**Supplementary Materials**

**Data analysis**

**Re-parameterized regression model:** Whether or not the significant MGPS🞨parenting interaction was consistent with the hypotheses of differential susceptibility or diathesis-stress was examined using the re-parameterized regression model with linear🞨linear interaction developed by Widaman et al. (2012) in R. The model was constructed as follows: *Y*= *B*0 + *B*1(*X1* - *C*) + *B*2((*X1* - *C*) • X*2*) + *B3X3* + *B4X4* + *B5X5*;

where *Y*is dependent variable of internalizing/externalizing symptoms, *X*1 maternal/paternal parenting (mean-centered); *X*2 MGPS; *X3*, *X4* and *X5* controlled variables— adolescent sex, age and the other type of parenting; *B0* the intercept, *B1* and *B*2 slopes for the effects of maternal/paternal parenting and the product term—MGPS×maternal/paternal parenting; *B3*, *B4* and *B5* slope for the controlled sex, age and parenting; *C* crossover point where the slopes for MGPS subgroups cross. Additionally, although we did not present here, the interaction effects for covariates survived in split half replication would be also included into this model.

What distinguishes the diathesis-stress and differential susceptibility models is the location of the crossover point *C* (Widaman et al. 2012). Specifically, if this crossover point C and its 95 % conﬁdential interval (CI) fall within the range of the maternal and paternal parenting variables, the G×E interaction is disordinal, consistent with the differential susceptibility model. Otherwise, if these values of C fall at or over the maximum of the maternal and paternal parenting variables, the G×E interaction is ordinal, in accordance with the diathesis-stress model (Widaman et al. 2012). Because the diathesis-stress model was nested within the differential susceptibility model, the *ΔF* test was used to test whether the differential susceptibility model fitted better than the diathesis-stress model.

**Equal gene model:** If a MGPS for multiple genes is calculated, the interpretation can be confounded if genes have differential effects. For example, different genes could have significantly different main effects or interactive effects with environmental factors on the phenotype of interest. In both cases, the significant G×E findings with the use of a MGPS might be driven by the effects of only one or two genes. Another possibility is that the effects of one gene may be counteracted by opposite effects of another gene. Although the computation of the additive MGPS (e.g., determination of the specific susceptible or risk alleles) was mainly based on previous literature (i.e., theory-driven perspective), the interpretation of its effect estimates could be confounded if different genes have differential effects. Therefore, an equal gene model was conducted to test whether differential effects across six candidate genes in this study might undermine the use of our MGPS. This confirmatory statistical approach has been developed in the study of Stocker et al. (2017), which supported the use of MGPS by *5-HTTLPR*, *DRD2*, *DRD4* and *COMT* genes.

The examination of an equal gene model comprised of two steps. First, a disaggregated regression model was constructed, where the main effects and interactions of six candidate genes and parenting, as well as covariates, were freely estimated. In the second step, a nested, equal gene regression model was constructed. This model has ten restrictions, constraining the regression weights for main effects of the six candidate genes (five restrictions), and their interactions with parenting (five restrictions) to equality. If the disaggregated model fitted better than the equal gene model, this would imply that at least one genetic marker might have differential effects. Otherwise, equal effects across different genetic markers were supported.

**Sensitivity analyses using MGPSs based on core genes:** The *CRHR1*, *NR3C1*, *NR3C2* and *FKBP5* genes are considered as core genes that directly regulate the HPA-axis function, whereas the *COMT* and *HTR1A* genes are important peripheral genes that indirectly regulate the HPA-axis function (see Table 1). In line with previous MGPS research (Pagliaccio et al., 2014; Feurer et al., 2017; Mckenna et al., 2020), we conducted a sensitivity analysis for the MGPSs including only core (versus peripheral) SNPs.

**Results**

**Sensitivity analyses using MGPSs based on core genes**

As shown in Table S10, our results demonstrated that, the MGPS🞨parenting interactions based on the MGPS including core SNPs of *CRHR1*, *NR3C1*, *NR3C2* and *FKBP5* remained significant on adolescent internalizing symptoms (for mothers: *ΔR*2 = .006, *p* = .022, *q* =.044; for fathers: *ΔR*2= .011, *p* = .001, *q* =.004). However, it is worth noting that our MGPS based on only core (versus peripheral) SNPs (*CRHR1*, *NR3C1*, *NR3C2* and *FKBP5*; *β*MGPS×maternal parenting = -.08, *β*MGPS×paternal parenting = -.11), as well as the MGPS based on core SNPs that were previously included by Di Iorio et al. (2017) (*CRHR1*, *NR3C2* and *FKBP5*; *β*MGPS×maternal parenting = -.09, *β*MGPS×paternal parenting = -.10), showed a slightly, albeit not significantly, smaller interaction effect than the MGPS based on both core and peripheral SNPs as used in our main analyses (*β*MGPS×maternal parenting = -.11, *β*MGPS×paternal parenting = -.13; *z* ≤ 1.31, *p* ≥ .095).

**Table S1** Single nucleotide polymorphism data

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Gene | SNP | MISSING | Alleles | MAF | Genotype frequency | | | Hardy-Weinberg equilibrium | |
| 11 | 12 | 22 | *χ2* | *p* |
| *CRHR1* | rs110402 | 0 | A > G | 0.12 | 589 | 174 | 9 | 0.94 | .332 |
| *NR3C1* | rs41423247 | 6 | G > C | 0.22 | 470 | 261 | 35 | 0.03 | .872 |
| *NR3C2* | rs5522 | 0 | A > G | 0.17 | 538 | 208 | 26 | 1.12 | .290 |
| *FKBP5* | rs1360780 | 0 | C > T | 0.25 | 441 | 278 | 53 | 1.02 | 312 |
| *COMT* | rs4680 | 2 | Val > Met | 0.28 | 392 | 321 | 57 | 0.62 | .430 |
| *5-HTR1A* | rs6295 | 0 | G>C | 0.28 | 406 | 305 | 61 | 0.12 | .724 |

*Note.* Missing = Missing number of participants due to genotyping failure; Alleles = Alleles presented in the current sample (major > minor);

MAF = minor allele frequency for the current sample; 11 = frequency of homozygotes constituted by major alleles, 12 = frequency of heterozygotes,

22 = frequency of homozygotes constituted by minor alleles.

**Table S2 (a)** Internal replication analysis of interactions between multilocus genetic profile score and maternal parenting

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Predictors | Internalizing symptoms | | | | | Externalizing symptoms | | | | |
| *ΔR2* | *b (S.E.)* | *ß* | *p* | *qc* | *ΔR2* | *b (S.E.)* | *ß* | *p* | *qc* |
| Subsample 1a | MGPS | .015 | –0.09 (0.09) | –.05 | .347 | — | .026 | 0.06 (0.12) | .03 | .582 | — |
| MPQ |  | –0.52 (0.22) | –.18 | .018 | — |  | –0.90 (0.27) | –.25 | .001 | — |
| MGPS×MPQ | .012 | –0.30 (0.13) | –.12 | .018 | .036 | .006 | –0.25 (0.16) | –.08 | .115 | .115 |
| Covariates |  |  |  |  |  |  |  |  |  |  |
| Sex | .109 | 0.99 (0.22) | .22 | <.001 | — | .087 | –0.19 (0.28) | –.03 | .499 | — |
| Age |  | 0.01 (0.08) | .01 | .857 | — |  | –0.09 (0.10) | –.05 | .345 | — |
| PPQ |  | –0.69 (0.14) | –.25 | <.001 | — |  | –0.97 (0.17) | –.28 | <.001 | — |
| Sex×MPQb |  | –0.42 (0.28) | –.11 | .133 | — |  | — | — | — | — |
| Subsample 2a | MGPS | .009 | –0.02 (0.10) | –.01 | .800 | — | .023 | 0.11 (0.12) | .04 | .397 | — |
| MPQ |  | –0.40 (0.20) | –.14 | .049 | — |  | –0.82 (0.27) | –.23 | .002 | — |
| MGPS×MPQ | .010 | –0.25 (0.10) | –.11 | .016 | .032 | .001 | –0.07 (0.14) | –.02 | .622 | .622 |
| Covariates |  |  |  |  |  |  |  |  |  |  |
| Sex | .206 | 1.45 (0.24) | .30 | <.001 | — | .116 | 0.43 (0.31) | .07 | .170` | — |
| Age |  | –0.08 (0.09) | –.04 | .388 | — |  | –0.13 (0.12) | –.06 | .268 | — |
| PPQ |  | –1.11 (0.14) | –.38 | <.001 | — |  | –1.21 (0.18) | –.33 | <.001 | — |
| Sex×MPQb |  | –0.65 (0.27) | –.18 | .015 | — |  | — | — | — | — |

*Note.* MGPS = multilocus genetic profile score; MPQ = maternal parenting quality; PPQ = paternal parenting quality;

a The full sample was randomly split into two subsamples (*N1* = 386, *N2* = 386). There were no significant differences on sex, age, maternal and paternal parenting quality and adolescent internalizing and externalizing symptoms between subsamples 1 and 2;

b Non-significant interaction effects for covariates (e.g., sex×MGPS) were removed from the models by backward elimination;

*c* The false discovery rate (FDR, *q* < 0.05) was used to control for multiple testing; 2 models (MGPS×MPQ and MGPS×PPQ models) × 2 outcomes (internalizing and externalizing symptoms) = 4.

**Table S2 (b)** Internal replication analysis for interactions between multilocus genetic profile score and paternal parenting

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Predictors | Internalizing symptoms | | | | | Externalizing symptoms | | | | |
| *ΔR2* | *b (S.E.)* | *ß* | *p* | *qc* | *ΔR2* | *b (S.E.)* | *ß* | *p* | *qc* |
| Subsample 1a | MGPS | .007 | –0.09 (0.09) | –.05 | .347 | — | .003 | 0.06 (0.12) | .03 | .582 | — |
| PPQ |  | –0.30 (0.21) | –.11 | .167 | — |  | –0.29 (0.27) | –.09 | .269 | — |
| MGPS×PPQ | .025 | –0.39 (0.12) | –.16 | .001 | .004 | .007 | –0.26 (0.15) | –.09 | .085 | .113 |
| Covariates |  |  |  |  |  |  |  |  |  |  |
| Sex | .112 | 0.86 (0.22) | .19 | <.001 | — | .110 | –0.38 (0.27) | –.07 | .164 | — |
| Age |  | 0.01 (0.08) | –.01 | .879 | — |  | –0.09 (0.10) | –.05 | .340 | — |
| MPQ |  | –0.76 (0.14) | –.26 | <.001 | — |  | –1.13 (0.17) | –.32 | <.001 | — |
| Sex×PPQb |  | –0.27 (0.27) | –.07 | .299 | — |  | — | — | — | — |
| Subsample 2a | MGPS | .031 | –0.02 (0.10) | –.01 | .800 | — | .013 | 0.11 (0.12) | .04 | .397 | — |
| PPQ |  | –0.80 (0.21) | –.28 | <.001 | — |  | –0.58 (0.27) | –.16 | .034 | — |
| MGPS×PPQ | .013 | –0.31 (0.11) | –.13 | .005 | .020 | .004 | –0.19 (0.15) | –.06 | .196 | .261 |
| Covariates |  |  |  |  |  |  |  |  |  |  |
| Sex | .182 | 1.41 (0.24) | .29 | <.001 | — | .126 | 0.23 (0.31) | .04 | .450 | — |
| Age |  | –0.09 (0.09) | –.05 | .323 | — |  | –0.13 (0.11) | –.06 | .259 | — |
| MPQ |  | –0.99 (0.13) | –.35 | <.001 | — |  | –1.22 (0.17) | –.34 | <.001 | — |
| Sex×PPQb |  | –0.93 (0.27) | –.24 | .001 | — |  | — | — | — | — |

*Note.* MGPS = multilocus genetic profile score; MPQ = maternal parenting quality; PPQ = paternal parenting quality;

a The full sample was randomly split into two subsamples (*N1* = 386, *N2* = 386). There were no significant differences on sex, age, maternal and paternal parenting quality and adolescent internalizing and externalizing symptoms between subsample 1 and 2;

b Non-significant interaction effects for covariates (e.g., sex×MGPS) were removed from the models by backward elimination;

*c* The false discovery rate (FDR, *q* < 0.05) was used to control for multiple testing; 2 models (MGPS×MPQ and MGPS×PPQ models) × 2 outcomes (internalizing and externalizing symptoms) = 4.

**Table S3** Results for regression models predicting adolescents’ internalizing symptoms from interactions between modified MGPS excluding one SNP and paternal parenting

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Outcomes | Modified MGPS  excluding one SNP | MGPS×MPQ | | | | | MGPS×PPQ | | | | |
| *ΔR2* | *b (S.E.)* | *ß* | *p* | *qa* | *ΔR2* | *b (S.E.)* | *ß* | *p* | *qa* |
| Internalizing symptoms | MGPSexcluding *CRHR1* rs110402 | .006 | –0.21 (0.08) | –.09 | .011 | .026 | .013 | –0.30 (0.09) | –.12 | <.001 | <.001 |
| MGPSexcluding *NR3C1* rs41423247 | .011 | –0.30 (0.09) | –.11 | .001 | <.001 | .015 | –0.35 (0.09) | –.13 | <.001 | <.001 |
| MGPSexcluding *NR3C2* rs5522 | .005 | –0.20 (0.09) | –.08 | .024 | .048 | .009 | –0.28 (0.09) | –.11 | .001 | .003 |
| MGPSexcluding *FKBP5* rs1360780 | .007 | –0.30 (0.10) | –.10 | .004 | .011 | .014 | –0.36 (0.09) | –.13 | <.001 | <.001 |
| MGPSexcluding *COMT* rs4680 | .010 | –0.27 (0.09) | –.10 | .003 | .009 | .014 | –0.32 (0.09) | –.12 | <.001 | <.001 |
| MGPSexcluding *5-HTR1A* rs6295 | .006 | –0.21 (0.09) | –.08 | .017 | .037 | .013 | –0.33 (0.09) | –.12 | <.001 | <.001 |
| Externalizing symptoms | MGPSexcluding *CRHR1* rs110402 | .0004 | –0.06 (0.11) | –.02 | .569 | .569 | .002 | –0.15 (0.11) | –.05 | .182 | .218 |
| MGPSexcluding *NR3C1* rs41423247 | .001 | –0.09 (0.11) | –.03 | .408 | .426 | .003 | –0.20 (0.12) | –.06 | .087 | .123 |
| MGPSexcluding *NR3C2* rs5522 | .002 | –0.16 (0.11) | –.05 | .156 | .197 | .006 | –0.25 (0.11) | –.08 | .027 | .050 |
| MGPSexcluding *FKBP5* rs1360780 | .002 | –0.14 (0.12) | –.04 | .248 | .283 | .004 | –0.22 (0.12) | –.06 | .064 | .102 |
| MGPSexcluding *COMT* rs4680 | .003 | –0.18 (0.11) | –.05 | .119 | .159 | .004 | –0.22 (0.11) | –.07 | .050 | .086 |
| MGPSexcluding *5-HTR1A* rs6295 | .001 | –0.10 (0.12) | –.03 | .405 | .426 | .004 | –0.21 (0.12) | –.06 | .075 | .113 |

*Note.* MGPS = multilocus genetic plasticity score; MPQ = maternal parenting quality; PPQ = paternal parenting quality;

*a* The false discovery rate (FDR, *q* < 0.05) was used to control for multiple testing; 6 MPGSs × 2 models (MGPS×MPQ and MGPS×PPQ models) × 2 outcomes (internalizing and externalizing symptoms) = 24;

**Table S4** Regression models predicting adolescent internalizing and externalizing symptoms when controlling for each other

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Predictors | Internalizing symptoms | | | | | Externalizing symptoms | | | | |
| *ΔR2* | *b (S.E.)* | *ß* | *p* | *qb* | *ΔR2* | *b (S.E.)* | *ß* | *p* | *qb* |
| MPQ model |  |  |  |  |  |  |  |  |  |  |
| MGPS | .003 | –0.09 (0.06) | –.05 | .103 | — | .012 | 0.12 (0.07) | .05 | .098 | — |
| MPQ |  | –0.12 (0.13) | –.04 | .365 | — |  | –0.55 (0.16) | –.16 | .001 | — |
| MGPS×MPQ | .005 | –0.19 (0.07) | –.08 | .005 | .010 | .0001 | 0.04 (0.09) | .01 | .647 | .863 |
| Covariates |  |  |  |  |  |  |  |  |  |  |
| Externalizing or internalizing symptoms | .382 | 0.40 (0.02) | .50 | <.001 | — | .339 | 0.66 (0.04) | .53 | <.001 |  |
| Sex |  | 1.15 (0.14) | .25 | <.001 | — |  | –0.69 (0.18) | –.12 | <.001 | — |
| Age |  | 0.02 (0.05) | .01 | .740 | — |  | –0.09 (0.06) | –.04 | .172 | — |
| PPQ |  | –0.47 (0.09) | –.17 | <.001 | — |  | –0.49 (0.11) | –.14 | <.001 | — |
| Sex×MPQa |  | –0.56 (0.17) | –.15 | .001 | — |  | 0.43 (0.21) | .09 | .045 | — |
| FPQ model |  |  |  |  |  |  |  |  |  |  |
| MGPS | .009 | –0.09 (0.06) | –.05 | .103 | — | .003 | 0.12 (0.07) | .05 | .098 | — |
| PPQ |  | –0.38 (0.13) | –.13 | .004 | — |  | –0.08 (0.17) | –.02 | .612 | — |
| MGPS×PPQ | .008 | –0.24 (0.07) | –.10 | .001 | .004 | .0001 | –0.01 (0.09) | –.004 | .901 | .901 |
| Covariates |  |  |  |  |  |  |  |  |  |  |
| Externalizing or internalizing symptoms | .376 | 0.40 (0.03) | .50 | <.001 | — | .345 | 0.65 (0.04) | .52 | <.001 | — |
| Sex |  | 1.07 (0.14) | .23 | <.001 | — |  | –0.76 (0.18) | –.13 | <.001 | — |
| Age |  | 0.01 (0.05) | .01 | .827 | — |  | –0.08 (0.06) | –.04 | .188 | — |
| MPQ |  | –0.41 (0.09) | –.14 | <.001 | — |  | –0.61 (0.11) | –.17 | <.001 | — |
| Sex×PPQa |  | –0.56 (0.17) | –.15 | <.001 | — |  | — | — | — | — |

*Note.* MGPS = multilocus genetic profile score; MPQ = maternal parenting quality; PPQ = paternal parenting quality;

a Non-significant interaction effects for covariates (e.g., sex×MGPS) were removed from the models by backward elimination;

*b* The false discovery rate (FDR, *q* < 0.05) was used to control for multiple testing; 2 models (MGPS×MPQ and MGPS×PPQ models) × 2 outcomes (internalizing and externalizing symptoms) = 4.

**Table S5** Regression models predicting adolescent internalizing and externalizing symptoms without maternal and paternal parenting being mutually adjusted for

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Predictors | Internalizing symptoms | | | | | Externalizing symptoms | | | | |
| *ΔR2* | *b (S.E.)* | *ß* | *p* | *qb* | *ΔR2* | *b (S.E.)* | *ß* | *p* | *qb* |
| MPQ Model |  |  |  |  |  |  |  |  |  |  |
| MGPS | .095 | –0.06 (0.07) | –.03 | .395 | — | .109 | 0.08 (0.08) | .03 | .332 | — |
| MPQ |  | –0.64 (0.14) | –.23 | <.001 | — |  | –1.18 (0.12) | –.33 | <.001 | — |
| MGPS×MPQ | .006 | –0.20 (0.08) | –.09 | .011 | .022 | .001 | –0.10 (0.10) | –.03 | .352 | .352 |
| Covariates |  |  |  |  |  |  |  |  |  |  |
| Sex | .056 | 1.07 (0.17) | .23 | <.001 | — | .007 | –0.04 (0.22) | –.01 | .841 | — |
| Age |  | –0.08 (0.06) | –.05 | .170 | — |  | –0.17 (0.08) | –.08 | .025 | — |
| Sex×MPQa |  | –0.44 (0.19) | –.12 | .022 | — |  | — | — | — | — |
| PPQ Model |  |  |  |  |  |  |  |  |  |  |
| MGPS | .100 | –0.07 (0.07) | –.04 | .293 | — | .092 | 0.06 (0.09) | .03 | .450 | — |
| PPQ |  | –0.90 (0.10) | –.32 | <.001 | — |  | –1.09 (0.12) | –.31 | <.001 | — |
| MGPS×PPQ | .013 | –0.30 (0.08) | –.12 | <.001 | <.001 | .003 | –0.16 (0.11) | –.05 | .123 | .164 |
| Covariates |  |  |  |  |  |  |  |  |  |  |
| Sex | .062 | 1.07 (0.17) | .23 | <.001 | — | .007 | –0.04 (0.22) | –.01 | .841 | — |
| Age |  | –0.08 (0.06) | –.05 | .170 | — |  | –0.17 (0.08) | –.08 | .025 | — |
| Sex×PPQa |  | –0.64 (0.19) | –.16 | .001 | — |  | — | — | — | — |

*Note.* MGPS = multilocus genetic profile score; MPQ = maternal parenting quality; PPQ = paternal parenting quality;

a Non-significant interaction effects for covariates (e.g., sex×MGPS) were removed from the models by backward elimination;

*b* The false discovery rate (FDR, *q* < 0.05) was used to control for multiple testing; 2 models (MGPS×MPQ and MGPS×PPQ models) × 2 outcomes (internalizing and externalizing symptoms) = 4.

**Table S6** Results for regression models predicting adolescent internalizing and externalizing symptoms from interactions between multilocus genetic

profile score and the individual parenting dimensions

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Predictors*a* | Internalizing symptoms | | | | | Externalizing symptoms | | | | |
| *ΔR2* | *b (S.E.)* | *ß* | *p* | *qc* | *ΔR2* | *b (S.E.)* | *ß* | *p* | *qc* |
| MW model |  |  |  |  |  |  |  |  |  |  |
| MGPS | .003 | –0.08 (0.07) | –.04 | .244 | — | .007 | 0.07 (0.09) | .03 | .452 | — |
| MW |  | –0.19 (0.26) | –.05 | .439 | — |  | –0.72 (0.32) | –.14 | .024 | — |
| MGPS×MW | .005 | –0.28 (0.12) | –.08 | .022 | .035 | .0001 | –0.01 (0.16) | –.003 | .930 | .930 |
| MH model |  |  |  |  |  |  |  |  |  |  |
| MGPS | .018 | –0.07 (0.07) | –.03 | .319 | — | .028 | 0.07 (0.08) | .03 | .403 | — |
| MH |  | 0.49 (0.13) | .19 | <.001 | — |  | 0.79 (0.16) | .24 | <.001 | — |
| MGPS×MH*b* | .007 | 0.19 (0.07) | .09 | .010 | .027 | .003 | 0.14 (0.09) | .05 | .136 | .181 |
| PW model |  |  |  |  |  |  |  |  |  |  |
| MGPS | .013 | –0.08 (0.07) | –.04 | .244 | — | .007 | 0.07 (0.09) | .03 | .452 | — |
| PW |  | –0.73 (0.24) | –.18 | .002 | — |  | –0.64 (0.30) | –.13 | .031 | — |
| MGPS×PW | .010 | –0.36 (0.12) | –.11 | .002 | .008 | .0004 | –0.09 (0.15) | –.02 | .529 | .605 |
| PH model |  |  |  |  |  |  |  |  |  |  |
| MGPS | .016 | –0.07 (0.07) | –.03 | .319 | — | .007 | 0.07 (0.08) | .03 | .403 | — |
| PH |  | 0.47 (0.13) | .18 | <.001 | — |  | 0.39 (0.16) | .12 | .019 | — |
| MGPS×PH*b* | .013 | 0.26 (0.07) | .12 | <.001 | .004 | .007 | 0.22 (0.09) | .08 | .018 | .035*d* |

*Note.* MGPS = multilocus genetic plasticity score; MW = maternal warmth; MH = maternal harsh discipline; PW = paternal warmth;

PH = paternal harsh discipline;

*a* The main and interactive effect of the covariates were comparable to the main analyses and not shown here.

*b* Because the correlations between punishment and rejection dimension for mothers (*r* =.75) and fathers (*r* =.73) were both high, we combined these two dimensions into one harsh discipline dimension for mothers and fathers, respectively, and conducted the interaction regression model.

*c* The false discovery rate (FDR, *q* < 0.05) was used to control for multiple testing; 4 models (MGPS×PW, MGPS×PH, MGPS×MW, and MGPS×MH models) × 2 outcomes (internalizing and externalizing symptoms) = 8.

*d* Although the MGPS interacted with paternal harsh discipline on adolescent externalizing symptoms in the full sample (*b* (*S.E.*) = 0.22 (0.09), *p* = .018, *q* = .035, *R*2 = .007), but failed to be internally replicated in two random subsamples (subsample 1: *b* (*S.E.*) = 0.26 (0.14), *p* = .071, *q* = .142, *R*2 = .008; subsample 2: *b* (*S.E.*) = 0.23 (0.13), *p* = .082, *q* = .328, *R*2 = .007).

**Table S7** Regression models predicting adolescent internalizing and externalizing symptoms from interactions between multilocus genetic profile score (range = 0~6) and parenting

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Predictors | Internalizing symptoms | | | | | Externalizing symptoms | | | | |
| *ΔR2* | *b (S.E.)* | *ß* | *p* | *qb* | *ΔR2* | *b (S.E.)* | *ß* | *p* | *qb* |
| MPQ Model |  |  |  |  |  |  |  |  |  |  |
| MGPS | .012 | –0.07 (0.07) | –.04 | .301 | — | .024 | 0.08 (0.08) | .03 | .339 | — |
| MPQ |  | –0.45 (0.15) | –.16 | .002 | — |  | –0.85 (0.19) | –.24 | <.001 | — |
| MGPS×MPQ | .009 | –0.24 (0.08) | –.10 | .003 | .006 | .001 | –0.11 (0.10) | –.04 | .258 | .258 |
| Covariates |  |  |  |  |  |  |  |  |  |  |
| Sex | .157 | 1.19 (0.16) | .25 | <.001 | — | .099 | 0.10 (0.21) | .02 | .635 | — |
| Age |  | –0.03 (0.06) | –.02 | .668 | — |  | –0.10 (0.07) | –.05 | .164 | — |
| PPQ |  | –0.90 (0.10) | –.32 | <.001 | — |  | –1.08 (0.12) | –.31 | <.001 | — |
| Sex×MPQa |  | –0.53 (0.19) | –.14 | .006 | — |  | — | — | — | — |
| PPQ Model |  |  |  |  |  |  |  |  |  |  |
| MGPS | .016 | –0.07 (0.07) | –.04 | .301 | — | .007 | 0.08 (0.08) | .03 | .339 | — |
| PPQ |  | –0.55 (0.15) | –.19 | <.001 | — |  | –0.44 (0.19) | –.12 | .021 | — |
| MGPS×PPQ | .015 | –0.32 (0.08) | –.13 | <.001 | <.001 | .005 | –0.20 (0.10) | –.07 | .049 | .065 |
| Covariates |  |  |  |  |  |  |  |  |  |  |
| Sex | .160 | 1.04 (0.16) | .22 | <.001 | — | .115 | –0.09 (0.20) | –.02 | .655 | — |
| Age |  | –0.03 (0.06) | –.02 | .599 | — |  | –0.10 (0.07) | –.05 | .161 | — |
| MPQ |  | –0.88 (0.10) | –.31 | <.001 | — |  | –1.17 (0.12) | –.33 | <.001 | — |
| Sex×PPQa |  | –0.63 (0.19) | –.16 | .001 | — |  | — | — | — | — |

*Note.* MGPS = multilocus genetic profile score; MPQ = maternal parenting quality; PPQ = paternal parenting quality;

a Non-significant interaction effects for covariates (e.g., sex×MGPS) were removed from the models by backward elimination;

*b* The false discovery rate (FDR, *q* < 0.05) was used to control for multiple testing; 2 models (MGPS×MPQ and MGPS×PPQ models) × 2 outcomes (internalizing and externalizing symptoms) = 4.

**Table S8** Regression models predicting adolescent internalizing and externalizing symptoms from interactions between multilocus genetic profile score and parenting based on a linear genetic modela

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Predictorsb | Internalizing symptoms | | | | | Externalizing symptoms | | | | |
| *ΔR2* | *b (S.E.)* | *ß* | *p* | *qc* | *ΔR2* | *b (S.E.)* | *ß* | *p* | *qc* |
| MPQ model |  |  |  |  |  |  |  |  |  |  |
| MGPS | .012 | –0.07 (0.06) | –.04 | .231 | — | .026 | 0.07 (0.07) | .03 | .321 | — |
| MPQ |  | –0.45 (0.15) | –.16 | .002 | — |  | –0.85 (0.19) | –.24 | <.001 | — |
| MGPS×MPQ | .005 | –0.16 (0.07) | –.08 | .023 | .046 | .001 | –0.07 (0.09) | –.03 | .405 | .405 |
| FPQ model |  |  |  |  |  |  |  |  |  |  |
| MGPS | .017 | –0.07 (0.06) | –.04 | .231 | — | .007 | 0.07 (0.07) | .03 | .321 | — |
| PPQ |  | –0.55 (0.15) | –.19 | <.001 | — |  | –0.44 (0.19) | –.12 | .022 | — |
| MGPS×PPQ | .011 | –0.22 (0.07) | –.11 | .002 | .008 | .003 | –0.15 (0.09) | –.06 | .091 | .121 |

*Note.* MGPS = multilocus genetic plasticity score; MPQ = maternal parenting quality; PPQ = paternal parenting quality;

a HPA-axis related multilocus genetic score was calculated based on a linear genetic model. Specifically, each candidate gene included in the polygenic index score was scored 0, 1, or 2 for the number of susceptibility alleles. This genetic score based on a linear genetic model ranged from 0 to 9 in the current sample. We combined the three groups with the highest genetic scores due to low numbers (*N8* = 4, 0.5%; *N*9= 1, 0.1%). Finally, the HPA-axis related multilocus genetic score based on a linear genetic model in this study resulted in eight score groups: 0 susceptibility alleles (*N* = 9, 1.2%), 1 susceptibility alleles (*N* = 56, 7.3%), 2 susceptibility alleles (*N* = 123, 15.9%), 3 susceptibility alleles (*N* = 194, 25.1%), 4 susceptibility alleles (*N* = 200, 25.9%), 5 susceptibility alleles (*N* = 129, 16.7%), 6 susceptibility alleles (*N* = 43,5.6%), 7~9 susceptibility alleles (*N* = 18, 2.3%). This MGPS based on a linear genetic model strongly correlated with the MGPS based on a dominant and recessive genetic model used in the main analysis (*r* = .94, *p* < .001).

b The main and interactive effect of the covariates were comparable to the main analyses and not shown here.

*c* The false discovery rate (FDR, *q* < 0.05) was used to control for multiple testing; 2 models (MGPS×MPQ, MGPS×FPQ) × 2 outcomes (internalizing and externalizing symptoms) = 4.

**Table S9** Regression models predicting adolescent internalizing and externalizing symptoms from interactions between multilocus genetic profile score used in Di Iorio et al. (2017) and parenting

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Predictorsa | Internalizing symptoms | | | | | Externalizing symptoms | | | | |
| *ΔR2* | *b (S.E.)* | *ß* | *p* | *q b* | *ΔR2* | *b (S.E.)* | *ß* | *p* | *q b* |
| MPQ model |  |  |  |  |  |  |  |  |  |  |
| MGPS | .015 | –0.19 (0.09) | –.07 | .047 | — | .024 | 0.12 (0.12) | .03 | .326 | — |
| MPQ |  | –0.44 (0.15) | –.16 | .003 | — |  | –0.85 (0.19) | –.24 | <.001 | — |
| MGPS×MPQ | .008 | –0.30 (0.11) | –.09 | .008 | .016 | .001 | –0.12 (0.15) | –.03 | .427 | .427 |
| MFQ model |  |  |  |  |  |  |  |  |  |  |
| MGPS | .019 | –0.19 (0.09) | –.07 | .047 | — | .007 | 0.12 (0.12) | .03 | .326 | — |
| PPQ |  | –0.54 (0.15) | –.19 | <.001 | — |  | –0.43 (0.19) | –.12 | .024 | — |
| MGPS×PPQ | .010 | –0.35 (0.12) | –.10 | .003 | .012 | .002 | –0.22 (0.15) | –.05 | .153 | .204 |

*Note.* MGPS = multilocus genetic profile score; MPQ = maternal parenting quality; PPQ = paternal parenting quality;

a The main and interactive effect of the covariates were comparable to the main analyses and not shown here.

*b* The false discovery rate (FDR, *q* < 0.05) was used to control for multiple testing; 2 models (MGPS×MPQ, MGPS×FPQ) × 2 outcomes (internalizing and externalizing symptoms) = 4.

**Table S10** Regression models predicting adolescent internalizing and externalizing symptoms from interactions between multilocus genetic profile score based on core genes of HPA axis and parenting

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Predictorsb | Internalizing symptoms | | | | | Externalizing symptoms | | | | |
| *ΔR2* | *b (S.E.)* | *ß* | *p* | *q c* | *ΔR2* | *b (S.E.)* | *ß* | *p* | *q c* |
| MPQ model |  |  |  |  |  |  |  |  |  |  |
| MGPS | .014 | –0.14 (0.08) | –.06 | .092 | — | .023 | 0.07 (0.10) | .02 | .517 | — |
| MPQ |  | –0.45 (0.15) | –.16 | .002 | — |  | –0.85 (0.19) | –.24 | <.001 | — |
| MGPS×MPQ | .006 | –0.23 (0.10) | –.08 | .022 | .044 | .002 | –0.16 (0.13) | –.04 | .222 | .222 |
| MFQ model |  |  |  |  |  |  |  |  |  |  |
| MGPS | .018 | –0.14 (0.08) | –.06 | .092 | — | .007 | 0.07 (0.10) | .02 | .517 | — |
| PPQ |  | –0.56 (0.15) | –.20 | <.001 | — |  | –0.43 (0.19) | –.12 | .022 | — |
| MGPS×PPQ | .011 | –0.31 (0.10) | –.11 | .001 | .004 | .003 | –0.21 (0.13) | –.06 | .089 | .119 |

*Note.* MGPS = multilocus genetic profile score; MPQ = maternal parenting quality; PPQ = paternal parenting quality;

aThe main and interactive effect of the covariates were comparable to the main analyses and not shown here.

*b* The false discovery rate (FDR, *q* < 0.05) was used to control for multiple testing; 2 models (MGPS×MPQ, MGPS×FPQ) × 2 outcomes (internalizing and externalizing symptoms) = 4.

**Table S11** Results for regression models predicting adolescent conduct problems and hyperactivity from interactions between multilocus genetic

profile score and parenting

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Predictors | Conduct problems | | | | | Hyperactivity | | | | |
| *ΔR2* | *b (S.E.)* | *ß* | *p* | *qb* | *ΔR2* | *b (S.E.)* | *ß* | *p* | *qb* |
| MGPS×MPQ | .001 | –0.06 (0.07) | –.03 | .365 | .525 | .001 | –0.05 (0.05) | –.03 | .327 | .525 |
| MGPS×PPQ | .004 | –0.10 (0.06) | –.07 | .062 | .308 | .003 | –0.11 (0.07) | –.06 | .147 | .427 |
| MGPS×MW | .0001 | –0.004 (0.08) | –.002 | .960 | .960 | .0001 | –0.01 (0.11) | –.003 | .609 | .731 |
| MGPS×MHa | .002 | 0.07 (0.05) | .05 | .178 | .427 | .002 | 0.07 (0.07) | .04 | .259 | .518 |
| MGPS×FW | .001 | –0.07 (0.08) | –.03 | .394 | .525 | .0001 | –0.03 (0.10) | –.01 | .793 | .866 |
| MGPS×FHa | .006 | 0.11 (0.05) | .08 | .030 | .308 | .004 | 0.12 (0.07) | .06 | .077 | .308 |

*Note.* MGPS = multilocus genetic plasticity score; MPQ = maternal parenting quality; PPQ = parental parenting quality; MW = maternal warmth;

MH = maternal harsh discipline; PW = paternal warmth; FH = paternal harsh discipline;

*a* Because the correlations between punishment and rejection dimension for mothers (*r* =.75) and fathers (*r* =.73) were both high, we combined these two dimensions into one harsh discipline dimension for mothers and fathers, respectively, and conducted the interaction regression model.

*b* The false discovery rate (FDR, *q* < 0.05) was used to control for multiple testing; 6 models (MGPS×MPQ, MGPS×PPQ, MGPS×PW, MGPS×PH, MGPS×MW, and MGPS×MH models) × 2 outcomes (conduct problems and hyperactivity) = 12.

**Table 12** Regression models predicting adolescent internalizing and externalizing symptoms when testing sex moderation effect

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Predictors | Internalizing symptoms | | | | | Externalizing symptoms | | | | |
| *ΔR2* | *b (S.E.)* | *ß* | *p* | *qb* | *ΔR2* | *b (S.E.)* | *ß* | *p* | *qb* |
| MPQ model |  |  |  |  |  |  |  |  |  |  |
| Sex | .073 | 1.14 (0.16) | .24 | <.001 | — | .024 | –0.03 (0.21) | –.01 | .870 | **—** |
| MGPS |  | –0.06 (0.07) | –.03 | .358 | — |  | 0.08 (0.08) | .03 | .335 | **—** |
| MPQ |  | –0.46 (0.15) | –.16 | .002 | — |  | –0.85 (0.19) | –.24 | <.001 | **—** |
| MGPS×MPQ | .017 | –0.24 (0.08) | –.10 | .003 | — | .002 | –0.11 (0.10) | –.04 | .265 | **—** |
| Sex×MGPS |  | 0.05 (0.13) | .02 | .733 | — |  | 0.09 (0.25) | .02 | .704 | **—** |
| Sex×MPQ |  | –0.53 (0.19) | –.14 | .006 | — |  | –0.09 (0.17) | –.03 | .578 | **—** |
| Sex×MGPS×MPQ | .0001 | 0.03 (0.16) | .01 | .876 | .919 | .0001 | 0.02 (0.21) | .01 | .919 | .919 |
| Covariates |  |  |  |  |  |  |  |  |  |  |
| Agea | .087 | 0.06 (0.06) | .04 | .284 | — | .098 | –0.10 (0.07) | –.05 | .185 | **—** |
| PPQ |  | –0.85 (0.10) | –.30 | <.001 | — |  | –1.08 (0.12) | –.30 | <.001 | **—** |
| FPQ model |  |  |  |  |  |  |  |  |  |  |
| Sex | .063 | 1.14 (0.16) | .24 | <.001 | — | .008 | –0.03 (0.21) | –.01 | .870 | — |
| MGPS |  | –0.06 (0.07) | –.03 | .358 | — |  | 0.08 (0.08) | .03 | .335 | — |
| PPQ |  | –0.55 (0.15) | –.19 | <.001 | — |  | –0.44 (0.19) | –.12 | .021 | — |
| MGPS×PPQ | .028 | –0.33 (0.08) | –.13 | <.001 | — | .005 | –0.20 (0.11) | –.07 | .051 | — |
| Sex×MGPS |  | 0.09 (0.13) | .03 | .497 | — |  | –0.06 (0.17) | –.02 | .713 | — |
| Sex×PPQ |  | –0.63 (0.19) | –.16 | .001 | — |  | 0.01 (0.24) | .001 | .982 | — |
| Sex×MGPS×PPQ | .001 | –0.13 (0.16) | –.04 | .439 | .919 | .0001 | –0.13 (0.21) | –.03 | .531 | .919 |
| Covariates |  |  |  |  |  |  |  |  |  |  |
| Agea | . 097 | 0.05 (0.06) | .03 | .387 | — | .115 | –0.11 (0.07) | –.05 | .124 | — |
| MPQ |  | –0.89 (0.10) | –.31 | <.001 | — |  | –1.17 (0.12) | –.33 | <.001 | — |

*Note.* MGPS = multilocus genetic profile score; MPQ = maternal parenting quality; PPQ = paternal parenting quality;

a Non-significant interaction effects for covariates (e.g., age×MGPS) were removed from the models by backward elimination;

*b* The false discovery rate (FDR, *q* < 0.05) was used to control for multiple testing; 2 models (sex×MGPS×MPQ and sex×MGPS×PPQ models) × 2 outcomes (internalizing and externalizing symptoms) = 4.

**Table S13** Results for regression models predicting adolescent internalizing and externalizing symptoms from three-way interactions

between multilocus genetic profile score, maternal and paternal parenting

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Predictors | Internalizing symptoms | | | | | Externalizing symptoms | | | | |
| *ΔR2* | *b (S.E.)* | *ß* | *p* | *qb* | *ΔR2* | *b (S.E.)* | *ß* | *p* | *qb* |
| MGPS | .110 | –0.06 (0.07) | –.03 | .358 | — | .115 | 0.08 (0.08) | .03 | .335 | — |
| MPQ |  | –0.46 (0.15) | –.16 | .002 | — |  | –0.85 (0.19) | –.24 | <.001 | — |
| PPQ |  | –0.55 (0.15) | –.19 | <.001 | — |  | –0.44 (0.19) | –.12 | .021 | — |
| MGPS×MPQ | .019 | 0.09 (0.14) | .04 | .533 | — | .014 | 0.18 (0.18) | .06 | .319 | — |
| MGPS×PPQ |  | –0.35 (0.14) | –.15 | .013 | — |  | –0.31 (0.18) | –.10 | .092 | — |
| MPQ×PPQ |  | –0.16 (0.10) | –.07 | .092 | — |  | –0.33 (0.12) | –.11 | .006 | — |
| MGPS×MPQ×PPQ | .002 | –0.12 (0.08) | –.07 | .156 | .312 | .0004 | –0.07 (0.11) | –.03 | .536 | .536 |
| Covariates |  |  |  |  |  |  |  |  |  |  |
| Sexa | .050 | 1.07 (0.17) | .23 | <.001 | — | .007 | –0.04 (0.22) | –.01 | .841 | — |
| Age |  | –0.08 (0.06) | –.05 | .170 | — |  | –0.17 (0.08) | –.08 | .025 | — |

*Note.* MGPS = multilocus genetic plasticity score; MPQ = maternal parenting quality; PPQ = parental parenting quality;

a Non-significant interaction effects for covariates (e.g., sex×MGPS) were removed from the models by backward elimination.

*b* The false discovery rate (FDR, *q* < 0.05) was used to control for multiple testing; 2 outcomes (internalizing and externalizing symptoms) = 2.

**Table S14** Regression models predicting adolescent internalizing and externalizing symptoms from interactions between the multilocus genetic

profile score and maternal and paternal parenting simultaneously

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Predictors | Internalizing symptoms | | | | | Externalizing symptoms | | | | |
| *ΔR2* | *b (S.E.)* | *ß* | *p* | *qb* | *ΔR2* | *b (S.E.)* | *ß* | *p* | *qb* |
| MGPS | .110 | –0.06 (0.07) | –.03 | .358 | — | .115 | 0.08 (0.08) | .03 | .335 | — |
| MPQ |  | –0.46 (0.15) | –.16 | .002 | — |  | –0.85 (0.19) | –.24 | <.001 | — |
| PPQ |  | –0.55 (0.15) | –.19 | <.001 | — |  | –0.44 (0.19) | –.13 | .021 | — |
| MGPS×MPQ | .016 | 0.07 (0.14) | .03 | .596 | .596 | .005 | 0.15 (0.18) | .05 | .398 | .596 |
| MGPS×PPQ |  | –0.37 (0.14) | –.15 | .010 | .020 |  | –0.33 (0.18) | –.11 | .067 | .067 |
| Covariates |  |  |  |  |  |  |  |  |  |  |
| Sexa | .050 | 1.07 (0.17) | .23 | <.001 | — | .007 | –0.04 (0.22) | –.01 | .841 | — |
| Age |  | –0.08 (0.06) | –.05 | .170 | — |  | –0.17 (0.08) | –.08 | .025 | — |

*Note.* MGPS = multilocus genetic profile score; MPQ = maternal parenting quality; PPQ = paternal parenting quality;

a Non-significant interaction effects for covariates (e.g., sex×MGPS) were removed from the models by backward elimination.

*b* The false discovery rate (FDR, *q* < 0.05) was used to control for multiple testing; 2 outcomes (internalizing and externalizing symptoms) = 2.