternal positive parenting significantly and positively predicted cognitive empathy, which in turn positively predicted prosocial behavior; however, this mediating effect was not significant for adolescents carrying the AG genotype. This study provides evidence for understanding how parenting environments, prosocial candidate genes, and individual empathy characteristics influence the mechanisms and individual differences in human prosocial behavior.

Mediation analysis revealed a significant positive association between maternal positive parenting and prosocial behavior, consistent with previous research (e.g., Hastings et al., 2015; Padilla-Walker et al., 2016), indicating that maternal positive parenting is an important environmental factor promoting prosocial behavior development. It should be noted that given the possible bidirectional relationship between maternal positive parenting and prosocial behavior (Newton et al., 2014), we conducted supplementary analyses controlling for early prosocial behavior to more accurately reveal the mechanisms of prosocial behavior. Due to the high stability of prosocial behavior development, this approach somewhat attenuated the effect size and significance level of positive parenting, rendering its direct effect on prosocial behavior non-significant.

Contrary to our expectations, this study only found that maternal positive parenting could indirectly influence adolescent prosocial behavior through cognitive empathy, but did not find a mediating role for emotional empathy. According to the dual-process model of empathy (Huang & Su, 2012), this may be related to the developmental decline in emotional empathy capacity during adolescence. As noted earlier, adolescents' cognitive empathy capacity is at a developmental peak while emotional empathy is at a relatively low level, resulting in a stronger association between cognitive empathy and prosocial behavior and diminished predictive power of emotional empathy for prosocial behavior. From a neurophysiological perspective, positive parenting (such as supportive responses to children' s negative emotions) not only regulates medial prefrontal cortex function related to cognitive empathy (Kopala-Sibley et al., 2018) but also influences activation in brain regions related to emotional empathy (e.g., amygdala) (Chen et al., 2020). However, fMRI research has shown that only medial prefrontal cortex activation is associated with prosocial behavior expression, while amygdala activation related to emotional empathy is not associated with prosocial behavior expression (Masten et al., 2011). Therefore, it can be inferred that during adolescence, cognitive empathy plays a stronger role in the link between parenting and prosocial behavior expression.

It should be noted that our stepwise regression analysis showed that positive parenting significantly predicted emotional empathy, and emotional empathy significantly predicted prosocial behavior. Although this pattern suggests that emotional empathy might mediate the relationship between positive parenting

and prosocial behavior, bootstrap tests and latent variable structural equation modeling showed non-significant or marginally significant effects. Considering the overall stability of results, we report that the mediating effect of emotional empathy was not significant. However, this does not imply that emotional empathy is unimportant for adolescent prosocial behavior development; rather, it suggests that cognitive and emotional empathy play different roles in how family environments influence the emergence and development of prosocial behavior in adolescents. Thus, differentiating the components of empathy is important for revealing the mechanisms of prosocial behavior. However, because developmental patterns of cognitive and emotional empathy differ across age stages, our findings cannot be generalized to other developmental stages. Future research should consider using larger age-span longitudinal designs to examine the dynamic roles of different empathy components in prosocial behavior development across ages.

More importantly, this study found that OXTR gene rs53576 polymorphism moderated the mediating pathway from maternal positive parenting to prosocial behavior via adolescent cognitive empathy. Specifically, for adolescents carrying GG and AA genotypes, maternal positive parenting significantly and positively predicted cognitive empathy, which in turn positively predicted prosocial behavior, whereas this mediating pathway was not significant for adolescents carrying the AG genotype. Our findings are consistent with most OXTR gene-environment interaction studies (Hostinar et al., 2014; Luo et al., 2019; McQuaid et al., 2013), which have found that the GG genotype shows higher environmental sensitivity. Consistent with social salience theory, the high environmental sensitivity of GG carriers makes them more susceptible to environmental influences, resulting in higher or lower empathy capacity and prosocial behavior. Since OXTR gene rs53576 polymorphism is located in an intronic (non-coding) region, the physiological functions of each genotype have not been clearly delineated. However, genetic neuroimaging research has shown that compared to A allele carriers, GG carriers exhibit higher amygdala activation and lower amygdala-hypothalamus coupling when processing emotional faces (Tost et al., 2010). This unique neurophysiological structure endows GG carriers with higher reward dependence, increasing their reliance on social approval and enhancing their sensitivity to interpersonal relationships (Tost et al., 2010). Consequently, GG carriers are more likely to attend to social environmental cues and show higher sensitivity to social environmental factors such as maternal parenting behaviors.

However, this study also found that AA carriers show environmental sensitivity, albeit slightly lower than that of GG carriers. Consistent with this result, Luo et al. (2019) found in their neuroimaging study of empathy that G allele carriers show higher sensitivity to environmental cues and are more receptive to subtle or ambiguous social cues, whereas AA carriers lack flexibility in receiving social cues but can also demonstrate environmental sensitivity when social cues are clear and explicit. This result also suggests that the A allele is not devoid of environmental sensitivity but rather shows sensitivity under specific envi-

ronmental conditions. The maternal positive parenting examined in this study may represent a relatively clear and explicit social environmental cue, enabling AA carriers to also demonstrate corresponding environmental sensitivity. To our knowledge, some studies examining OXTR gene-environment interactions using negative environments have found that the A allele is more susceptible to negative environments than the G allele (Poulin et al., 2012; van Roekel et al., 2013). This may be because the G allele' s higher reward dependence (Tost et al., 2010) makes it more likely to benefit from social support when coping with stress (Chen et al., 2011) and more likely to seek positive social support (Kim et al., 2010), buffering the impact of negative environments. In other words, the G allele' s high sensitivity to positive environments may partially offset the negative impact of adverse environments, thereby making the A allele appear more sensitive to negative environments.

Particular attention should be paid to the unique gene-environment interaction pattern revealed in this study—an overdominance effect (Aliev et al., 2014), or heterozygote advantage (heterosis). As our results show, AG heterozygote carriers demonstrate stronger adaptability than homozygote carriers (AA and GG genotypes), being less susceptible to environmental influences and maintaining consistently high levels of cognitive empathy. Previous research on the direct association between the OXTR gene and peer relationships has also found heterozygote advantage, with AG carriers showing higher peer acceptance than AA and GG carriers (He et al., 2018). Similar to our findings, Fang et al. (2020) found that compared to OXTR rs53576 homozygotes (AA and GG carriers), heterozygotes (AG carriers) showed the highest trust levels after experiencing work stress, demonstrating a protective effect. Zheng et al. (2020) also found that after experiencing childhood maltreatment, AA carriers had lower trust levels than AG carriers, with no difference between AA and GG carriers. One possible explanation for this heterozygote advantage phenomenon is that oxytocin function and psychological adaptation or brain function follow an inverted-U shaped dose-response relationship; for instance, both excessively high and low oxytocin function can reduce trust (Rilling et al., 2014) or left ventral caudate nucleus reactivity (Feng et al., 2015). Related research has also shown that the G allele is associated with higher oxytocin efficacy than the A allele (Moons et al., 2014). Thus, GG and AA genotypes may be associated with relatively high and low oxytocin efficacy, respectively, whereas the AG genotype may represent an intermediate level of oxytocin function that achieves optimal psychological adaptation. Another possible explanation for heterozygote advantage is that the two alleles have unique neurophysiological functions, such that heterozygous gene products have a broader range of expression and therefore greater developmental advantage (Comings & MacMurray, 2000). Previous research suggests that OXTR G and A alleles are separately associated with anterior cingulate cortex/supplementary motor area and nucleus accumbens function, respectively (Luo et al., 2015); the AG genotype may combine functions of both alleles, thereby showing higher adaptability. It is worth noting that due to the lack of research on the physiological mechanisms of the intronic (non-coding)

rs53576 polymorphism and the neglect of heterozygote (AG genotype) function in most studies, these hypotheses require verification in future research. Additionally, these findings suggest that arbitrarily grouping genotypes based on distribution frequencies (e.g., combining GG and AG genotypes) is problematic, as inconsistent coding approaches contribute to divergent conclusions in current OXTR gene research and may obscure the true effects of each genotype (Reiner et al., 2016).

Contrary to our expectations, we did not find a moderating effect of the OXTR gene on the direct path between maternal positive parenting and prosocial behavior. This may be because genes and their interactions with the environment typically do not directly encode behavioral phenotypes but rather influence behavioral phenotypes indirectly by affecting neurophysiological functions, endocrine systems, or cognitive components (Caspi & Moffitt, 2006; Meyer-Lindenberg & Weinberger, 2006). That is, the effects of genetic factors and their interactions with the environment on behavioral phenotypes (such as prosocial behavior) may be smaller than their effects on cognitive factors (such as cognitive empathy) and other endophenotypes. Moreover, our results suggest that cognitive empathy may be an endophenotype closer to neurophysiological mechanisms or genetic predispositions. Selecting traits that are closer to genetic structures can not only increase the penetrance of genetic effects but also help future research identify candidate genes (Meyer-Lindenberg & Weinberger, 2006). Consequently, an increasing number of researchers are exploring endophenotype mechanisms that lie between genes and behavioral phenotypes to clarify how genes and gene-environment interactions influence behavioral phenotypes. Our findings provide some insight for constructing this "Gene × Environment → Endophenotype → Behavioral Phenotype" pathway. However, due to the limited research on the functions of OXTR gene rs53576 polymorphism and its neurophysiological mechanisms related to empathy and prosocial behavior, our findings require direct verification in future studies. This also highlights the urgent need for future research to adopt imaging genetics designs within the "Gene-Endophenotype-Behavior" framework to reveal the neurophysiological mechanisms linking OXTR gene function to prosocial behavior, providing new evidence for enriching existing theories.

Several limitations of this study should be noted. First, although we used a longitudinal design to examine the moderated mediation model, empathy data were only collected at T2 in this large-scale longitudinal project. Our analysis of concurrent mediation and outcome variables prevents us from inferring causal relationships. Second, prosocial behavior is multi-dimensional, and different types of prosocial behavior may have different genetic mechanisms. For example, Knafo et al. (2011) found that compliant prosocial behavior is primarily explained by additive genetic effects, whereas spontaneous prosocial behavior is influenced by gene-environment interactions. This study did not distinguish between different types of prosocial behavior, so our findings may not generalize to all prosocial behavior types. Third, this study' s single-gene design has clear limitations. Candidate gene studies based on single SNPs typically have small ef-

fect sizes and low replicability, potentially producing false positive results (Dick et al., 2015; Duncan et al., 2014). For complex psychological and behavioral phenotypes like prosocial behavior, single-gene designs may also oversimplify the process by which genetic factors influence prosocial behavior. Although single-gene studies have faced increasing criticism, this research paradigm still provides preliminary evidence for revealing gene-environment interactions, and their small effect sizes and low replicability have spurred the development of polygenic research paradigms and the "Gene-Endophenotype-Behavior"approach (Caspi & Moffitt, 2006; Duncan et al., 2014). Moreover, single-gene studies still hold value: First, they typically select functional polymorphisms based on the neurophysiological functions of psychological and behavioral development, offering interpretive advantages over gene variants of unknown clinical significance identified by genome-wide association studies (GWAS), and providing a basis for candidate gene-polygenic research while avoiding the data-driven and genetic indicator misuse risks faced by GWAS (Vrshek-Schallhorn et al., 2015). Second, single-gene studies have value for intervention and treatment of psychopathology. Many candidate genes for psychopathology are identified based on drug research targeting neurotransmitter systems. Since the mechanisms of psychopathology development and treatment may differ, GWAS may fail to replicate these candidate genes (Duncan et al., 2014), but single-gene × intervention studies provide insights, as these genes may be important factors moderating the association between interventions (e.g., medication) and treatment efficacy. Fourth, this study only measured maternal parenting behavior and did not assess parenting behaviors of other family members such as fathers or grandparents. However, existing research shows that paternal parenting and grandparental involvement (such as emotional engagement) can also effectively promote prosocial behavior development in children and adolescents (Padilla-Walker et al., 2012; Yorgason & Gustafson, 2014) and may play different roles than maternal parenting (Hastings et al., 2007; Padilla-Walker et al., 2012). Therefore, future research should measure parenting behaviors and family relationships of other family members in the family system to more comprehensively reveal the role and unique mechanisms of family socialization in children' s and adolescents' prosocial behavior. Finally, we used multiple methods including internal validation, k-fold testing, and meta-analysis to examine result reliability. Although internal validation and k-fold testing supported our findings, the meta-analysis did not find significant gene-environment interactions. Due to extremely low researcher response rates, this meta-analysis was based on only four studies, which may introduce substantial bias. Future research should conduct meta-analyses with richer data to verify OXTR gene-environment interactions and this heterozygote advantage effect. Additionally, the meta-analysis results suggest that current findings of gene-environment interactions cannot exclude the possibility of false positives and should be interpreted cautiously. Furthermore, due to the lack of external samples with matching measurement tools and sample characteristics, we could not conduct external validation, and our findings require replication in other samples.

5. Conclusion

In summary, this study found that: (1) Adolescent cognitive empathy (perspective-taking), but not emotional empathy (empathic concern), mediated the relationship between maternal positive parenting and prosocial behavior; (2) The OXTR gene rs53576 polymorphism did not significantly moderate the direct path between maternal positive parenting and prosocial behavior; (3) The OXTR gene rs53576 polymorphism moderated the first half of the "maternal positive parenting—cognitive empathy—prosocial behavior" mediating effect. Specifically, among adolescents carrying GG and AA genotypes, maternal positive parenting significantly and positively predicted cognitive empathy, which in turn increased prosocial behavior, whereas this mediating effect was not significant among adolescents carrying the AG heterozygous genotype, demonstrating an overdominance genetic effect.

References

Aliev, F., Latendresse, S. J., Bacanu, S. A., Neale, M. C., & Dick, D. M. (2014). Testing for measured gene-environment interaction: Problems with the use of cross-product terms and a regression model reparameterization solution. *Behavior Genetics, 44*(2), 165–181.

Augustine, M. E., & Stifter, C. A. (2015). Temperament, parenting, and moral development: Specificity of behavior and context. *Social Development, 24*(2), 285—303.

Bakermans-Kranenburg, M. J., & van Ijzendoorn, M. H. (2014). A sociability gene? Meta-analysis of oxytocin receptor genotype effects in humans. *Psychiatric Genetics, 24*(2), 45—51.

Bartz, J. A., Zaki, J., Bolger, N., & Ochsner, K. N. (2011). Social effects of oxytocin in humans: Context and person matter. *Trends in Cognitive Sciences, 15*(7), 301–309.

Batson, C. D., Eklund, J. H., Chermok, V. L., Hoyt, J. L., & Ortiz, B. G. (2007). An additional antecedent of empathic concern: Valuing the welfare of the person in need. *Journal of Personality and Social Psychology, 93*(1), 65–74.

Bradley, B., Davis, T. A., Wingo, A. P., Mercer, K. B., & Ressler, K. J. (2013). Family environment and adult resilience: Contributions of positive parenting and the oxytocin receptor gene. *European Journal of Psychotraumatology, 4*(1), 21659.

Cao, C., Cao, L., & Chen, J. (2019). Differences in sensitivity to environment depending on Catechol-O-Methyltransferase (COMT) Gene? A meta-analysis of child and adolescent gene-by-environment studies. *Journal of Youth and Adolescence, 48*(4), 655–667.

Cao, C., Rijlaarsdam, J., van der Voort, A., Ji, L., Zhang, W., & Bakermans-Kranenburg, M. J. (2018). Associations between dopamine D2 receptor (DRD2) gene, maternal positive parenting and trajectories of depressive symptoms from early to mid-adolescence. *Journal of Abnormal Child Psychology, 46*(2), 365-379.

Carlo, G., White, R. M. B., Streit, C., Knight, G. P., & Zeiders, K. H. (2017). Longitudinal relations among parenting styles, prosocial behaviors, and academic outcomes in U.S. Mexican adolescents. *Child Development, 89*(2), 577-592.

Caspi, A., & Moffitt, T. E. (2006). Gene-environment interactions in psychiatry: Joining forces with neuroscience. *Nature Reviews Neuroscience, 7*(7), 583-590.

Chen, B., Zhu, Z., Wang, Y., Ding, X., Guo, X., He, M., ···& Huang, A. (2018). Nature vs. nurture in human sociality: Multi-level genomic analyses of social conformity. *Journal of Human Genetics, 63*(5), 605-619.

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*(50), 19937-19942.

Chen, L., Zhang, W. X., Ji, L. Q., & Deater-Deckard, K. (2019). Developmental trajectories of Chinese adolescents' relational aggression: Associations with changes in social-psychological adjustment. *Child Development, 90*(6), 1939-1954.

Chen, X., Bian, Y., Xin, T., Wang, L., & Silbereisen, R. K. (2010). Perceived social change and childrearing attitudes in China. *European Psychologist, 15*(4), 260-270.

Chen, X., McCormick, E. M., Ravindran, N., McElwain, N. L., & Telzer, E. H. (2020). Maternal emotion socialization in early childhood predicts adolescents' amygdala-vmPFC functional connectivity to emotion faces. *Developmental Psychology, 56*(3), 503-515.

Comings, D. E., & MacMurray, J. P. (2000). Molecular heterosis: A review. *Molecular Genetics and Metabolism, 71*(1-2), 19-31.

Costa, B., Pini, S., Gabelloni, P., Abelli, M., Lari, L., Cardini, A., ···& Martini, C. (2009). Oxytocin receptor polymorphisms and adult attachment style in patients with depression. *Psychoneuroendocrinology, 34*(10), 1506-1514.

Davis, A. N., & Carlo, G. (2018). The roles of parenting practices, sociocognitive/emotive traits, and prosocial behaviors in low-income adolescents. *Journal of Adolescence, 62*, 140-150.

Davis, M. H. (1980). A multidimensional approach to individual differences in empathy. *Journal of Personality and Social Psychology, 10*(85).

Decety, J., Bartal, I. B-A., Uzefovsky, F., & Knafo-Noam, A. (2015). Empathy as a driver of prosocial behaviour: Highly conserved neurobehavioural mechanisms across species. *Philosophical Transactions of the Royal Society B: Biological Sciences, 371*(1686), 20150077.

de Waal, F. B., & Preston, S. D. (2017). Mammalian empathy: Behavioural manifestations and neural basis. *Nature Reviews Neuroscience, 18*(8), 498–509.

Dick, D. M., Agrawal, A., Keller, M. C., Adkins, A., Aliev, F., Monroe, S., ···& Sher, K. J. (2015). Candidate gene-environment interaction research: Reflections and recommendations. *Perspectives on Psychological Science, 10*, 37–59.

Duncan, L. E., Pollastri, A. R., & Smoller, J. W. (2014). Mind the gap: Why many geneticists and psychological scientists have discrepant views about gene-environment interaction (G×E) research. *American Psychologist, 69*(3), 249–268.

Eisenberg, N., Spinrad, T. L., & Knafo-Noam, A. (2015). Prosocial development. In M.E. Lamb, & C. Garcia Coll (Vol. Eds.), R.M. Lerner (Series Ed.), *Handbook of Child Psychology, Vol. 3, Social, emotional, and personality development* (7th edn, pp. 610–656). New York: Wiley.

Fan, X. H., Fang, X. Y., Liu, Y., Lin, X. Y., & Yuan, X. J. (2012). The effect of social support and social identity on the relationship between perceived discrimination and socio-cultural adjustment among Chinese migrant children. *Acta Psychologica Sinica, 44*(5), 647-663.

Fang, Y., Li, Z., Wu, S., Wang, C., Dong, Y., & He, S. (2020). Oxytocin receptor gene polymorphisms moderate the relationship between job stress and general trust in Chinese Han university teachers. *Journal of Affective Disorders, 260*, 18–23.

Feng, C., Lori, A., Waldman, I. D., Binder, E. B., Haroon, E., & Rilling, J. K. (2015). A common oxytocin receptor gene (OXTR) polymorphism modulates intranasal oxytocin effects on the neural response to social cooperation in humans. *Genes, Brain and Behavior, 14*(7), 516–525.

Field, A. P. (2005). Intraclass correlation. In B. S. Everitt & D. C. Howell (Eds.), *Encyclopedia of statistics in the behavioral sciences* (pp. 1296–1305). Chichester, England: Wiley.

Flasbeck, V., Moser, D., Kumsta, R., & Brüne, M. (2018). The OXTR single-nucleotide polymorphism rs53576 moderates the impact of childhood maltreatment on empathy for social pain in female participants: Evidence for differential susceptibility. Frontiers in Psychiatry, 9*, 359.

Fortuna, K., & Knafo, A. (2014). Parental and genetic contributions to prosocial behavior during childhood. In L.M. Padilla Walker & G. Carlo (Eds.), *Prosocial development: A multidimensional approach* (pp. 70–89). Oxford: Oxford University Press.

Gong, P., Fan, H., Liu, J., Yang, X., Zhang, K., & Zhou, X. (2017). Revisiting the impact of OXTR rs53576 on empathy: A population-based study and a meta-analysis. *Psychoneuroendocrinology, 80*, 131–136.

Grusec, J. E., & Goodnow, J. J. (1994). Impact of parental discipline methods on the child' s internalization of values: A reconceptualization of current points of view. *Developmental Psychology, 30*(1), 4—19.

Hackel, L. M., Zaki, J., & Van Bavel, J. J. (2017). Social identity shapes social valuation: Evidence from prosocial behavior and vicarious reward. *Social Cognitive and Affective Neuroscience, 12*(8), 1219–1228.

Hastings, P. D., McShane, K. E., Parker, R., & Ladha, F. (2007). Ready to make nice: Parental socialization of young sons' and daughters' prosocial behaviors with peers. *The Journal of Genetic Psychology, 168*(2), 177–200.

Hastings, P., Miller, J., & Troxel, N. R. (2015). Making good: The socialization of children' s prosocial development. In J. Grusec & P.D. Hastings (Eds.), *Handbook of Socialization: Theory and Research* (pp. 637–666). New York, NY: Guilford Press.

Hayes, A. F. (2013). *An introduction to mediation, moderation, and conditional process analysis: A regression-based approach*. New York: Guilford Press.

He, J., Buil, J. M., Koot, H. M., & van Lier, P. A. (2018). Associations between oxytocin receptor (OXTR) genotype and elementary school children' s likability, dis-likability and friendship among classroom peers: A longitudinal study. *Journal of Youth and Adolescence, 47*(9), 1799–1812.

Hoffman, M. L. (1970). Moral development. In P. H. Mussen (Ed.), *Carmichael' s manual of child development* (Vol. 2, pp. 261–359). New York: Wiley.

Hoffman, M. L. (1983). Affective and cognitive processes in moral internalization. In E. T. Higgins, D. N. Ruble, and W. W. Hartup (Eds.), *Social cognition and social development* (pp. 236–274). Cambridge, England: Cambridge University Press.

Hoffman, M. L. (2001). *Empathy and moral development: Implications for caring and justice*. Cambridge University Press.

Hostinar, C. E., Cicchetti, D., & Rogosch, F. A. (2014). Oxytocin receptor gene (OXTR) polymorphism, perceived social support, and psychological symptoms in maltreated adolescents. *Development and Psychopathology, 26*(2), 465–477.

Huang, Y. Q., & Su, Y. J. (2012). The development of empathy across the lifespan: A perspective of double processes. *Psychological Development and Education, 28*(4), 434–441.

Kennedy, D., & Norman, C. (2005). What don' t we know? *Science, 309*(5731), 75.

Kiang, L., Moreno, A. J., & Robinson, J. L. (2004). Maternal preconceptions about parenting predict child temperament, maternal sensitivity, and children' s empathy. *Developmental Psychology, 40*(6), 1081–1092.

Kim, E. K., You, S., & Knox, J. (2019). The mediating effect of empathy on the relation between child self-expressiveness in family and prosocial behaviors. *Journal of Child and Family Studies, 1–10.

Kim, H. S., Sherman, D. K., Sasaki, J. Y., Xu, J., Chu, T. Q., Ryu, C., ···& Taylor, S. E. (2010). Culture, distress, and oxytocin receptor polymorphism (OXTR) interact to influence emotional support seeking. *Proceedings of the National Academy of Sciences, 107*(36), 15717–15721.

Knafo, A., Israel, S., & Ebstein, R. P. (2011). Heritability of children's prosocial behavior and differential susceptibility to parenting by variation in the dopamine receptor D4 gene. *Development and Psychopathology, 23*(1), 53–67.

Knafo-Noam, A., Vertsberger, D., & Israel, S. (2018). Genetic and environmental contributions to children's prosocial behavior: Brief review and new evidence from a reanalysis of experimental twin data. *Current Opinion in Psychology, 20*, 60–65.

Kopala-Sibley, D. C., Cyr, M., Finsaas, M. C., Orawe, J., Huang, A., Tottenham, N., & Klein, D. N. (2018). Early childhood parenting predicts late childhood brain functional connectivity during emotion perception and reward processing. *Child Development, 91*(1), 110–128.

Lim, D., & DeSteno, D. (2016). Suffering and compassion: The links among adverse life experiences, empathy, compassion, and prosocial behavior. *Emotion, 16*(2), 175–182.

Luo, S., Li, B., Ma, Y., Zhang, W., Rao, Y., & Han, S. (2015). Oxytocin receptor gene and racial ingroup bias in empathy-related brain activity. *NeuroImage, 110*, 22–31.

Luo, S., Zhang, T., Li, W., Yu, M., Hein, G., & Han, S. (2019). Interactions between oxytocin receptor gene and intergroup relationship on empathic neural responses to others' pain. *Social Cognitive and Affective Neuroscience, 14*(5), 505–517.

Masten, C. L., Morelli, S. A., & Eisenberger, N. I. (2011). An fMRI investigation of empathy for 'social pain' and subsequent prosocial behavior. *NeuroImage, 55*(1), 381–388.

Mcdonald, N. M., Baker, J. K., & Messinger, D. S. (2016). Oxytocin and parent-child interaction in the development of empathy among children at risk for autism. *Developmental Psychology, 52*(5), 735–745.

McQuaid, R. J., McInnis, O. A., Stead, J. D., Matheson, K., & Anisman, H. (2013). A paradoxical association of an oxytocin receptor gene polymorphism:

Early-life adversity and vulnerability to depression. *Frontiers in Neuroscience, 7*, 128.

Meyer-Lindenberg, A., & Weinberger, D. R. (2006). Intermediate phenotypes and genetic mechanisms of psychiatric disorders. *Nature Reviews Neuroscience, 7*(10), 818–827.

Moons, W. G., Way, B. M., & Taylor, S. E. (2014). Oxytocin and vasopressin receptor polymorphisms interact with circulating neuropeptides to predict human emotional reactions to stress. *Emotion, 14*(3), 562–572.

Newton, E. K., Laible, D., Carlo, G., Steele, J. S., & McGinley, M. (2014). Do sensitive parents foster kind children, or vice versa? Bidirectional influences between children' s prosocial behavior and parental sensitivity. *Developmental Psychology, 50*(6), 1808–1816.

Padilla-Walker, L. M., & Christensen, K. J. (2011). Empathy and self-regulation as mediators between parenting and adolescents' prosocial behavior toward strangers, friends, and family. *Journal of Research on Adolescence, 21*(3), 545—551.

Padilla-Walker, L. M., Carlo, G., Christensen, K. J., & Yorgason, J. B. (2012). Bidirectional relations between authoritative parenting and adolescents' prosocial behaviors. *Journal of Research on Adolescence, 22*(3), 400–408.

Padilla-Walker, L. M., Nielson, M. G., & Day, R. D. (2016). The role of parental warmth and hostility on adolescents' prosocial behavior toward multiple targets. *Journal of Family Psychology, 30*(3), 331–340.

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*(5), 446–452.

Reiner, I., Frieling, H., Beutel, M., & Michal, M. (2016). Gene–environment interaction of the oxytocin receptor gene polymorphism (rs53576) and unresolved attachment status predict depersonalization symptoms: An exploratory study. *Psychological Studies, 61*(4), 295–300.

Rilling, J. K., DeMarco, A. C., Hackett, P. D., Chen, X., Gautam, P., Stair, S., ···& Pagnoni, G. (2014). Sex differences in the neural and behavioral response to intranasal oxytocin and vasopressin during human social interaction. *Psychoneuroendocrinology, 39*, 237–248.

Singer, T. (2006). The neuronal basis and ontogeny of empathy and mind reading: Review of literature and implications for future research. *Neuroscience & Biobehavioral Reviews, 30*(6), 855–863.

Siu, A. M. H., & Shek, D. T. L. (2005). Validation of the interpersonal reactivity index in a Chinese context. *Research on Social Work Practice, 15*(2), 118–126.

Shamay-Tsoory, S. G., & Abu-Akel, A. (2016). The social salience hypothesis of oxytocin. *Biological Psychiatry, 79*(3), 194–202.

Smearman, E. L., Winiarski, D. A., Brennan, P. A., Najman, J., & Johnson, K. C. (2015). Social stress and the oxytocin receptor gene interact to predict antisocial behavior in an at-risk cohort. *Development and Psychopathology, 27*(1), 309–318.

Starr, L. R., Hammen, C., Conway, C. C., Raposa, E., & Brennan, P. A. (2014). Sensitizing effect of early adversity on depressive reactions to later proximal stress: Moderation by polymorphisms in serotonin transporter and corticotropin releasing hormone receptor genes in a 20-year longitudinal study. *Development and Psychopathology, 26*(4), 1241–1254.

Steinberg, L., Lamborn, S. D., Dornbusch, S. M., & Darling, N. (1992). Impact of parenting practices on adolescent achievement: Authoritative parenting, school involvement, and encouragement to succeed. *Child Development, 63*(5), 1266–1281.

Tost, H., Kolachana, B., Hakimi, S., Lemaitre, H., Verchinski, B. A., Mattay, V. S., Weinberger, D. R., & Meyer-Lindenberg, A. (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 of the United States of America, 107*(31), 13936–13941.

Uzefovsky, F., Shalev, I., Israel, S., Edelman, S., Raz, Y., Mankuta, D., Knafo-Noam, A., & Ebstein, R. P. (2015). Oxytocin receptor and vasopressin receptor 1a genes are respectively associated with emotional and cognitive empathy. *Hormones and Behavior, 67*, 60–65.

van Roekel, E., Verhagen, M., Scholte, R. H., Kleinjan, M., Goossens, L., & Engels, R. C. (2013). The oxytocin receptor gene (OXTR) in relation to state levels of loneliness in adolescence: Evidence for micro-level gene-environment interactions. *PLoS ONE, 8*(11), e77689.

Vrshek-Schallhorn, S., Stroud, C. B., Mineka, S., Zinbarg, R. E., Adam, E. K., Redei, E. E., ···& Craske, M. G. (2015). Additive genetic risk from five serotonin system polymorphisms interacts with interpersonal stress to predict depression. *Journal of Abnormal Psychology, 124*(4), 776–790.

Wang, S. Q., Zhang, W. X., Chen, L., Li, H. L., Li, C., & Zhou, L. N. (2011). A multitrait-multimethod analysis of aggressive behaviors in middle childhood. *Acta Psychologica Sinica, 43*(3), 294–307.

Wen, Z. L., & Ye, B. J. (2014). Different methods for testing moderated mediation models: Competitors or backups? *Acta Psychologica Sinica, 46*(5), 714–726.

Wu, N., & Su, Y. (2015). Oxytocin receptor gene relates to theory of mind and prosocial behavior in children. *Journal of Cognition and Development, 16*(2), 302–313.

Yamasue, H. (2013). Function and structure in social brain regions can link oxytocin-receptor genes with autistic social behavior. *Brain and Development,*

35(2), 111–118.

Yan, Z. Q., & Su, Y. J. (2021). Difference between cognitive empathy and affective empathy in development: Meta-analysis preliminary exploration. *Psychological Development and Education, 37*(1), 1–9.

Yorgason, J. B., & Gustafson, K. B. (2014). Linking grandparent involvement with the development of prosocial behavior in adolescents. In *Prosocial development: A multidimensional approach* (pp. 201–217).

Yu, X. Q., Dong. Y., Li, Z. N., Fang, Y., Wu, S., Wang, C., & He, S. C. (2020). Work stress and general trust: The mediating effect of depression and the moderating effect of the OXTR gene rs53576. Journal of Affective Disorders, 272*, 283–288.

Zhang, F. F., Dong. Y., Wang, K., Zhan, Z. Y., & Xie, L. F. (2010). Reliability and validity of the Chinese version of the Interpersonal Reactivity Index-C. *Chinese Journal of Clinical Psychology, 18*(2), 155–157.

Zhang, W., Wei, X., Ji, L., Chen, L., & Deater-Deckard, K. (2017). Reconsidering parenting in Chinese culture: Subtypes, stability, and change of maternal parenting style during early adolescence. *Journal of Youth and Adolescence, 46*(5), 1117–1136.

Zheng, S., Masuda, T., Matsunaga, M., Noguchi, Y., Ohtsubo, Y., Yamasue, H., & Ishii, K. (2020). Oxytocin receptor gene (OXTR) and childhood adversity influence trust. Psychoneuroendocrinology, 121*, 104840.

Note: Figure translations are in progress. See original paper for figures.