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EMPIRICAL RESEARCH

Monoamine Oxidase A (*MAOA*) and Catechol-O-Methyltransferase (*COMT*) Gene Polymorphisms Interact with Maternal Parenting in Association with Adolescent Reactive Aggression but not Proactive Aggression: Evidence of Differential Susceptibility

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Abstract To date, whether and how gene-environment (G × E) interactions operate differently across distinct subtypes of aggression remains untested. More recently, in contrast with the diathesis-stress hypothesis, an alternative hypothesis of differential susceptibility proposes that individuals could be differentially susceptible to environments depending on their genotypes in a "for better and for worse" manner. The current study examined interactions between monoamine oxidase A (*MAOA*) T941G and catechol-O-methyltransferase (*COMT*) Val158Met polymorphisms with maternal parenting on two types of aggression: reactive and proactive. Moreover, whether these potential G × E interactions would be consistent with the diathesis-stress versus the differential susceptibility hypothesis was tested. Within the sample of 1399 Chinese Han adolescents (47.2 % girls, $M_{age} = 12.32$ years, $SD = 0.50$), *MAOA* and *COMT* genes both interacted with positive parenting in their associations with reactive but not proactive aggression. Adolescents with T alleles/TT homozygotes of *MAOA* gene or Met alleles of *COMT* gene exhibited more reactive aggression when exposed to low positive parenting, but less reactive aggression when exposed to high positive parenting. These findings provide the first evidence for distinct G × E interaction effects on reactive versus proactive aggression and lend further support for the differential susceptibility hypothesis.

Keywords *MAOA* gene · *COMT* gene · Reactive aggression · Proactive aggression · Differential susceptibility

Introduction

Aggression is a significant problem among adolescents throughout the world. It has been reported that as many as 17.7 % of adolescents aged 12 to 17 in the United States engaged in a serious flight at school or at work in the past year (SAMHSA 2014), and 17.9 % of adolescents in China committed a serious aggressive behavior (Wang et al. 2012). Although the level and frequency of aggression decreases when individuals enter adolescence (Bongers et al. 2004), its severity and perniciousness increases during this period (Tremblay 2010). Besides, it is during early adolescence that the later-onset developmental path of aggression and related behaviors emerges (Moffitt 1993; Odgers et al. 2008). Aggression among early adolescents is associated with important life-long outcomes, such as antisocial behavior, substance use and internalizing behavior (Hubbard et al. 2010; Odgers et al. 2008). Together, these data and evidence highlight the need to better understand the etiology of adolescent aggression.

Expressions of problem behaviors such as aggression are influenced by a complex interplay of biological, psychological and social factors (Anholt and Mackay 2012). With

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the upsurge of interest on the genetic underpinning of human aggression during the last decade, researchers have demonstrated that certain candidate genes such as *monoamine oxidase A* (*MAOA*) (Buckholtz and Meyer-Lindenberg 2008; McDermott et al. 2009) and *catechol-O-methyltransferase* (*COMT*) (Albaugh et al. 2010; Volavka et al. 2004) are associated with individual differences in human aggression (also see Anholt and Mackay 2012 for a review). However, the fact that almost no major effect size of any single gene has been observed indicates that these genes do not work independently, but interact with environmental factors to affect aggression (Moffitt 2005). Recent empirical research on gene-environment (G × E) interaction has shown that genes interact with environmental factors in their associations with aggression (e.g., Caspi et al. 2002; DiLalla et al. 2015; Thompson et al. 2012; Widom and Brzustowicz 2006).

Although they are related to one another (see Hubbard et al. 2010 for a review), proactive aggression and reactive aggression represent two distinct subtypes of aggressive behavior. Proactive aggression refers to initiative and instrumental aggression without emotional arousal. Reactive aggression, in contrast, refers to an anger defensive response to real or perceived provocation (Dodge and Coie 1987). Recent twin studies have revealed that both proactive and reactive aggression could be explained by unique genetic and environmental effects, in addition to their common underpinnings, which highlights the necessity to distinguish these two types of aggression in exploring the underlying mechanism of aggression (Baker et al. 2008; Brendgen et al. 2006; Tuvblad et al. 2009). However, to date, very few studies have tested whether G × E interactions operate differently across these two distinct subtypes of aggression.

Existing evidence has shown that enhanced functioning of dopaminergic and noradrenergic pathways are related to the increased risk for aggression (Volavka et al. 2004). The *MAOA* and *COMT* genes, both responsible for encoding the monoamine degradation enzyme, have been thought to confer vulnerability to aggression (e.g., Albaugh et al. 2010; Caspi et al. 2002). Specifically, the *MAOA* gene, located on the Xp11.23–11.4, is involved in the catabolism of dopamine, serotonin and noradrenaline. To date, the overwhelming majority of studies on the effect of *MAOA* gene on aggression have focused on variable number tandem repeat polymorphism in the promoter region of *MAOA* gene (*MAOA-uVNTR)* (Buckholtz and Meyer-Lindenberg 2008). However, it should be noted that the T941G polymorphism in exon 8 has also been identified as a common functional polymorphism, especially among Asians (Fan et al. 2010; http://www.ensembl.org/Homo_sapiens/Variation/Population?db=core;g=ENSG00000189221;r=X:43515467-43606068;v=rs6323;vdb=variation;vf=8347). Synonymous substitution of *T* to *G* at this location could improve MAOA activity as much as about 75 % (Hotamisligil and Breakefield 1991). The *COMT* gene, mapping to 22q11.1–11.2, plays an important role in the degradation of dopamine, epinephrine and noradrenaline. A substitution of methionine (Met) in place of valine (Val) at codon 158 (Val158Met) can result in a three to fourfold decrease in COMT activity (Lachman et al. 1996).

Both *MAOA* and *COMT* genes have been shown to be involved in excessive emotional sensitivity (Buckholtz and Meyer-Lindenberg 2008; Smolka et al. 2005) and hostile attributional biases (Wakschlag et al. 2010; Gohier et al. 2014), which uniquely underlie reactive aggression (Hubbard et al. 2010). Therefore, it is reasonable to infer that *MAOA* and *COMT* genes could be more likely to be disposed toward reactive aggression, instead of proactive aggression. Indeed, one recent study found that low-activity alleles of *MAOA-uVNTR* were related to reactive aggression, but not proactive aggression (Kuepper et al. 2013), providing first direct evidence for the differential associations between *MAOA* gene with reactive and proactive aggression. To our knowledge, this is the only study to directly compare the molecular genetic underpinnings between these two types of aggression. Although this study represents an advance in understanding the differential associations between *MAOA* gene and reactive and proactive aggression, it did not directly examine whether G × E interactions operated differently across proactive versus reactive aggression. In the present study, we aimed to address this issue by examining how *MAOA* and *COMT* genes interacted with parenting environments on these two types of aggression.

It has been well established that maternal parenting plays a crucial role in the development of child and adolescent aggression and other psychological problems. Negative parenting including abuse and punishment contributes to the increase in adolescent aggression by modeling violent behavior and promoting hostile attributions (Gershoff 2002). In contrast, positive parenting, such as warmth and support, can foster the development of adolescent negotiation and conflict-resolution skills (Pettit et al. 1997), and hence has protective effects against aggression (Chen et al. 2002; Gershoff 2002). In addition to its independent role, the bulk of G × E studies have provided ample evidence that maternal parenting interacts with genes to affect aggression (e.g., Caspi et al. 2002; Moffitt 2005; Widom and Brzustowicz 2006).

To be noted, to date, most of the extant studies regarding gene-parenting interactions have been conducted under the framework of diathesis-stress and "risk allele" assumptions (Monroe and Simons 1991; Burmeister et al. 2008), and thus have largely focused on negative rearing environments (e.g., Caspi et al. 2002; Widom and Brzustowicz

2006). However, the genes could be "plasticity" rather than "risk" according to the differential susceptibility hypothesis (Bakermans-Kranenburg and van IJzendoorn 2011; Belsky and Pluess 2009). That is, individuals with "plasticity alleles" not only suffer from adverse environments, but also benefit from supportive environments. Because the essential for investigating differential susceptibility hypothesis is an assessment of positive/supportive environments, not merely the absence of negative environmental conditions (Buil et al. 2015), we included both positive and negative maternal parenting in examining the G × E interaction in their associations with proactive aggression and reactive aggression in the present study.

Current Study

This study investigated the interactions between *MAOA* T941G and *COMT* Val158Met polymorphisms with maternal positive/negative parenting on adolescent two types of aggression: proactive and reactive aggression. We addressed two aims. First, we examined whether and how G × E interactions may operate distinctly across these two types of aggression. Based on the evidence that the *MAOA* and *COMT* genes are uniquely involved in reactive aggression/reactive aggression-related endophenotypes (Buckholtz and Meyer-Lindenberg 2008; Gohier et al. 2014; Kuepper et al. 2013; Smolka et al. 2005; Wakschlag et al. 2010), we expected that the G × E effect may vary across proactive and reactive aggression. However, due to the lack of relevant empirical findings, we do not have a specific hypothesis for this issue. Second, by focusing on both positive and negative parenting, we tested two competing hypotheses about G × E interaction: diathesis-stress hypothesis and differential susceptibility hypothesis. According to the diathesis-stress hypothesis, in the present study, individuals with risk alleles of the *MAOA* T941G and *COMT* Val158Met genes would suffer from low positive parenting or high negative parenting environments compared with others and hence exhibit more aggression, whereas no differences between individuals would be expected in response to high positive parenting or low negative parenting environments. Otherwise, according to the differential susceptibility hypothesis, individuals with plasticity alleles of these two genes would not only exhibit more aggression when exposed to low positive parenting or high negative parenting, but also exhibit less aggression when exposed to high positive parenting or low negative parenting. To this end, after identifying the interaction patterns using traditional regression analysis, the robustness of these interactive effects were tested in an additional sensitivity analysis of re-parameterized regression to maximize the statistical power.

Materials and Methods

Participants

Participants consisted of 1433 early adolescents (47.2 % girls, $M_{age} = 12.32$ years, $SD = 0.49$), recruited from 39 classes in grade 6 of 14 primary schools in Jinan, P.R. China. Of them, 97.6 % ($N = 1399$, 47.2 % girls, $M_{age} = 12.32$ years, $SD = 0.50$) were of Chinese Han ethnicity, and 2.4 % ($N = 34$, 50.0 % girls, $M_{age} = 12.35$ years, $SD = 0.49$) were of Chinese minorities. We limited analyses on the subsample of Chinese Han ethnicity in order to minimize the effect of population stratification. The majority (90.0 %) of the sample were adolescents without siblings. The mean age of mothers was 39.10 years ($SD = 2.40$ years) and family income per month varied moderately (2.1 % < ¥1000; 22.5 % = ¥1001–¥3000; 45.6 % = ¥3001–¥6000; 29.8 % > ¥6001). Adolescents were asked to provide their saliva samples for DNA extraction under the instructions of trained research investigators. Mothers and teachers were recruited in classroom to complete maternal parenting and adolescent aggression questionnaires, respectively. This study was approved by the local ethics committee, and informed assent from adolescents themselves and consent from their mothers and school principals were obtained prior to data collection.

Measures

Reactive and Proactive Aggression

Adolescent proactive and reactive aggression were assessed by teachers via the widely used instrument in this regard: Proactive and Reactive Aggression Questionnaire (PRQ) (Dodge and Coie 1987). Teachers were asked to what extent the adolescent involved in proactive aggression (3 items; e.g., "Use physical force to dominate") and reactive aggression (3 items; e.g., "When teased, strikes back"); responses were given on a 3-point scale (0 = never, 1 = sometimes, 2 = often). Confirmatory factor analysis (CFA) indicated that the two-factor construct ($\chi^2 = 80.11$, $df = 8$, RMSEA = .08, NFI = .99, NNFI = .99, CFI = .99, AGFI = .95) was better than the single-factor construct ($\chi^2 = 2520.04$, $df = 9$, RMSEA = .44, NFI = .87, NNFI = .79, CFI = .87, AGFI = .14). The Cronbach's alphas for proactive and reactive aggression were both .95.

Maternal Parenting

The mothers reported their parenting on the Chinese version of Child Rearing Practices of Report (CRPR) with response ranging from 0 (not all at true) to 4 (almost always true). This Chinese version was revised by Chen and his colleagues (Chen et al. 2000, 2002) to assess

maternal *warmth* (e.g., "My child and I have warm, intimate times together"), *induction* (e.g., "I talk it over and reason with my child when s/he misbehaves"), *rejection* (e.g., "I yell at my child when I am angry") and *punishment orientation* (e.g., "I believe physical punishment to be the best way of disciplining"). These dimensions were combined to form two broad-band scores: *positive parenting* (i.e., warmth and induction) and *negative parenting* (i.e., rejection and punishment orientation). CFA indicated that the two-factor model provided a good fit to the data ($\chi^2 = 2146.19$, $df = 251$, RMSEA = .07, NFI = .92, NNFI = .92, CFI = .93, AGFI = .87). The Cronbach's alphas for positive and negative parenting were .98 and .97, respectively.

Genotyping

Genomic DNA was extracted from each saliva sample using standard techniques. The T941G and Val158Met polymorphisms were genotyped by the analysis of primer extension products generated from amplified genomic DNA using a Sequenom (San Diego, CA, USA) chip-based MALDI-TOF mass spectrometry platform. The T941G polymorphism was amplified using the following primer sequences: forward ACGTTGGATGTGCACTTAAAT GACAGTCCC and reverse ACGTTGGATGGATTCACT TCAGACCAGAGC. The primer sequences for Val158Met polymorphism were as follows: forward ACGTTGGAT GACCCAGCGGATGGTGGATTT and reverse ACGTTG GATGTTTTCCAGGTCTGACAACGG. With regard to *COMT* gene, 0.6 % failed for genotyping.

Data Analysis

A set of MANOVAs were conducted to test the associations between genes with aggression and maternal parenting, followed by traditional linear regressions to provide initial testing for G × E interactions. Then, re-parameterized regression models, a newly-developed approach, were fitted to test the nature of G × E interactions (Belsky et al. 2013; Widaman et al. 2012), which had the form:

$$Y: \begin{cases} GROUP = 1 & Y = B_0 + B_1(X_1 - C) + B_3X_3 + B_4X_4 + E \\ GROUP = 2 & Y = B_0 + B_2(X_1 - C) + B_3X_3 + B_4X_4 + E \end{cases}$$

where Y is the dependent variable of proactive/reactive aggression, *GROUP* allelic groups, X_1 positive/negative parenting (mean centered; ranged from −2.37 to 0.92 and −1.03 to 2.07, respectively), X_3 and X_4 controlled variables—the other type of parenting and aggression, B_0 the intercept, B_1 slope for positive/negative parenting for non-risk/non-plasticity alleles, B_2 slope for positive/negative parenting for risk/plasticity alleles, B_3 and B_4 slopes for controlled variables, C the crossover point where the slopes for allelic groups cross.

What distinguishes the diathesis-stress and differential susceptibility models is the location of the crossover point C, while the two models make identical predictions about the slopes for two allele subgroups—the slope only for risk/plasticity alleles is significant (Widaman et al. 2012). So if the point and 95 % confidential interval (CI) of C fall within the range of parenting, the G × E interaction is *crossover* in forms consistent with the differential susceptibility model. Otherwise, if these values of C fall at or over the maximum of parenting, the G × E interaction is *ordinal*, according with the diathesis-stress model (Widaman et al. 2012). These two models can be further subdivided into "strong" and "weak" versions. Strong versions assume that "non-risk/non-plasticity alleles" carriers are not susceptible to environments (i.e., constraining $B_1 = 0$), whereas weak versions assume that these individuals are to a lesser extent susceptible to environments than others with "risk/plasticity alleles" (i.e., relaxing $B_1 = 0$). When these models are nested within each other, F test can be used to compare if one model explain more or less variance than another one. Moreover, lower values of Akaike information criterion (AIC) and Bayesian information criterion (BIC) in a model indicate a better fit to the data. SAS and R procedures were both used and provided identical results in this study. Consistent with previous studies (Belsky et al. 2013; Hartman et al. 2015), we did not control Type I error rate, as it is not a prerequisite of re-parameterized regressions. To be noted, the major advantage of this approach is that it can avoid the negative bias of omnibus tests from exploratory methods (e.g., hierarchical regressions) and maximize statistical power by aligning analyses with hypotheses of interest, thereby detect G × E interaction that exploratory methods do not (Belsky et al. 2013).

Finally, we conducted an internal replication analysis by randomly splitting the total sample into two subsamples. Besides, it should be noted that, as recommended by prior studies (Verma et al. 2014; Wakschlag et al. 2010), analyses involving *MAOA* gene were conducted separately for each gender, because of the uncertainties about epigenetic mechanisms and inactivation of one of the X chromosomes. Gender was controlled as covariate in analyses involving *COMT* gene.

Results

Preliminary Analyses

Among boys, genotype frequencies for T941G polymorphism were G allele: 58.5 %, T allele: 41.5 %; among girls, the frequencies were GG: 36.7 %, GT: 47.3 %, TT:

16.0 %, which accorded with Hardy–Weinberg equilibrium. Because of uncertain X-inactivation and resulting in vivo MAOA activity levels, heterozygous girls were excluded from further analyses involving *MAOA* gene (Pickles et al. 2013; Widom and Brzustowicz 2006). Distribution of Val158Met polymorphism was Val/Val = 55.8 %, Val/Met = 36.7 %, Met/Met = 7.5 %. Genotype frequencies for Val158Met polymorphism accorded with Hardy–Weinberg equilibrium.

The descriptive statistics of research variables are shown in Table 1. *MANOVA* revealed no main effects of T941G (boys: *Wilk's* $\lambda = 1.00$, $F(2, 736) = 0.23$, $p > .05$; girls: *Wilk's* $\lambda = 1.00$; $F(2, 344) = 0.38$, $p > .05$) or Val158Met polymorphism (*Wilk's* $\lambda = 1.00$, $F(4, 2772) = 0.14$, $p > .05$) on proactive and reactive aggression. Neither significant relationship between parenting with T941G (boys: *Wilk's* $\lambda = 1.00$, $F(2, 721) = 1.03$, $p > .05$; girls: *Wilk's* $\lambda = 1.00$; $F(2, 343) = 0.45$, $p > .05$) or Val158Met (*Wilk's* $\lambda = 1.00$, $F(4, 2732) = 0.42$, $p > .05$) was observed. Positive and negative parenting were both related to proactive and reactive aggression ($|rs| \geq .12$, $ps < .001$). Besides, the two types of aggression were correlated ($r = .65$, $p < .001$) and boys reported higher levels of proactive and reactive aggression than girls ($t(1395)s \geq 6.99$, $ps < .001$).

Interactions Between T941G Polymorphism and Maternal Parenting on Aggression

Reactive Aggression

In line with Hartman et al. (2015), we firstly conducted traditional linear regressions predicting reactive aggression from maternal parenting for different allelic groups. Among boys, the slopes for positive parenting on reactive aggression were as follows: G allele group, $\beta = -.00$, $t = -0.08$, $p > .05$; T allele group, $\beta = -.09$, $t = -1.97$, $p < .05$; among girls, the slopes for positive parenting on reactive aggression were as follows: GG homozygote group, $\beta = -.04$, $t = -0.57$, $p > .05$; TT homozygote group, $\beta = -.23$, $t = -2.20$, $p < .05$. None of the slopes for negative parenting in allelic groups were significant for boys and girls ($|\beta|s \leq .07$, $|t|s \leq 1.43$, $ps > .05$). These results indicated that associations between positive parenting and reactive aggression only existed among T allele/TT homozygote carries, but not among G allele/GG homozygote carries, providing initial indication of T941G × positive parenting interactions (see Fig. 1).

Next, re-parameterized regressions were conducted with T alleles/TT homozygotes assumed to be the plasticity/risk group. Results involving T941G × positive parenting interactions (see Table 2) showed that, *for boys*, the strong

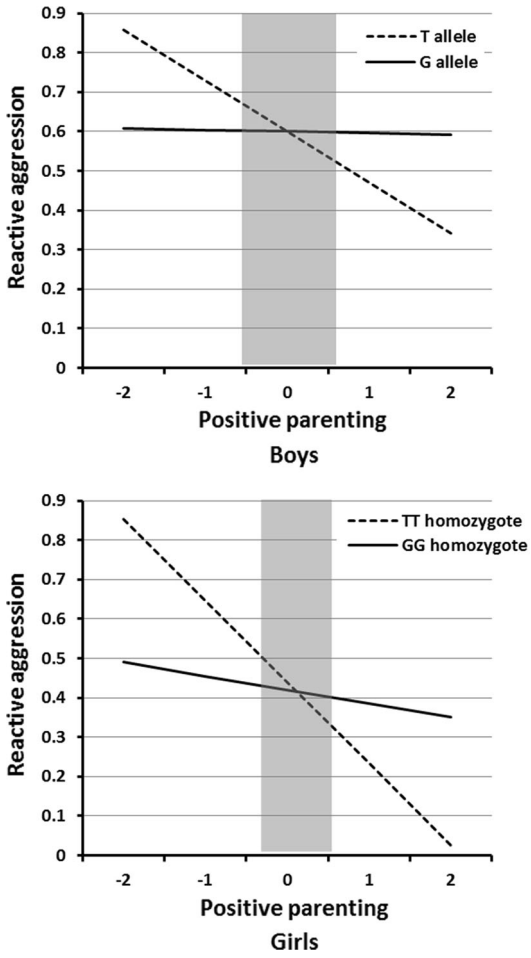

Fig. 1 Simple slopes on reactive aggression from positive parenting in MAOA T941G allelic groups. *Grey shaded* area represents 95 % CI of the cross over point *C* of the interaction on the positive parenting axis. For boys, 95 % CI of *C* ranged from −0.54 to 0.64; for girls, 95 % CI of *C* ranged from −0.29 to 0.53

Table 1 Mean and SD for aggression and maternal parenting among different allelic groups

	T941G				Val158Met		
	G	T	GG	TT	Val/Val	Val/Met	Val/Met
RA	0.66 (0.63)	0.69 (0.66)	0.33 (0.45)	0.34 (0.46)	0.51 (0.58)	0.52 (0.60)	0.48 (0.56)
PA	0.23 (0.47)	0.25 (0.48)	0.09 (0.24)	0.07 (0.22)	0.17 (0.39)	0.18 (0.42)	0.15 (0.38)
PP	3.03 (0.51)	3.03 (0.47)	3.13 (0.46)	3.09 (0.51)	3.08 (0.48)	3.06 (0.50)	3.11 (0.54)
NP	1.06 (0.47)	1.11 (0.49)	0.98 (0.49)	0.97 (0.42)	1.02 (0.46)	1.04 (0.49)	0.99 (0.51)

RA reactive aggression, *PA* proactive aggression, *PP* positive parenting, *NP* negative parenting

Table 2 Results for re-parameterized regression models examining T941G × positive parenting interactions on reactive aggression

Parameter	Boys				Girls			
	Differential susceptibility		Diathesis-stress		Differential susceptibility		Diathesis-stress	
	Strong	Weak	Strong	Weak	Strong	Weak	Strong	Weak
B_1	0.00 (–)[a]	−0.01 (0.05)	0.00 (–)[a]	−0.04 (0.04)	0.00 (–)[a]	−0.03 (0.06)	0.00 (–)[a]	−0.07 (0.05)
C	0.05 (0.30)	0.06 (0.33)	0.92 (–)[a]	0.92 (–)[a]	0.12 (0.21)	0.12 (0.24)	0.92 (–)[a]	0.92 (–)[a]
95 % CI of C	[−0.54, 0.64]	[−0.59, 0.71]	–	–	[−0.29, 0.53]	[−0.35, 0.59]	–	–
B_2	−0.12 (0.06)*	−0.12 (0.06)*	−0.04 (0.03)	−0.08 (0.05)	−0.22 (0.08)**	−0.22 (0.08)**	−0.08 (0.04)*	−0.14 (0.06)*
B_3	0.07 (0.04)	0.06 (0.04)	0.08 (0.04)*	0.06 (0.04)	0.01 (0.05)	−0.00 (0.05)	0.04 (0.04)	−0.00 (0.05)
B_4	0.86 (0.04)***	0.86 (0.04)***	0.87 (0.04)***	0.86 (0.04)***	0.98 (0.09)***	0.98 (0.09)***	0.99 (0.09)***	0.98 (0.09)***
R^2	.43	.43	.42	.42	.29	.29	.28	.28
F	133.30***	106.51***	176.61***	132.72***	34.32***	27.44***	43.83***	33.44***
df	4, 719	5, 718	3, 720	4, 719	4, 340	5, 339	3, 341	4, 340
F versus a	–	0.06	2.38	–	–	0.24	4.46*	–
df	–	1, 718	1, 719	–	–	1, 339	1, 340	–
AIC	1007.21	1009.15	1007.59	1008.55	323.74	325.50	326.24	326.31
BIC	1034.71	1041.24	1030.52	1036.06	346.81	352.40	345.46	349.37

Model: $RA = (T941G = \text{G/GG})(B_0 + B_1(X_{PP} - C)) + (T941G = \text{T/TT})(B_0 + B_2(X_{PP} - C)) + B_3X_{NP} + B_4PA + E$; F versus a stands for F tests of the difference in R^2 for a given model versus the strong differential susceptibility model

RA reactive aggression, *PP* positive parenting, *NP* negative parenting, *PA* proactive aggression, *CI* confidential interval

[a] Parameter fixed at reported value; *SE* is not applicable, so is listed as –

* $p < .05$; ** $p < .01$; *** $p < .001$

differential susceptibility model with $B_1 = 0$ explained a significant amount of variance in reactive aggression ($R^2 = .43$, $p < .001$), in which the slope for positive parenting in T allele group (i.e., the assumed plasticity group) was significant ($B_2 = -0.12$, $SE = 0.06$, $t = -2.00$, $p < .05$). The estimated point and 95 % CI of the crossover point C both fell within the range of positive parenting, $C = 0.05$ ($SE = 0.30$), 95 % CI = [−0.54, 0.64]. Furthermore, although the weak differential susceptibility model had one more parameter than the strong model, it did not explained more variance, $\Delta R^2 = .00$, $p > .05$. Neither strong nor weak diathesis-stress model had significant slopes for positive parenting in T allele group (i.e., the assumed plasticity/risk group) ($|B_2|$s ≤ 0.08, $|SE|$s ≤ 0.05, $|t|$s ≤ 1.64, ps $> .05$), thus were both rejected. In sum, all the statistical indexes support for the strong differential susceptibility model, in which boys with T alleles functions in a "for better and for worse" manner (see Fig. 1).

For girls (see Table 2), the strong differential susceptibility model involving T941G × positive parenting interactions also had strong fit to the data ($R^2 = .29$, $p < .001$). The slope for positive parenting in TT homozygote group was significant ($B_2 = -0.22$, $SE = 0.08$, $t = -2.85$, $p < .01$), and the point and 95 % CI of C fell within the range of positive parenting, $C = 0.12$ ($SE = 0.21$), 95 % CI = [−0.29, 0.53]. Moreover, the strong differential susceptibility model fitted better to the data than other models, which demonstrated that TT homozygotes were susceptive to positive parenting (see Fig. 1).

With regard to T941G × negative parenting interactions, none of the slopes for negative parenting in T allele/TT homozygote group (i.e., the assumed plasticity/risk group) were significant ($|B_2|$s ≤ 0.13, $|SE|$s ≤ 0.10, $|t|$s ≤ 1.37, ps $> .05$), therefore no significant interactions were observed in four models both for boys and girls (see Table 4 in the "Appendix").

Proactive Aggression

None of the slopes for positive/negative parenting on proactive aggression in different allelic groups were significant for boys and girls ($|\beta|$s $\leq .07$, $|t|$s ≤ 1.31, ps $> .05$). In re-parameterized regression models, none of the slopes for parenting in T allele/TT homozygote group were significant ($|B_2|$s ≤ 0.05, $|SE|$s ≤ 0.05, $|t|$s ≤ 1.42, ps $> .05$). In brief, all the statistical indexes indicated no significant T941G × parenting interactions on proactive aggression (see Tables 5, 6 in the "Appendix").

Interactions Between Val158Met Polymorphism and Maternal Parenting on Aggression

As previous study recommended (Hartman et al. 2015), the Val158Met × maternal parenting interactions were tested

in three genetic models: *dominant* (Met allele vs. Val/Val homozygote), *recessive* (Met/Met homozygote vs. Val allele) and *additive* (Met/Met vs. Val/Met vs. Val/Val genotype) models. Here, we present the results of the dominant genetic model, because this model provided better fit to the data.

Reactive Aggression

The slopes for maternal positive parenting on reactive aggression were as follows: Val/Val homozygotes, $\beta = -.03$, $t = -0.93$, $p > .05$; Met alleles, $\beta = -.10$, $t = -2.72$, $p < .01$. The slopes for negative parenting in allelic groups were non-significant (Val/Val homozygotes, $\beta = .04$, $t = 1.33$, $p > .05$; Met alleles, $\beta = .05$, $t = 1.31$, $p > .05$). These regression results provided initial indication of Val158Met × positive parenting interactions (see Fig. 2). Then, the same sets of re-parameterized regressions indicated that the strong differential susceptibility model fitted better to the data for Val158Met × positive parenting interactions on reactive aggression, where the Met allele carriers were sensitive to positive parenting (see Table 3, Fig. 2). However, no significant Val158Met × negative parenting interactions on reactive aggression were observed ($|B_2|$s ≤ 0.07, $|SE|$s ≤ 0.04, $|t|$s ≤ 1.88, ps $> .05$) (see Table 7 in the "Appendix").

Proactive Aggression

None of the slopes for positive and negative parenting on proactive aggression in different allelic groups was significant ($|\beta|$s $\leq .03$, $|t|$s ≤ 1.04, ps $> .05$) and none of the slopes for parenting in Met allele group (i.e., the assumed plasticity/risk group) were significant in re-parameterized regression models ($|B_2|$s ≤ 0.03, $|SE|$s ≤ 0.03, $|t|$s ≤ 1.29, ps $> .05$). Briefly, no significant Val158Met × parenting interactions on proactive aggression were observed (see Table 8 in the "Appendix").

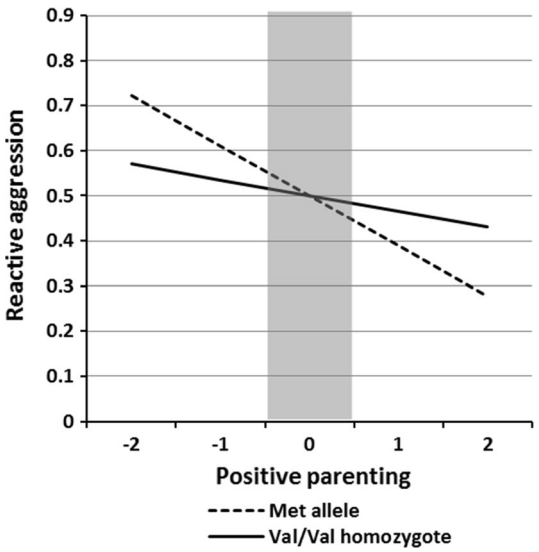

Fig. 2 Simple slopes on reactive aggression from positive parenting in COMT Val158Met allelic groups. *Grey shaded* area represents 95 % CI of the cross over point *C* of the interaction on the positive parenting axis and the 95 % CI of *C* ranged from −0.41 to 0.49

Internal Replication Analyses

With regard to the *COMT* Val158Met polymorphism ($N_{subsample1} = 701$, $N_{subsample2} = 698$), the findings obtained from the total sample were fully replicated in the two randomly split subsamples (see Table 9, Fig. 3 in the "Appendix"). Specifically, the *COMT* Val158Met polymorphism interacted with maternal positive parenting in its association with reactive aggression, but not proactive aggression. Compared to Val/Val homozygotes, adolescents with Met alleles of *COMT* gene exhibited more reactive aggression when exposed to low positive parenting, while less reactive aggression when experiencing high positive parenting.

With regard to the *MAOA* T941G polymorphism (boys: $N_{subsample1} = 369$, $N_{subsample2} = 370$; girls: $N_{subsample1} = 175$, $N_{subsample2} = 173$), only the results of re-parameterized regressions among girls were replicated in the two randomly split samples (see Tables 10, 11; Figs. 4, 5 in the "Appendix"). For girls, the significant interactive effect of *MAOA* gene and positive parenting was only found on reactive aggression but not on proactive aggression. Girls with TT homozygotes of *MAOA* gene were more likely to engage in reactive aggression when exposed to low levels of positive parenting, but less likely to engage in reactive aggression when exposed to high levels of positive parenting. For boys, such interaction between *MAOA* gene and positive parenting was not observed in the two subsamples. However, it should be noted that, although the interactions between *MAOA* gene and positive parenting on reactive aggression among boys did not reach statistical significance, the interactive patterns among both boys and girls in both subsamples exhibited very similar trends with those observed in the total sample (see Figs. 4, 5 in the "Appendix").

Discussion

Building on previous studies examining G × E effects on aggression, we investigated the interactions between *MAOA* T941G and *COMT* Val158Met polymorphisms with maternal parenting on proactive and reactive aggression, and further explored the nature of gene × maternal parenting by testing two competing models: diathesis-stress versus differential susceptibility. The former one suggests that individuals with "risky alleles" may suffer from the

Table 3 Results for re-parameterized regression models examining Val158Met × positive parenting interactions on reactive aggression

Parameter	Differential susceptibility		Diathesis-stress	
	Strong	Weak	Strong	Weak
B_1	0.00 (–)	−0.04 (0.04)	0.00 (–)	−0.06 (0.03)*
C	0.04 (0.23)	0.05 (0.34)	0.92 (–)[a]	0.92 (–)[a]
95 % CI of C	[−0.41, 0.49]	[−0.62, 0.71]	–	–
B_2	−0.10 (0.04)**	−0.11 (0.04)**	−0.04 (0.02)	−0.08 (0.03)**
B_3	0.07 (0.03)*	0.05 (0.03)	0.08 (0.03)**	0.06 (0.03)
B_4	0.89 (0.03)***	0.89 (0.03)***	0.89 (0.03)***	0.89 (0.03)***
B_5	0.20 (0.02)***	0.20 (0.02)***	0.20 (0.02)***	0.20 (0.02)***
R^2	.69	.69	.69	.69
F	504.65***	432.82***	603.03***	504.55***
df	6, 1371	7, 1370	5, 1372	6, 1371
F versus a	–	1.14	4.50*	–
df	–	1, 1363	1, 1364	–
AIC	1588.22	1589.07	1590.73	1588.51
BIC	1624.78	1630.85	1622.07	1625.07

Model: $RA = (Val158Met = Val/Val)(B_0 + B_1(X_{PP} - C)) + (Val158Met = Met)(B_0 + B_2(X_{PP} - C)) + B_3X_{NP} + B_4PA + B_5Gender + E$; F versus a stands for F tests of the difference in R^2 for a given model versus the strong differential susceptibility model

RA reactive aggression, *PP* positive parenting, *NP* negative parenting, *PA* proactive aggression, CI confidential interval

[a] Parameter fixed at reported value; *SE* is not applicable, so is listed as –

* $p < .05$; ** $p < .01$; *** $p < .001$

poor environmental experiences (e.g., insensitive parenting, stressful life experiences) and deviate from the developmental pathway of their peers (Monroe and Simons 1991; Burmeister et al. 2008). In contrast, the differential susceptibility model proposes that individuals with "plasticity alleles" could be susceptible to both adverse and positive environments and develop in a "for better and for worse" manner (Bakermans-Kranenburg and van IJzendoorn 2011; Belsky and Pluess 2009).

As expected, we found that gene × maternal parenting interaction operated differently across proactive and reactive aggression. Both T941G and Val158Met polymorphisms interacted with maternal positive parenting in their associations with reactive aggression, but not proactive aggression. Specifically, adolescents with T alleles/TT homozygotes of *MAOA* gene or Met alleles of *COMT* gene exhibited more reactive aggression when exposed to low positive parenting, while less reactive aggression when experiencing high positive parenting. These findings provide the first evidence for distinct gene-parenting environment interaction effects on proactive aggression versus reactive aggression, and suggest that the two types of aggression may have distinct underlying mechanisms.

It is not surprising that G × E effects were only found on reactive aggression but not on proactive aggression, given that both *COMT* and *MAOA* genes play important roles in emotion regulation, which is only associated with reactive aggression instead of proactive aggression (see Hubbard et al. 2010 for a review). More specifically, there is evidence that carriers with Met alleles of *COMT* gene show heightened activation in amygdala and medial prefrontal regions to negative emotional and social cues (e.g., fearful faces) (Drabant et al. 2006; Smolka et al. 2005). These dysfunctions would render such individuals more susceptible to low levels of positive parenting, resulting in hyperactive impulsivity and deleterious hostile attribution bias (Buckholtz and Meyer-Lindenberg 2008; Williams et al. 2010) that are characteristics of reactive aggression. On the other hand, the Met allele carriers also exhibit diminished activation in amygdala and medial prefrontal regions to positively valenced emotional stimuli (e.g., happy faces) (Williams et al. 2010). Thus, these carriers could be more likely to be affected by high positive parenting and decrease the tendency to experience anger and frustration; therefore, exhibiting low levels of reactive aggression. Similarly, *MAOA* gene is related to dopamine and serotonin functioning (Hotamisligil and Breakefield 1991), the deficit of which in low-activity allele could labialize corticolimbic regions involved in emotional regulation (Buckholtz and Meyer-Lindenberg 2008). These central nervous systems involved in emotional regulation and social evaluation could amplify individuals' emotional response to environmental stimuli among low-activity allele carriers (Eisenberger et al. 2007; Meyer-Lindenberg et al. 2006). It is possible that carriers of T alleles/TT

homozygotes are particularly susceptible to the variations in maternal parenting and, therefore, may vary in reactive aggression in low and high levels of positive parenting environments. This is consistent with the notion of "gene-brain-behavior" model (Buckholtz and Meyer-Lindenberg 2008; Eisenberger et al. 2007) and might be a reasonable explanation.

To be noted, our finding does not mean that proactive aggression has no genetic underpinnings. Previous twin studies have indicated that proactive and reactive aggression have unique genetic and environmental underpinnings (Baker et al. 2008; Brendgen et al. 2006; Tuvblad et al. 2009). Future studies should examine other candidate genes and environmental indicators to further detect the underlying mechanisms of proactive and reactive aggression.

These findings also lend further support for the importance of the distinction between these two subtypes of aggression. Indeed, inconsistent findings about genes and aggression have been reported in previous studies. For example, McDermott and colleagues (2009) found that subjects only with low activity alleles of *MAOA* gene reported high levels of aggression under provocations. However, Manuck et al. (2000) found a strong association between high activity alleles and aggression. It should be noted that the inconsistent findings may be related to the distinct constructs or types of aggression measured in the two studies. While the study of McDermott et al. assessed reactive aggression, the study of Manucka et al. used a composite score of aggression including aggression/antisocial factor, impulsiveness and hostility. Therefore, the findings of the present study may provide new meaningful cues for explaining the paradox findings about gene and aggression in literature.

Turning to our second question, whether G × E interactions found in our study would be consistent with the diathesis-stress model or differential susceptibility model, all the indexes in the re-parameterized regressions indicated that T941G × positive parenting interactions were consistent with the strong differential susceptibility model among both boys and girls, such that adolescents with T alleles/TT homozygotes were sensitive to maternal parenting. The interaction between Val158Met and positive parenting was also accorded with the strong differential susceptibility model, in which Met alleles functioned in a "for better and for worse" manner. Our findings that T alleles/TT homozygotes in T941G polymorphism and Met alleles in Val158Met polymorphism may be the "susceptibility alleles" but not "risk alleles" are in concordance with previous literature. With regard to *MAOA* T941G polymorphism, TT homozygote patients with major depression have shown a significantly faster and better treatment response to antidepressant mirtazapine (Tadic et al. 2007). Similarly, Leuchter et al. (2009) found that MDD patients with T alleles/TT homozygotes exhibited more heightened sensitivity to placebo than those with G alleles/GG homozygotes. Evidence has also been provided that Met alleles of *COMT* gene not only suffer from adverse environments, but also benefit from supportive environments (e.g., Laucht et al. 2012; Thompson et al. 2012).

Inconsistent with previous studies (e.g., Caspi et al. 2002; Widom and Brzustowicz 2006), we did not find any significant gene × negative parenting interactions on adolescent aggression. One probability may be that, in the general population sample, especially in the case of the present study in which the overwhelming majority of the sample were adolescents without siblings, mothers reared their children with relatively low levels of negative parenting ($M = 1.03$, $SD = 0.47$), which might minimize our ability to detect its effect. In contrast, previous literature with significant gene × negative parenting interactions has often focused on adolescents experiencing extreme levels of risk (e.g., Caspi et al. 2002; Widom and Brzustowicz 2006), enhancing the power to find the effect. Some researchers may suggest that there could be other theoretical interpretation for the results—"vantage sensitivity hypothesis" (Pluess and Belsky 2013). This newly-proposed and non-mainstream hypothesis assumes that individuals with vantage-sensitivity factors exclusively benefit from supportive environments compared with others, whereas no differences between individuals expected in response to adversities or the absence of positive environments. We also tested this possibility by using re-parameterized regression models where we fixed *C* to the minimum of parenting as recommended by Belsky et al. (2013). However, finally we ruled out this possibility because both the strong and weak vantage sensitivity models fitted worse than the strong differential susceptibility model.

With regard to the internal replication analyses, the findings about *COMT* gene obtained from the total sample were fully replicated in the two randomly split subsamples. Regarding *MAOA* gene, the findings obtained from the total sample were only partially replicated in the two female subsamples. However, the interactive patterns of *MAOA* gene and positive parenting on reactive aggression among boys and girls in both randomly split subsamples exhibited very similar trends with those observed in the total sample. By and large, these results indicate that our findings are relatively robust. Besides, one strength of our study lies in that we used two different strategies in our analysis. That is, we first used traditional regression analysis to identify the interaction patterns and then the robustness of these interactive effects observed was further tested in an additional sensitivity analysis of re-parameterized regressions. The consistency in the findings yielded by these two different strategies also, to a certain extent, provides evidence for the robustness of our findings.

The current study contributes to the existing literature by providing valuable information about the underlying mechanism of two subtypes of aggression: proactive and reactive aggression and has several notable strengths. First, to our knowledge, this study is the first to examine the G × E interactions on two subtypes of adolescent aggression, providing preliminary evidence for the distinct G × E interactions on proactive versus reactive aggression. Second, with the newly-developed approach of re-parameterized regression analysis, the present study is likely to maximize the statistical power by aligning analyses with hypotheses of interest and can directly compare and evaluate different G × E hypotheses (Belsky et al. 2013). Third, by focusing on both positive and negative parenting, the present study tested whether the G × E interactions would be consistent with the diathesis-stress model or the differential susceptibility model in a more comprehensive manner (Buil et al. 2015).

However, it is important to consider the limitations of this study. First, perhaps the most important limitation is that we were unable to obtain the external replication evidence due to the unavailability of a matched independent sample using the same measurement. In literature of G × E interaction, there have been concerns regarding the lack of direct replication; however, this issue has been shown to be mainly due to variations in research designs including different measurements of the environments or outcomes and different sample characteristics (Munafò et al. 2009). Therefore, although the pattern of our results in this study was generally consistent with the previous evidence with regard to reactive aggression/reactive aggression related endophenotypes (Buckholtz and Meyer-Lindenberg 2008; Eisenberger et al. 2007; Kuepper et al. 2013; Smolka et al. 2005), these findings still need to be interpreted with caution until directly replicated. Second, our data on the associations between genes, parenting and aggression were cross-sectional, which did not allow for cross-lagged relationships between parenting and aggression across different genotypes to be tested. Moreover, recent studies investigating the G × E interactions have shown that effects can change over time and the differential susceptibility model works in a developmental perspective (Belsky and Pluess 2013; Windhorst et al. 2015). For example, Zhang et al. (2015) found that the *DRD2 TaqIA* polymorphism only interacted with maternal parenting in predicting concurrent depressive symptoms at age 11 and 12, but not at age 13. Therefore, future research with longitudinal design will be needed to explore whether the G × E interaction observed in our study would change with age. Third, adolescent aggression was only measured by teacher report in this study. Although teachers are valid raters for these aggression subtypes during childhood and adolescence (Dodge and Coie 1987; Hubbard et al. 2010), multiple informants are needed to reduce confounds of rater biases and increase the validation of our findings. Fourth, restricting the present study to the sample of Chinese Han adolescents also means that our findings need to be replicated with other ethnic groups before they are presumed to be fully generalizable. In addition, genetic contributions to these two subtypes of aggression may operate in ways not tested in this study. Future studies can use Genome-wide analyses (GWAS) to uncover genetic associations beyond the usual suspects. Also epigenetic processes such as DNA methylation merit consideration, as these can modify gene expression and neural function without changing nucleotide sequence (van IJzendoorn et al. 2010).

Conclusion

With a large Chinese Han sample, the present study provides preliminary evidence for distinct G × E interactions for proactive aggression versus reactive aggression in adolescents, such that the *MAOA* T941 and *COMT* Val158Met polymorphisms both interacted with maternal positive parenting on adolescent reactive aggression, rather than proactive aggression. These findings contribute to a more comprehensive view of the complex genetic etiology of adolescent aggression and provide further evidence for the distinction between these two subtypes of aggression. With regard to the nature of G × E interaction on reactive aggression observed in the present study, our findings were in accordance with the differential susceptibility hypothesis, i.e., adolescents were differentially susceptible to maternal positive parenting depending on their *MAOA* or *COMT* genotypes. These empirical findings provide further evidence for the differential susceptibility hypothesis and have important implications for interpreting genetic moderation of maternal parenting on individual differences of adolescent aggression.

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Author Contributions WZ conceived of the study, participated in its design and coordination and drafted the manuscript; CC participated in its design, performed the statistical analysis and drafted the manuscript; MW participated in the design and helped to draft the manuscript; LJ helped to draft the manuscript; YC helped to draft the manuscript. All authors read and approved the final manuscript.

Conflict of interest All authors declare no conflicts of interest.

Ethical Approval All procedures followed were in accordance with the ethical standards of the ethics committee on human experimentation of Shandong Normal University and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed assent (adolescents) and consent (mothers, teachers and school principals) were obtained from all participants for being included in the study.

Appendix

See Tables 4, 5, 6, 7, 8, 9, 10, 11; Figs. 3, 4, 5.

Table 4 Results for re-parameterized regression models examining T941G × negative parenting interactions on reactive aggression

Parameter	Boys				Girls			
	Differential susceptibility		Diathesis-stress		Differential susceptibility		Diathesis-stress	
	Strong	Weak	Strong	Weak	Strong	Weak	Strong	Weak
B_1	0.00 (–)[a]	0.05 (0.06)	0.00 (–)[a]	0.06 (0.04)	0.00 (–)[a]	−0.04 (0.06)	0.00 (–)[a]	−0.00 (0.05)
C	−0.15 (0.57)	−0.46 (2.15)	2.07 (–)[a]	2.07 (–)[a]	−0.20 (0.35)	−0.17 (0.30)	1.57 (–)[a]	1.57 (–)[a]
95 % CI of C	[−1.23, 0.97]	[−4.67, 3.75]	–	–	[−0.89, 0.49]	[−0.76, 0.42]	–	–
B_2	0.07 (0.06)	0.08 (0.06)	−0.00 (0.02)	0.08 (0.05)	0.13 (0.10)	0.12 (0.10)	−0.00 (0.03)	−0.00 (0.06)
B_3	−0.07 (0.04)	−0.06 (0.04)	−0.08 (0.04)*	−0.06 (0.04)	−0.07 (0.05)	−0.09 (0.05)	−0.10 (0.04)*	−0.10 (0.05)
B_4	0.86 (0.04)***	0.86 (0.04)***	0.87 (0.04)***	0.87 (0.04)***	0.98 (0.09)***	0.98 (0.09)***	0.98 (0.09)***	0.98 (0.09)***
R^2	.43	.42	.42	.42	.28	.28	.28	.28
F	132.05***	105.77***	175.43***	132.33***	33.47***	26.81***	43.80***	32.76***
df	4, 719	5, 718	3, 720	4, 719	4, 340	5, 339	3, 341	4, 340
F versus a	–	0.82	1.52	–	–	0.42	2.06	–
df	–	1, 718	1, 719	–	–	1, 339	1, 340	–
AIC	1010.11	1011.29	1009.64	1009.45	326.21	327.78	326.29	328.28
BIC	1037.62	1043.38	1032.56	1036.96	349.27	354.68	345.51	351.34

Model: $RA = (T941G = \text{G/GG})(B_0 + B_1(X_{NP} - C)) + (T941G = \text{T/TT})(B_0 + B_2(X_{NP} - C)) + B_3X_{PP} + B_4PA + E$; *F* versus a stands for *F* tests of the difference in R^2 for a given model versus the strong differential susceptibility model

RA reactive aggression, *PP* positive parenting, *NP* negative parenting, *PA* proactive aggression, CI confidential interval

[a] Parameter fixed at reported value; *SE* is not applicable, so is listed as –

* $p < .05$; ** $p < .01$; *** $p < .001$

Table 5 Results for re-parameterized regression models examining T941G × positive parenting interactions on proactive aggression

Parameter	Boys				Girls			
	Differential susceptibility		Diathesis-stress		Differential susceptibility		Diathesis-stress	
	Strong	Weak	Strong	Weak	Strong	Weak	Strong	Weak
B_1	0.00 (–)[a]	−0.01 (0.04)	0.00 (–)[a]	−0.01 (0.03)	0.00 (–)[a]	−0.01 (0.03)	0.00 (–)[a]	−0.00 (0.03)
C	0.45 (1.81)	0.89 (5.57)	0.92 (–)[a]	0.92 (–)[a]	0.46 (0.64)	0.39 (0.53)	0.92 (–)[a]	0.92 (–)[a]
95 % CI of C	[−3.10, 4.00]	[−10.03, 11.81]	–	–	[−0.79,1.70]	[−0.65, 1.43]	–	–
B_2	−0.02 (0.05)	−0.02 (0.05)	−0.01 (0.02)	−0.02 (0.03)	0.05 (0.04)	0.04 (0.04)	0.03 (0.02)	0.03 (0.03)
B_3	0.07 (0.03)	0.05 (0.03)	0.05 (0.03)*	0.05 (0.03)	0.00 (0.02)	−0.00 (0.03)	0.00 (0.02)	−0.00 (0.03)
B_4	0.46 (0.02)***	0.46 (0.02)***	0.46 (0.02)***	0.46 (0.02)***	0.28 (0.02)***	0.28 (0.02)***	0.27 (0.02)***	0.27 (0.02)***
R^2	.42	.42	.42	.42	.27	.27	.28	.27
F	131.02***	104.70***	174.92***	131.05***	31.76***	25.37***	42.36***	31.68***
df	4, 719	5, 718	3, 720	4, 719	4, 340	5, 339	3, 341	4, 340
F versus a	–	0.07	0.03	–	–	0.14	0.24	–
df	–	1, 718	1, 719	–	–	1, 339	1, 340	–
AIC	558.92	560.85	556.96	558.85	−113.55	−111.69	−115.31	−113.32
BIC	586.43	592.94	579.88	586.36	−90.49	−84.78	−96.09	−90.26

Model: $PA = (T941G = \text{G/GG})(B_0 + B_1(X_{PP} - C)) + (T941G = \text{T/TT})(B_0 + B_2(X_{PP} - C)) + B_3X_{NP} + B_4RA + E$; *F* versus a stands for *F* tests of the difference in R^2 for a given model versus the strong differential susceptibility model

RA reactive aggression, *PP* positive parenting, *NP* negative parenting, *PA* proactive aggression, CI confidential interval

[a] Parameter fixed at reported value; *SE* is not applicable, so is listed as –

* $p < .05$; ** $p < .01$; *** $p < .001$

Table 6 Results for re-parameterized regression models examining T941G × negative parenting interactions on proactive aggression

Parameter	Boys				Girls			
	Differential susceptibility		Diathesis-stress		Differential susceptibility		Diathesis-stress	
	Strong	Weak	Strong	Weak	Strong	Weak	Strong	Weak
B_1	0.00 (–)[a]	0.05 (0.04)	0.00 (–)[a]	0.05 (0.03)	0.00 (–)[a]	0.01 (0.03)	0.00 (–)[a]	−0.00 (0.03)
C	−0.23 (0.75)	2.39 (31.40)	2.07 (–)[a]	2.07 (–)[a]	−0.57 (0.89)	−0.49 (0.73)	1.57 (–)[a]	1.57 (–)[a]
95 % CI of C	[−1.70, 1.24]	[−59.15, 63.93]	–	–	[−2.31, 1.17]	[1.92, 0.94]	–	–
B_2	0.04 (0.04)	0.05 (0.04)	−0.00 (0.01)	0.05 (0.03)	−0.04 (0.05)	−0.04 (0.05)	0.01 (0.01)	0.01 (0.03)
B_3	−0.03 (0.03)	−0.01 (0.03)	−0.04 (0.03)	−0.01 (0.03)	0.01 (0.02)	0.00 (0.03)	0.01 (0.02)	0.01 (0.03)
B_4	0.47 (0.02)***	0.46 (0.02)***	0.46 (0.02)***	0.46 (0.02)***	0.27 (0.02)***	0.27 (0.02)***	0.27 (0.03)***	0.27 (0.02)***
R^2	.43	.42	.42	.42	.27	.27	.27	.27
F	130.37***	104.69***	173.47***	131.04***	31.56***	25.20***	41.75***	31.22***
df	4, 719	5, 718	3, 720	4, 719	4, 340	5, 339	3, 341	4, 340
F versus a	–	1.56	1.02	–	–	0.10	0.99	–
df	–	1, 718	1, 719	–	–	1, 339	1, 340	–
AIC	560.46	560.88	559.49	558.87	−112.95	−111.05	−113.95	−111.96
BIC	587.96	592.97	582.41	586.38	−89.89	−84.15	−94.73	−88.89

Model: $PA = (T941G = \text{G/GG})(B_0 + B_1(X_{NP} - C)) + (T941G = \text{T/TT})(B_0 + B_2(X_{NP} - C)) + B_3X_{PP} + B_4RA + E$, *RA*: reactive aggression; *F* versus a stands for *F* tests of the difference in R^2 for a given model versus the strong differential susceptibility model

PP positive parenting, *NP* negative parenting, *PA* proactive aggression, CI confidential interval

[a] Parameter fixed at reported value; *SE* is not applicable, so is listed as –

* $p < .05$; ** $p < .01$; *** $p < .001$

Table 7 Results for re-parameterized regression models examining Val158Met × negative parenting interactions on reactive aggression

Parameter	Differential susceptibility		Diathesis-stress	
	Strong	Weak	Strong	Weak
B_1	0.00 (–)	0.04 (0.04)	0.00 (–)	0.06 (0.03)
C	−0.07 (0.36)	−0.13 (0.75)	2.07 (–)[a]	2.07 (–)[a]
95 % CI of C	[−0.78, 0.64]	[−1.60, 1.34]	–	–
B_2	0.07 (0.04)	0.07 (0.04)	−0.04 (0.02)	0.06 (0.03)
B_3	−0.08 (0.03)**	−0.07 (0.03)*	0.08 (0.03)**	−0.07 (0.03)*
B_4	0.90 (0.03)***	0.89 (0.03)***	0.89 (0.03)***	0.89 (0.03)***
B_5	0.20 (0.02)***	0.20 (0.02)***	0.20 (0.02)***	0.20 (0.02)***
R^2	.69	.69	.69	.69
F	503.72***	432.02***	602.96***	504.14***
df	6, 1371	7, 1370	5, 1372	6, 1371
F versus a	–	1.17	2.91	–
df	–	1, 1363	1, 1364	–
AIC	1589.94	1590.76	1590.86	1589.23
BIC	1626.49	1632.54	1622.20	1625.78

Model: $RA = (Val158Met = Val/Val)(B_0 + B_1(X_{PP} - C)) + (Val158Met = Met)(B_0 + B_2(X_{PP} - C)) + B_3X_{NP} + B_4PA + B_5Gender + E$; *F* versus a stand for *F* tests of the difference in R^2 for a given model versus the strong differential susceptibility model

RA reactive aggression, *PP* positive parenting, *NP* negative parenting, *PA* proactive aggression, CI confidential interval

[a] Parameter fixed at reported value; *SE* is not applicable, so is listed as –

* $p < .05$; ** $p < .01$; *** $p < .001$

Table 8 Results for re-parameterized regression models examining Val158Met × parenting interactions on proactive aggression

Parameter	Val158Met × positive parenting models[b]				Val158Met × negative parenting models[c]			
	Differential susceptibility		Diathesis-stress		Differential susceptibility		Diathesis-stress	
	Strong	Weak	Strong	Weak	Strong	Weak	Strong	Weak
B_1	0.00 (–)[a]	0.01 (0.02)	0.00 (–)[a]	0.01 (0.02)	0.00 (–)[a]	0.02 (0.03)	0.00 (–)[a]	0.03 (0.02)
C	−1.13 (53.70)	0.11 (2.74)	0.92 (–)[a]	0.92 (–)[a]	−0.03 (0.59)	−0.09 (1.87)	2.07 (–)[a]	2.07 (–)[a]
95 %CI of C	[−106.38, 104.20]	[−5.26, 5.48]	–	–	[−1.18, 1.13]	[−3.76, 3.58]	–	–
B_2	0.00 (0.03)	0.00 (0.03)	−0.00 (0.01)	0.00 (0.02)	0.03 (0.02)	0.03 (0.03)	0.00 (0.01)	0.03 (0.02)
B_3	0.03 (0.01)	0.03 (0.02)	0.02 (0.02)	0.03 (0.02)	−0.00 (0.02)	0.00 (0.02)	−0.01 (0.02)	0.00 (0.02)
B_4	0.43 (0.01)***	0.43 (0.01)***	0.43 (0.02)***	0.43 (0.01)***	0.43 (0.01)***	0.43 (0.01)***	0.43 (0.01)***	0.43 (0.01)***
B_5	−0.01 (0.02)	−0.01 (0.02)	−0.01 (0.02)	−0.01 (0.02)	−0.01 (0.02)	−0.01 (0.02)	−0.01 (0.02)	−0.01 (0.02)
R^2	.51	.51	.51	.51	.51	.51	.51	.51
F	235.53***	201.77***	282.84***	235.56***	235.26***	201.70***	282.14***	235.46***
df	6, 1371	7, 1370	5, 1372	6, 1371	6, 1371	7, 1370	5, 1372	6, 1371
F versus a	–	0.08	0.00	–	–	0.74	1.00	–
df	–	1, 1363	1, 1364	–	–	1, 1363	1, 1364	–
AIC	593.56	595.47	591.56	593.49	594.18	595.44	593.18	593.51
BIC	630.11	637.25	622.89	630.05	630.74	637.22	624.51	630.07

RA reactive aggression, *PP* positive parenting, *NP* negative parenting, *PA* proactive aggression, *CI*: confidential interval

[a] Parameter fixed at reported value; *SE* is not applicable, so is listed as –

[b] Model: $PA = (Val158Met = \text{Val/Val})(B_0 + B_1(X_{PP} - C)) + (Val158Met = \text{Met})(B_0 + B_2(X_{PP} - C)) + B_3X_{NP} + B_4RA + B_5Gender + E$

[c] Model: $PA = (Val158Met = \text{Val/Val})(B_0 + B_1(X_{NP} - C)) + (Val158Met = \text{Met})(B_0 + B_2(X_{NP} - C)) + B_3X_{PP} + B_4RA + B_5Gender + E$; *F* versus a stands for *F* tests of the difference in R^2 for a given model versus the strong differential susceptibility model

* $p < .05$; ** $p < .01$; *** $p < .001$

Table 9 Cross validation results for re-parameterized regression models examining Val158Met × positive parenting interactions on reactive aggression

Parameter	Subsample 1 ($N = 701$)				Subsample 2 ($N = 698$)			
	Differential susceptibility		Diathesis-stress		Differential susceptibility		Diathesis-stress	
	Strong	Weak	Strong	Weak	Strong	Weak	Strong	Weak
B_1	0.00 (–)[a]	−0.02 (0.05)	0.00 (–)[a]	−0.05 (0.04)	0.00 (–)[a]	−0.07 (0.05)	0.00 (–)[a]	−0.08 (0.04)
C	−0.16 (0.33)	−0.19 (0.41)	0.92 (–)[a]	0.92 (–)[a]	0.20 (0.31)	0.39 (0.76)	0.92 (–)[a]	0.92 (–)[a]
95 % CI of C	[−0.81, 0.49]	[−0.99, 0.61]	–	–	[−0.41, 0.81]	[−1.10, 1.88]	–	–
B_2	−0.10 (0.05)*	−0.10 (0.05)*	−0.02 (0.03)	−0.06 (0.04)	−0.11 (0.06)*	−0.12 (0.06)*	−0.05 (0.03)	−0.11 (0.05)*
B_3	0.04 (0.04)	0.03 (0.04)	0.06 (0.04)	0.04 (0.04)	0.08 (0.04)*	0.06 (0.04)	0.10 (0.04)*	0.06 (0.04)
B_4	0.85 (0.04)***	0.85 (0.04)***	0.86 (0.04)***	0.85 (0.04)***	0.95 (0.05)***	0.95 (0.05)***	0.95 (0.05)***	0.95 (0.05)***
B_5	0.17 (0.03)***	0.17 (0.03)***	0.17 (0.03)***	0.17 (0.03)***	0.23 (0.03)***	0.23 (0.03)***	0.23 (0.03)***	0.23 (0.03)***
R^2	.70	.70	.69	.70	.69	.69	.68	.69
F	261.67***	224.04***	312.11***	260.70***	247.49***	212.62***	296.23***	248.33***
df	6, 684	7, 683	5, 685	6, 684	6, 681	7, 680	5, 682	6, 681
F versus a	–	0.15	3.55^+	–	–	1.61	1.78	–
df	–	1, 678	1, 679	–	–	1, 678	1, 679	–
AIC	760.72	762.57	762.29	762.50	828.69	829.07	828.47	827.23
BIC	792.43	798.80	789.47	794.20	860.39	865.30	855.66	858.94

Model: $PA = (Val158Met = \text{Val/Val})(B_0 + B_1(X_{PP} - C)) + (Val158Met = \text{Met})(B_0 + B_2(X_{PP} - C)) + B_3X_{NP} + B_4RA + B_5Gender + E$; *F* versus a stands for *F* tests of the difference in R^2 for a given model versus the strong differential susceptibility model

RA reactive aggression, *PP* positive parenting, *NP* negative parenting, *PA* proactive aggression, CI confidential interval

[a] Parameter fixed at reported value; *SE* is not applicable, so is listed as –

$^+$ $p < .10$; * $p < .05$; ** $p < .01$; *** $p < .001$

Table 10 Cross validation results for re-parameterized regressions examining T941G × positive parenting interactions on reactive aggression among girls

Parameter	Subsample 1 ($N = 175$)				Subsample 2 ($N = 173$)			
	Differential susceptibility		Diathesis-stress		Differential susceptibility		Diathesis-stress	
	Strong	Weak	Strong	Weak	Strong	Weak	Strong	Weak
B_1	0.00 (–)[a]	−0.03 (0.08)	0.00 (–)[a]	−0.08 (0.08)	0.00 (–)[a]	−0.04 (0.09)	0.00 (–)[a]	−0.08 (0.08)
C	0.07 (0.25)	0.07 (0.28)	0.92 (–)[a]	0.92 (–)[a]	0.19 (0.34)	0.23 (0.43)	0.92 (–)[a]	0.92 (–)[a]
95 % CI of C	[−0.42, 0.56]	[−0.41, 0.55]	–	–	[−0.48, 0.86]	[−0.61, 1.07]	–	–
B_2	−0.27 (0.12)*	−0.27 (0.11)*	−0.09 (0.06)**	−0.15 (0.08)$^+$	−0.19 (0.10)$^+$	−0.20 (0.11)$^+$	−0.08 (0.06)	−0.15 (0.09)$^+$
B_3	0.03 (0.06)	0.02 (0.07)	0.05 (0.06)	0.02 (0.07)	−0.01 (0.07)	−0.03 (0.08)	0.01 (0.07)	−0.03 (0.08)
B_4	0.93 (0.13)***	0.93 (0.13)***	0.94 (0.13)***	0.93 (0.13)***	1.03 (0.12)***	1.03 (0.12)***	1.03 (0.12)***	1.03 (0.12)***
R^2	.27	.27	.25	.26	.31	.31	.31	.31
F	15.52***	12.38***	19.35***	14.80***	18.77***	14.99***	24.46***	18.59***
df	4, 169	5, 168	3, 170	4, 169	4, 166	5, 165	3, 167	4, 166
F versus a	–	0.14	3.26$^+$	–	–	0.20	1.50	–
df	–	1, 168	1, 169	–	–	1, 165	1, 166	–
AIC	175.52	177.38	176.84	177.68	158.91	160.69	158.44	159.42
BIC	194.48	199.49	192.64	196.64	177.76	182.69	174.15	178.27

Model: $RA = (T941G = \text{GG})(B_0 + B_1(X_{PP} - C)) + (T941G = \text{TT})(B_0 + B_2(X_{PP} - C)) + B_3X_{NP} + B_4PA + E$; F versus a stands for F tests of the difference in R^2 for a given model versus the strong differential susceptibility model

RA reactive aggression, *PP* positive parenting, *NP* negative parenting, *PA* proactive aggression, *CI* confidential interval

[a] Parameter fixed at reported value; *SE* is not applicable, so is listed as –

$^+$ $p < .10$; *$p < .05$; **$p < .01$; ***$p < .001$

Table 11 Cross validation results for re-parameterized regressions examining T941G × positive parenting interactions on reactive aggression among boys

Parameter	Subsample 1 ($N = 369$)				Subsample 2 ($N = 370$)			
	Differential susceptibility		Diathesis-stress		Differential susceptibility		Diathesis-stress	
	Strong	Weak	Strong	Weak	Strong	Weak	Strong	Weak
B_1	0.00 (–)[a]	−0.02 (0.08)	0.00 (–)[a]	−0.04 (0.07)	0.00 (–)[a]	−0.00 (0.07)	0.00 (–)[a]	−0.05 (0.06)
C	0.17 (0.49)	0.19 (0.59)	0.92 (–)[a]	0.92 (–)[a]	−0.04 (0.39)	−0.04 (0.41)	0.92 (–)[a]	0.92 (–)[a]
95 % CI of C	[−0.79, 1.13]	[−0.97, 1.35]	–	–	[−0.80, 0.72]	[−0.84, 0.76]	–	–
B_2	−0.11 (0.09)	−0.12 (0.09)	−0.05 (0.05)	−0.08 (0.07)	−0.13 (0.08)	−0.13 (0.08)	−0.04 (0.05)	−0.07 (0.06)
B_3	0.09 (0.06)	0.08 (0.06)	0.10 (0.06)	0.08 (0.06)	0.05 (0.06)	0.05 (0.06)	0.06 (0.05)	0.04 (0.06)
B_4	0.88 (0.06)***	0.88 (0.06)***	0.89 (0.06)***	0.88 (0.06)***	0.84 (0.06)***	0.84 (0.06)***	0.85 (0.06)***	0.84 (0.06)***
R^2	.44	.44	.44	.44	.41	.41	.41	.41
F	70.47***	56.23***	93.80***	70.33***	62.32***	49.72***	82.30***	61.81***
df	4, 357	5, 356	3, 358	4, 357	4, 357	5, 356	3, 358	4, 357
F versus a	–	0.05	0.70	–	–	0.00	1.81	–
df	–	1, 356	1, 357	–	–	1, 356	1, 357	–
AIC	506.98	508.93	505.69	507.29	511.37	513.36	511.20	512.59
BIC	530.33	536.17	525.15	530.64	534.72	540.60	530.66	533.94

Model: $RA = (T941G = \text{G})(B_0 + B_1(X_{PP} - C)) + (T941G = \text{T})(B_0 + B_2(X_{PP} - C)) + B_3X_{NP} + B_4PA + E$; F versus a stands for F tests of the difference in R^2 for a given model versus the strong differential susceptibility model

RA reactive aggression, *PP* positive parenting, *NP* negative parenting, *PA* proactive aggression, *CI* confidential interval

[a] Parameter fixed at reported value; *SE* is not applicable, so is listed as –

* $p < .05$; ** $p < .01$; *** $p < .001$

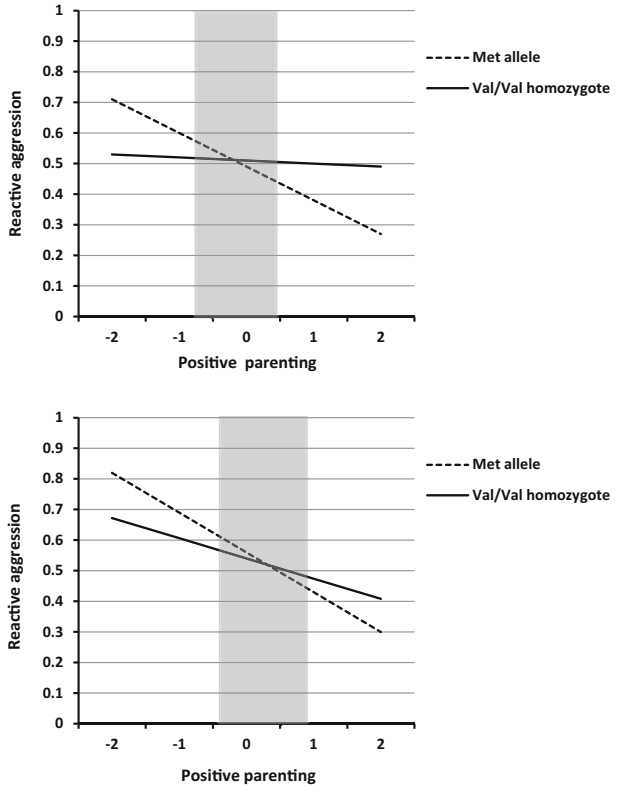

Fig. 3 Simple slopes on reactive aggression from positive parenting in COMT Val158Met allelic groups. *Grey shaded* area represents 95 % CI of the cross over point *C* of the interaction on the positive parenting axis. The 95 % CI of *C* ranged from −0.81 to 0.49 and −0.41 to 0.81 in subsample 1 and 2, respectively. The slopes for positive parenting on reactive aggression were as follows: (i) in subsample 1: Val/Val homozygotes, $\beta = .01$, $p > .05$; Met alleles, $\beta = -.10$, $p < .05$; (ii) in subsample 2: Val/Val homozygotes, $\beta = -.05$, $p > .05$; Met alleles, $\beta = -.10$, $p < .05$

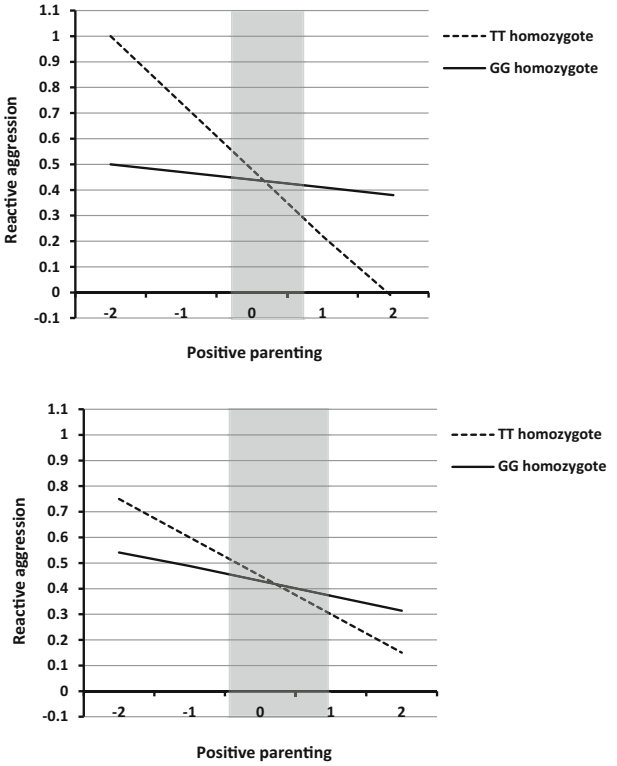

Fig. 4 Simple slopes on reactive aggression from positive parenting in MAOA T941G allelic groups among girls. *Grey shaded* area represents 95 % CI of the cross over point *C* of the interaction on the positive parenting axis. The 95 % CI of *C* ranged from −0.42 to 0.56 and −0.48 to 0.86 in subsample 1 and 2, respectively. The slopes for positive parenting on reactive aggression were as follows: (i) in subsample 1: GG homozygotes, $\beta = -.04$, $p = .69$; TT homozygotes, $\beta = -.28$, $p = .06$; (ii) in subsample 2: GG homozygotes, $\beta = -.06$, $p = .54$; TT homozygotes, $\beta = -.18$, $p = .29$

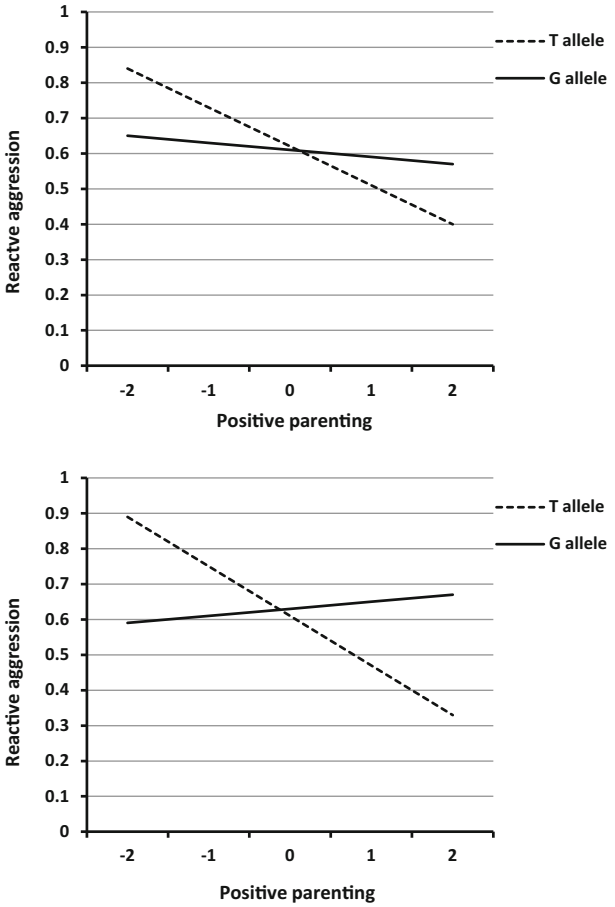

Fig. 5 Simple slopes on reactive aggression from positive parenting in MAOA T941G allelic groups among boys. The values of the cross over point *C* of the interaction on the positive parenting axis were 0.11 and −0.13 in subsample 1 and 2, respectively. The slopes for positive parenting on reactive aggression were as follows: (i) in subsample 1: GG homozygotes, $\beta = -.02$, $p = .79$; TT homozygotes, $\beta = -.08$, $p = .27$; (ii) in subsample 2: GG homozygotes, $\beta = .01$, $p = .84$; TT homozygotes, $\beta = -.11$, $p = .11$

References

Albaugh, M. D., Harder, V. S., Althoff, R. R., Rettew, D. C., Ehli, E. A., Lengyel-Nelson, T., & Hudziak, J. J. (2010). COMT Val158Met genotype as a risk factor for problem behaviors in youth. *Journal of the American Academy of Child and Adolescent Psychiatry, 49*, 841–849. doi:10.1016/j.jaac.2010.05.015.

Anholt, R. R., & Mackay, T. F. (2012). Genetics of aggression. *Annual Review of Genetics, 46*, 145–164. doi:10.1146/annurev-genet-110711-155514.

Baker, L., Raine, A., Liu, J., & Jacobson, K. C. (2008). Differential genetic and environmental influences on reactive and proactive aggression in children. *Journal of Abnormal Child Psychology, 36*, 1265–1278. doi:10.1007/s10802-008-9249-1.

Bakermans-Kranenburg, M. J., & van IJzendoorn, M. H. (2011). Differential susceptibility to rearing environment depending on dopamine-related genes: New evidence and a meta-analysis. *Development and Psychopathology, 23*, 39–52. doi:10.1017/S0954579410000635.

Belsky, J., & Pluess, M. (2009). Beyond diathesis stress: Differential susceptibility to environmental influences. *Psychological Bulletin, 135*, 885–908. doi:10.1037/a0017376.

Belsky, J., & Pluess, M. (2013). Genetic moderation of early child-care effects on social functioning across childhood: A developmental analysis. *Child Development, 84*, 1209–1225. doi:10.1111/cdev.12058.

Belsky, J., Pluess, M., & Widaman, K. F. (2013). Confirmatory and competitive evaluation of alternative gene-environment interaction hypotheses. *Journal of Child Psychology and Psychiatry, 54*, 1135–1143. doi:10.1111/jcpp.12075.

Bongers, I. L., Koot, H. M., Van Der Ende, J., & Verhulst, F. C. (2004). Developmental trajectories of externalizing behaviors in childhood and adolescence. *Child Development, 75*, 1523–1537. doi:10.1111/j.1467-8624.2004.00755.x.

Brendgen, M., Vitaro, F., Boivin, M., Dionne, G., & Pérusse, D. (2006). Examining genetic and environmental effects on reactive versus proactive aggression. *Developmental Psychology, 42*, 1299–1312. doi:10.1037/0012-1649.42.6.1299.

Buckholtz, J. W., & Meyer-Lindenberg, A. (2008). MAOA and the neurogenetic architecture of human aggression. *Trends in Neurosciences, 31*, 120–129. doi:10.1016/j.tins.2007.12.006.

Buil, J. M., Koot, H. M., Olthof, T., Nelson, K. A., & van Lier, P. A. C. (2015). DRD4 genotype and the developmental link of peer social preference with conduct problems and prosocial behavior across ages 9–12 years. *Journal of Youth and Adolescence, 44*, 1360–1378. doi:10.1007/s10964-015-0289-x.

Burmeister, M., McInnis, M. G., & Zöllner, S. (2008). Psychiatric genetics: Progress amid controversy. *Nature Reviews Genetics, 9*, 527–540. doi:10.1038/nrg2381.

Caspi, A., McClay, J., Moffitt, T. E., Mill, J., Martin, J., Craig, I. W., & Poulton, R. (2002). Role of genotype in the cycle of violence in maltreated children. *Science, 297*, 851–854. doi:10.1126/science.1072290.

Chen, X., Liu, M., & Li, D. (2000). Parental warmth, control and indulgence and their relations to adjustment in Chinese children: A longitudinal study. *Journal of Family Psychology, 14*, 401–419. doi:10.1037/0893-3200.14.3.401.

Chen, X., Wang, L., Chen, H., & Liu, M. (2002). Noncompliance and child-rearing attitudes as predictors of aggressive behaviour: A longitudinal study in Chinese children. *International Journal of Behavioral Development, 26*, 225–233. doi:10.1080/01650250143000012.

DiLalla, L. F., Bersted, K., & Gheyara, S. J. (2015). Peer victimization and DRD4 genotype influence problem behaviors in young children. *Journal of Youth and Adolescence, 44*, 1478–1493. doi:10.1007/s10964-015-0282-4.

Dodge, K. A., & Coie, J. D. (1987). Social information processing factors in reactive and proactive aggression in children's peer groups. *Journal of Personality and Social Psychology, 53*, 1146–1158. doi:10.1037/0022-3514.53.6.1146.

Drabant, E. M., Hariri, A. R., Meyer-Lindenberg, A., Munoz, K. E., Mattay, V. S., Kolachana, B. S., & Weinberger, D. R. (2006). Catechol O-methyltransferase val158met genotype and neural mechanisms related to affective arousal and regulation. *Archives of General Psychiatry, 63*, 1396–1406. doi:10.1001/archpsyc.63.12.1396.

Eisenberger, N. I., Way, B. M., Taylor, S. E., Welch, W. T., & Lieberman, M. D. (2007). Understanding genetic risk for aggression: Clues from the brain's response to social exclusion. *Biological Psychiatry, 61*, 1100–1108. doi:10.1016/j.biopsych.2006.08.007.

Fan, M., Liu, B., Jiang, T., Jiang, X., Zhao, H., & Zhang, J. (2010). Meta-analysis of the association between the monoamine oxidase-A gene and mood disorders. *Psychiatric Genetics, 20*, 1–7. doi:10.1097/YPG.0b013e3283351112.

Gershoff, E. T. (2002). Corporal punishment by parents and associated child behaviors and experiences: A meta-analytic and theoretical review. *Psychological Bulletin, 128*, 539–579. doi:10.1037//0033-2909.128.4.539.

Gohier, B., Senior, C., Radua, J., EI-Hage, W., Reichenberg, A., Proitsi, P., & Surquladze, S. A. (2014). Genetic modulation of the response bias towards facial displays of anger and happiness. *European Psychiatry, 29*, 197–202. doi:10.1016/j.eurpsy.2013.03.003.

Hartman, S., Widaman, K. F., & Belsky, J. (2015). Genetic moderation of effects of maternal sensitivity on girl's age of menarche: Replication of the Manuck et al. study. *Development and Psychopathology, 27*, 747–756. doi:10.1017/S0954579414000856.

Hotamisligil, G. S., & Breakefield, X. O. (1991). Human monoamine oxidase A gene determines levels of enzyme activity. *American Journal of Human Genetics, 49*, 383–392.

Hubbard, J. A., McAuliffe, M. D., Morrow, M. T., & Romano, L. J. (2010). Reactive and proactive aggression in childhood and adolescence: Precursors, outcomes, processes, experiences, and measurement. *Journal of Personality, 78*, 95–118. doi:10.1111/j.1467-6494.2009.00610.x.

Kuepper, Y., Grant, P., Wielpuetz, C., & Hennig, J. (2013). MAOA-uVNTR genotype predicts interindividual differences in experimental aggressiveness as a function of the degree of provocation. *Behavioural Brain Research, 247*, 73–78. doi:10.1016/j.bbr.2013.03.002.

Lachman, H. M., Papolos, D. F., Saito, T., Yu, Y. M., Szumlanski, C. L., & Weinshilboum, R. M. (1996). Human catechol-O-methyltransferase pharmacogenetics: Description of a functional polymorphism and its potential application to neuropsychiatric disorders. *Pharmacogenetics, 6*, 243–2450. doi:10.1097/00008571-199606000-00007.

Laucht, M., Blomeyer, D., Buchmann, A. F., Treutlein, J., Schmidt, M. H., Esser, G., & Banaschewski, T. (2012). Catechol-O-methyltransferase Val158 Met genotype, parenting practices and adolescent alcohol use: Testing the differential susceptibility hypothesis. *Journal of Child Psychology and Psychiatry, 53*, 351–359. doi:10.1111/j.1469-7610.2011.02408.x.

Leuchter, A. F., McCracken, J. T., Hunter, A. M., Cook, I. A., & Alpert, J. E. (2009). Monoamine oxidase a and catechol-o-methyltransferase functional polymorphisms and the placebo response in major depressive disorder. *Journal of Clinical Psychopharmacology, 29*, 372–377. doi:10.1097/JCP.0b013e3181ac4aaf.

Manuck, S. B., Flory, J. D., Ferrell, R. E., Mann, J. J., & Muldoon, M. F. (2000). A regulatory polymorphism of the monoamine oxidase-A gene may be associated with variability in aggression, impulsivity, and central nervous system serotonergic responsivity. *Psychiatry Research, 95*, 9–23. doi:10.1016/S0165-1781(00)00162-1.

McDermott, R., Tingley, D., Cowden, J., Frazzetto, G., & Johnson, D. D. (2009). Monoamine oxidase A gene (MAOA) predicts behavioral aggression following provocation. *Proceedings of the National Academy of Sciences, 106*, 2118–2123. doi:10.1073/pnas.0808376106.

Meyer-Lindenberg, A., Buckholtz, J. W., Kolachana, B., Hariri, A. R., Pezawas, L., Blasi, G., & Weinberger, D. R. (2006). Neural mechanisms of genetic risk for impulsivity and violence in humans. *Proceedings of the National Academy of Sciences, 103*, 6269–6274. doi:10.1073/pnas.0511311103.

Moffitt, T. E. (1993). Adolescence-limited and life-course-persistent antisocial behavior: A developmental taxonomy. *Psychological Review, 100*, 674–701. doi:10.1037/0033-295X.100.4.674.

Moffitt, T. E. (2005). The new look of behavioral genetics in developmental psychopathology: Gene-environment interplay in antisocial behaviors. *Psychological Bulletin, 131*, 533–554. doi:10.1037/0033-2909.131.4.533.

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. doi:10.1037//0033-2909.110.3.406.

Munafò, M. R., Durrant, C., Lewis, G., & Flint, J. (2009). Gene × environment interactions at the serotonin transporter locus. *Biological Psychiatry, 65*, 211–219. doi:10.1016/j.biopsych.2008.06.009.

Odgers, C. L., Moffitt, T. E., Broadbent, J. M., Dickson, N., Hancox, R. J., Harrington, H., & Caspi, A. (2008). Female and male antisocial trajectories: From childhood origins to adult outcomes. *Development and Psychopathology, 20*, 673–716. doi:10.1017/S0954579408000333.

Pettit, G. S., Bates, J. E., & Dodge, K. A. (1997). Supportive parenting, ecological context, and children's adjustment: A seven-year longitudinal study. *Child Development, 68*, 908–923. doi:10.1111/j.1467-8624.1997.tb01970.x.

Pickles, A., Hill, J., Breen, G., Quinn, J., Abbott, K., Jones, H., & Sharp, H. (2013). Evidence for interplay between genes and parenting on infant temperament in the first year of life: Monoamine oxidase A polymorphism moderates effects of maternal sensitivity on infant anger proneness. *Journal of Child Psychology and Psychiatry, 54*, 1308–1317. doi:10.1111/jcpp.12081.

Pluess, M., & Belsky, J. (2013). Vantage sensitivity: Individual differences in response to positive experiences. *Psychological Bulletin, 139*, 901–916. doi:10.1037/a0030196.

Smolka, M. N., Schumann, G., Wrase, J., Grusser, S. M., Flor, H., Mann, K., & Heinz, A. (2005). Catechol-O-methyltransferase val158met genotype affects processing of emotional stimuli in the amygdala and prefrontal cortex. *Journal of Neuroscience, 25*, 836–842. doi:10.1523/JNEUROSCI.1792-04.2005.

Substance Abuse and Mental Health Services Administration (SAMHSA). (2014). *Results from the 2013 national survey on drug use and the health: Summary of national findings* (Office of Applied Studies, NSDUH Series H-48, HHS Publication No. SMA 14-4683). Rockville, MD: SAMHSA.

Tadić, A., Müller, M. J., Rujescu, D., Kohnen, R., Stassen, H. H., Dahmen, N., & Szegedi, A. (2007). The MAOA T941G polymorphism and short-term treatment response to mirtazapine and paroxetine in major depression. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics, 144*, 325–331. doi:10.1002/ajmg.b.30462.

Thompson, J. M., Sonuga-Barke, E. J., Morgan, A. R., Cornforth, C. M., Turic, D., Ferguson, L. R., & Waldie, K. E. (2012). The catechol-O-methyltransferase (COMT) Val158Met polymorphism moderates the effect of antenatal stress on childhood behavioural problems: Longitudinal evidence across multiple ages. *Developmental Medicine and Child Neurology, 52*, 148–154. doi:10.1111/j.1469-8749.2011.04129.x.

Tremblay, R. E. (2010). Developmental origins of disruptive behaviour problems: The 'original sin' hypothesis, epigenetics and their consequences for prevention. *Journal of Child Psychology and Psychiatry, 51*, 341–367. doi:10.1111/j.1469-7610.2010.02211.x.

Tuvblad, C., Raine, A., Zheng, M., & Baker, L. A. (2009). Genetic and environmental stability differs in reactive and proactive aggression. *Aggressive Behavior, 35*, 437–452. doi:10.1002/ab.20319.

van Ijzendoorn, M. H., Caspers, K., Bakermans-Kranenburg, M. J., Beach, S. R., & Philibert, R. (2010). Methylation matters: Interaction between methylation density and serotonin transporter genotype predicts unresolved loss or trauma. *Biological Psychiatry, 68*, 405–407. doi:10.1016/j.biopsych.2010.05.008.

Verma, D., Chakraborti, B., Karmakar, A., Bandyopadhyay, T., Singh, A. S., Sinha, S., & Rajamma, U. (2014). Sexual

dimorphic effect in the genetic association of monoamine oxidase A (MAOA) makers with autism spectrum disorder. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 50*, 11–20. doi:10.1016/j.pnpbp.2013.11.010.

Volavka, J. A. N., Bilder, R., & Nolan, K. (2004). Catecholamines and aggression: The role of COMT and MAO polymorphisms. *Annals of the New York Academy of Sciences, 1036*, 393–398. doi:10.1196/annals.1330.023.

Wakschlag, L. S., Kistner, E. O., Pine, D. S., Biesecker, G., Pickett, K. E., Skol, A., & Cook, E. H. (2010). Interaction of prenatal exposure to cigarettes and MAOA genotype in pathways to youth antisocial behavior. *Molecular Psychiatry, 15*, 928–937. doi:10.1038/mp.2009.22.

Wang, F. M., Chen, J. Q., Xiao, W. Q., Ma, Y. T., & Zhang, M. (2012). Peer physical aggression and its association with aggressive beliefs, empathy, self-control, and cooperation skills among students in a rural town of china. *Journal of Interpersonal Violence, 27*, 3252–3267. doi:10.1177/0886260512441256.

Widaman, K. F., Helm, J. L., Castro-Schilo, L., Pluess, M., Stallings, M., & Belsky, J. (2012). Distinguishing ordinal and disordinal interactions. *Psychological Methods, 17*, 615–622. doi:10.1037/a0030003.

Widom, C. S., & Brzustowicz, L. M. (2006). MAOA and the "cycle of violence": Childhood abuse and neglect, MAOA genotype, and risk for violent and antisocial behavior. *Biological Psychiatry, 60*, 684–689. doi:10.1016/j.biopsych.2006.03.039.

Williams, L. M., Gatt, J. M., Grieve, S. M., Dobson-Stone, C., Paul, R. H., Gordon, E., & Schofield, P. R. (2010). COMT Val 108/158 Met polymorphism effects on emotional brain function and negativity bias. *Neuroimage, 53*, 918–925. doi:10.1016/j.neuroimage.2010.01.084.

Windhorst, D. A., Mileva-Seitz, V. R., Linting, M., Hofman, A., Jaddoe, V. W., Verhulst, F. C., & Bakermans-Kranenburg, M. J. (2015). Differential susceptibility in a developmental perspective: DRD4 and maternal sensitivity predicting externalizing behavior. *Developmental Psychobiology, 57*, 35–49. doi:10.1002/dev.21257.

Zhang, W., Cao, Y., Wang, M., Ji, L., Chen, L., & Deater-Deckard, K. (2015). The dopamine D2 receptor polymorphism (DRD2 TaqIA) interacts with maternal parenting in predicting early adolescent depressive symptoms: Evidence of different susceptibility and age differences. *Journal of Youth and Adolescence, 44*, 1428–1440. doi:10.1007/s10964-015-0297-x.

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