**Supplementary Materials**

**Equal gene model:** When an additive MGPS for multiple genes is calculated, the interpretation can be confounded if genes have differential effects (Stocker et al., 2017). For example, different genes may have significantly distinct main effects or interactive effects with environments on outcomes. Or the effects of one gene may be counteracted by opposite effects of another gene. Although the use of the additive MGPS was mainly derived theoretically from previous literature, the interpretation of its effects still might be confusing if effects varies across genes. Therefore, as suggested by Stocker et al. (2017), the equal gene model was established to test whether differential effects across six candidate genes might compromise the use of our MGPS.

The test of the equal gene model proceeded in two steps. First, the disaggregated model was constructed, where the main effects, two-way and three-way interactions of six SNPs, childhood maltreatment and recent stress, as well as covariates, were freely estimated. The level 1 (within-subject) model for the disaggregated model was as follows:

Dep*tij* = β0*j* + β1*j* (Dep*t–*1*ij*) + β2*j* (Stress*tij*) + e*ij*,

where Dep*tij* represents depressive symptoms at Time *t* for assessment *i* and adolescent *j*, Dep*t–*1*ij*represents depressive symptoms at Time *t–*1 for assessment *i* and adolescent *j*, and Stress*tij*represents the recent interpersonal or noninterpersonal stress between Time *t–*1 and time *t* for assessment *i* and adolescent *j*. In addition, β0*j* is the Dep*tij*intercept, β1*j* is the slope of the relation between depressive symptoms between Time *t* and Time *t–*1at each assessment *i* for adolescent *j* (i.e., the autocorrelation), β2*j*is the slope of the relation between recent interpersonal or noninterpersonal stress and depressive symptoms at Time *t*, and e*ij* represents the error term. Importantly, including depressive symptoms at Time *t–*1 in the model while predicting depressive symptoms at Time *t* allows us to determine whether recent interpersonal or noninterpersonal stress occurring between assessments predicts prospective changes in depressive symptom between those assessments.

The level 2 (between-subject) model for the disaggregated model was as follows:

β0*j* = γ00 + γ01 (CM) + ∑γ02w (Gw) + ∑γ03w (Gw × CM) + γ04 (sex) + γ05 (age) + u0*j*,

β1*j* = γ10 + γ11 (CM) + ∑γ12w (Gw) + ∑γ13w (Gw × CM) + u1*j*, and

β2*j*= γ20 + γ21 (CM) + ∑γ22w (Gw) + ∑γ23w (Gw × CM) + u2*j*,

where w is 1~6; G1 ~ G6 represents rs110402, rs41423247, rs5522, rs1360780, rs4680, rs6295, respectively. Besides, γ01 is the cross-level interaction term representing the effect of childhood maltreatment on the depressive symptoms intercept, γ11 is the cross-level interaction term representing the effect of childhood maltreatment on the slope of the relation between adolescent lagged and current depressive symptoms, and γ21 is the cross-level interaction representing the effect of childhood maltreatment on the slope of the relation between recent interpersonal or noninterpersonal stress and depressive symptoms. Similarly, γ02, γ12, and γ22 are the cross-level interaction terms representing the effect of the SNP on the depressive symptoms intercept, the slope of the relation between adolescent lagged and current depressive symptoms, and the slope of the relation between recent interpersonal or noninterpersonal stress and depressive symptoms, respectively. γ03, γ13, and γ23 are the cross-level interaction terms representing the effect of SNP × childhood maltreatment interaction on the depressive symptoms intercept, the slope of the relation between adolescent lagged and current depressive symptoms, and the slope of the relation between recent interpersonal or noninterpersonal stress and depressive symptoms, respectively. Finally, γ00, γ10, and γ20 are the intercept terms for each of their respective equations, and u0*j*, u1*j*, and u2*j*, are the error terms. Besides, γ04 and γ05 is the cross-level interaction term representing the effect of sex and age on the depressive symptoms intercept, respectively.

In the second step, the nested, equal gene model was constructed. This model had thirty restrictions; in specific, the regression weights for main effects of the six SNPs (five × three restrictions), and their interactions with childhood maltreatment (five × three restrictions) were constrained to equality. If the equal gene model did not fit significantly worse than the disaggregated model, the equal effects across six SNPs were supported and the MGPS of six genes was appropriate in this study. Otherwise, at least one SNP might have differential effects, and the MGPS might be not appropriate.

**Multilevel models:** The level 1 (within-subject) model for the HLM analysis was as follows:

Dep*tij* = β0*j* + β1*j* (Dep*t–*1*ij*) + β2*j* (Stress*tij*) + e*ij*,

where Dep*tij*, Dep*t–*1*ij,* Stress*tij*, and e*ij* represents the same meaning as described in the Supplementary Materials “Equal gene model” section.

The level 2 (between-subject) model for the HLM analysis was as follows:

β0*j* = γ00 + γ01 (CM) + γ02 (MGPS) + γ03 (MGPS × CM) + γ04 (sex) + γ05 (age) + u0*j*,

β1*j* = γ10 + γ11 (CM) + γ12 (MGPS) + γ13 (MGPS × CM ) + u1*j*, and

β2*j*= γ20 + γ21 (CM) + γ22 (MGPS) + γ23 (MGPS × CM) + u2*j*,

where γ01, γ11, γ21 is the cross-level interaction term representing the effect of childhood maltreatment on the depressive symptoms intercept, on the slope of the relation between adolescent lagged and current depressive symptoms, and on the slope of the relation between recent interpersonal or noninterpersonal stress and depressive symptoms. Similarly, γ02, γ12, and γ22 are the cross-level interaction terms representing the effect of the MGPS on the depressive symptoms intercept, the slope of the relation between adolescent lagged and current depressive symptoms, and the slope of the relation between recent interpersonal or noninterpersonal stress and depressive symptoms, respectively. γ03, γ13, and γ23 are the cross-level interaction terms representing the effect of MGPS × childhood maltreatment interaction on the depressive symptoms intercept, the slope of the relation between adolescent lagged and current depressive symptoms, and the slope of the relation between recent interpersonal or noninterpersonal stress and depressive symptoms, respectively. Finally, γ00, γ10, and γ20 are the intercept terms for each of their respective equations, and u0*j*, u1*j*, and u2*j*, are the error terms. Besides, γ04 and γ05 is the cross-level interaction term representing the effect of sex and age on the depressive symptoms intercept, respectively.

**Exposure number of childhood maltreatment and recent stress**

Maltreatment subtypes were first categorized separately into four hierarchical levels (i.e., “None or minimal”, “Low”, “Moderate” and “Severe”) according to the established subtype-specific thresholds of CTQ-SF (see Supplementary Table S2; Bernstein & Fink, 1998). Then, for each maltreatment subtype, adolescents with scores reaching or exceeding the corresponding “moderate” threshold were classified as positive for exposure. The number of maltreatment subtypes experienced was calculated by counting the number of five subtypes exposure, with a range of 0 to 5 (Bernstein & Fink, 1998).

Regarding recent stress assessed by the ASLEC, we recoded the response “the event had not happened” into 0, and any other responses about the extent to which “this life event negatively affected you” into 1. Then, sum score regarding the exposure number of each stress domain was calculated and used in the sensitivity analysis.

**Table S1.** Single nucleotide polymorphism data

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Gene | SNP | Major Allele | Mirror Allele | MISSING | MAF | Genotype frequency | | | Hardy-Weinberg equilibrium | |
| 11 | 12 | 22 | *χ2* | *p* |
| *CRHR1* | rs110402 | A | G | 0 | .12 | 634 | 184 | 9 | 1.17 | .279 |
| *NR3C1* | rs41423247 | G | C | 6 | .21 | 509 | 272 | 40 | 0.22 | .638 |
| *NR3C2* | rs5522 | A | G | 0 | .17 | 581 | 218 | 28 | 1.78 | .182 |
| *FKBP5* | rs1360780 | C | T | 0 | .25 | 474 | 294 | 59 | 2.04 | .153 |
| *COMT* | rs4680 | G | A | 2 | .28 | 418 | 345 | 62 | 0.63 | .426 |
| *HTR1A* | rs6295 | G | C | 0 | .28 | 434 | 328 | 65 | 0.08 | .783 |

*Note.* *N* = 827; Missing = Missing number of participants due to genotyping failure; MAF = Minor allele frequency; 11 = Frequency of homozygotes constituted by major alleles, 12 = Frequency of heterozygotes, 22 = Frequency of homozygotes constituted by minor alleles.

**Table S2.** CTQ-SF subtype-specific thresholds for the identification and severity of exposure to childhood maltreatment

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Levels of exposure | Maltreatment Subtypes | | | | |
| Emotional abuse | Physical  abuse | Sexual abuse | Emotional neglect | Physical neglect |
| None or minimal | 5~8 | 5~7 | 5 | 5~9 | 5~7 |
| Low | 9~12 | 8~9 | 6~7 | 10~14 | 8~9 |
| Moderate | 13~15 | 10~12 | 8~12 | 15~17 | 10~12 |
| Severe | 16~25 | 13~25 | 13~25 | 18~25 | 13~25 |

*Note.* CTQ-SF, childhood Trauma Questionnaire–Short Form;

For each maltreatment subtype, adolescents with scores reaching or exceeding the corresponding “moderate” threshold were classified as positive for exposure; otherwise, they were classified as negative for exposure.

**Table S3.** The other three main HPA-axis related MGPSs established in extant research

|  |  |  |
| --- | --- | --- |
| Study | SNPs in HPA-axis related MGPS | Note |
|
| 1.Pagliaccio et al. (2014, 2015) | *CRHR1*: rs4792887, **rs110402**, rs242941, rs242939, rs1876828;  *NR3C1*: **rs41423247**; rs10482605, rs10052957;  *NR3C2*: **rs5522**;  *FKBP5*: **rs1360780** | The work of Starr and colleagues  also used this MGPS (e.g., Huang & Starr, 2020; Starr & Huang, 2019; Starr et al., 2021) |
| 2.Di Iorio et al. (2017) | *CRHR1:* **rs110402**  *NR3C2:* **rs5522**/rs4635799 haplotype  *FKBP5:* **rs1360780** | Feurer et al. (2017) used a very similar MGPS:  *CRHR1:* **rs110402**/ rs7209436/rs242924 haplotype  *NR3C2:* **rs5522**/rs2070951 haplotype  *FKBP5:* **rs1360780** |
| 3.McKenna et al. (2021) | *CRHR1:* rs242924  *NR3C1:* rs6169  *FKBP5:* rs9296158 |  |

*Note.* Overlapping SNPs in the current and previous MGPSs are displayed in bold.

**Table S4.** Model comparisons testing equality of effects of individual SNPs on adolescent depressive symptoms

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Predictors | Regression model | Model Fit | | | | Change in Model Fit | | | |
|  |  | *F* (*df*) of | *F* (*df*) of | *Δ* | *Δ* | *F* (*df*) of *△* | *F2* (*df*) of *△* |
| G × CM × IS | Disaggregated | .246 | .254 | 18.31 (43, 2413)\*\*\* | 6.45 (41, 777)\*\*\* |  |  |  |  |
| Equal gene effect | .241 | .251 | 59.67 (13, 2443)\*\*\* | 24.59 (11, 807)\*\*\* | .005 | .003 | 0.53 (30, 2413) | 0.10 (30, 777) |
| G × CM × AS | Disaggregated | .235 | .254 | 17.24 (43, 2413)\*\*\* | 6.45 (41, 777)\*\*\* |  |  |  |  |
| Equal gene effect | .229 | .251 | 55.82 (13, 2443)\*\*\* | 24.59 (11, 807)\*\*\* | .006 | .003 | 0.63 (30, 2413) | 0.10 (30, 777) |
| G × CM × BP | Disaggregated | .236 | .254 | 17.33 (43, 2413)\*\*\* | 6.45 (41, 777)\*\*\* |  |  |  |  |
| Equal gene effect | .230 | .251 | 56.13 (13, 2443)\*\*\* | 24.59 (11, 807)\*\*\* | .006 | .003 | 0.63 (30, 2413) | 0.10 (30, 777) |
| G × CM × LO | Disaggregated | .233 | .254 | 17.05 (43, 2413)\*\*\* | 6.45 (41, 777)\*\*\* |  |  |  |  |
| Equal gene effect | .227 | .251 | 55.19(13, 2443)\*\*\* | 24.59 (11, 807)\*\*\* | .005 | .003 | 0.52 (30, 2413) | 0.10 (30, 777) |
| G × CM × ADS | Disaggregated | .246 | .254 | 18.31 (43, 2413)\*\*\* | 6.45 (41, 777)\*\*\* |  |  |  |  |
| Equal gene effect | .242 | .251 | 60.00 (13, 2443)\*\*\* | 24.59 (11, 807)\*\*\* | .004 | .003 | 0.43 (30, 2413) | 0.10 (30, 777) |

*Note*: G = Each SNP; CM = Childhood maltreatment; IS = Interpersonal stress; AS = Academic stress; BP = Being punished; LO = Loss, ADS = Adjustment stress;

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

**Table S5.** HLM predicting changes in depressive symptoms from three-way interactions between HPA-axis multilocus genetic score, childhood maltreatment and recent noninterpersonal stress

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Model |  |  | *b* | *SE* | *pa* | 95% CI of *b* |
| MGPS × CM × AS | .231 | .253 | 0.01 | 0.01 | .113 | [–0.003, 0.03] |
| MGPS × CM × BP | .232 | .253 | 0.01 | 0.004 | .020 | [0.001, 0.02] |
| MGPS × CM × LO | .229 | .253 | 0.01 | 0.01 | .042 | [0.00, 0.02] |
| MGPS × CM × ADS | .243 | .253 | 0.01 | 0.01 | .104 | [–0.002, 0.02] |

*Note*: MGPS = Multilocus genetic profile score; CM = Childhood maltreatment; AS = Academic stress; BP = Being punished; LO = Loss; ADS = Adjustment stress;

a The Bonferroni correction was used to control for multiple testing of three-way interactions: the significance threshold of *p* was .010 (.050/5 testing; five stress domains); the effect survived correction is displayed in bold.

**Table S6.** HLM predicting changes in depressive symptoms from three-way interactions between *n*–1 modified MGPSs, childhood maltreatment and recent interpersonal stress

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  |  | *b* | *SE* | *pa* | 95% CI of *b* |
| MGPS excluding rs110402 | .243 | .253 | 0.013 | 0.004 | **.003** | [0.004, 0.021] |
| MGPS excluding rs41423247 | .244 | .255 | 0.010 | 0.004 | **.010** | [0.002, 0.017] |
| MGPS excluding rs5522 | .243 | .252 | 0.013 | 0.004 | **.002** | [0.005, 0.021] |
| MGPS excluding rs1360780 | .244 | .253 | 0.015 | 0.006 | **.006** | [0.004, 0.026] |
| MGPS excluding rs4680 | .243 | .252 | 0.013 | 0.005 | **.010** | [0.003, 0.022] |
| MGPS excluding rs6295 | .243 | .253 | 0.012 | 0.004 | **.004** | [0.004, 0.021] |

*Note*: MGPS = Multilocus genetic profile score;

a The significance threshold of *p* for G × E1 × E2 interaction regarding interpersonal stress was .010, i.e., .050/(5 stress domains);

the effect survived correction is displayed in bold.

**Table S7.** HLM predicting changes in depressive symptoms from three-way interactions between HPA-axis MGPS, childhood maltreatment, and recent stress after inclusion of an open items for recent stress

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Model |  |  | *b* | *SE* | *pa* | 95% CI of *b* |
| MGPS × CM × IS | .243 | .253 | 0.01 | 0.004 | **.003** | [0.004, 0.02] |
| MGPS × CM × AS | .231 | .253 | 0.01 | 0.01 | .195 | [–0.004, 0.02] |
| MGPS × CM × BP | .232 | .253 | 0.01 | 0.004 | .023 | [0.001, 0.02] |
| MGPS × CM × LO | .229 | .253 | 0.01 | 0.01 | .045 | [0.00, 0.02] |
| MGPS × CM × ADS | .243 | .253 | 0.01 | 0.01 | .111 | [–0.002, 0.02] |

*Note*: MGPS = Multilocus genetic profile score; CM = Childhood maltreatment; IS = Interpersonal stress; AS = Academic stress; BP = Being punished; LO = Loss; ADS = Adjustment stress;

a The Bonferroni correction was used to control for multiple testing of three-way interactions: the significance threshold of *p* was .010 (.050/5 testing; five stress domains); the effect survived correction is displayed in bold.

**Table S8.** HLM predicting changes in depressive symptoms when interactive effects of covariates with both genetic and environmental variables were controlled for

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Model |  |  | *b* | *SE* | *pa* | 95% CI of *b* |
| MGPS × CM × IS | .252 | .259 | 0.01 | 0.004 | **.003** | [0.004, 0.02] |
| MGPS × CM × AS | .239 | .260 | 0.01 | 0.01 | .118 | [–0.003, 0.03] |
| MGPS × CM × BP | .242 | .260 | 0.01 | 0.004 | **.009** | [0.002, 0.02] |
| MGPS × CM × LO | .236 | .260 | 0.01 | 0.01 | .039 | [0.001, 0.02] |
| MGPS × CM × ADS | .251 | .260 | 0.01 | 0.01 | .083 | [–0.002, 0.03] |

*Note*: MGPS = Multilocus genetic profile score; CM = Childhood maltreatment; IS = Interpersonal stress; AS = Academic stress; BP = Being punished; LO = Loss; ADS = Adjustment stress;

a The Bonferroni correction was used to control for multiple testing of three-way interactions: the significance threshold of *p* was .010 (.050/5 testing; five stress domains); the effect survived correction is displayed in bold.

**Table S9.** HLM predicting changes in depressive symptoms when quadratic effects for genetic and environmental stress were controlled fora

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Model |  |  | *b* | *SE* | *pb* | 95% CI of *b* |
| MGPS × CM × IS | .251 | .264 | 0.01 | 0.004 | **.005** | [0.004, 0.02] |
| MGPS × CM × AS | .241 | .267 | 0.01 | 0.01 | .290 | [–0.007, 0.02] |
| MGPS × CM × BP | .237 | .259 | 0.01 | 0.004 | .142 | [–0.002, 0.01] |
| MGPS × CM × LO | .230 | .254 | 0.01 | 0.01 | .112 | [–0.002, 0.02] |
| MGPS × CM × ADS | .252 | .265 | 0.01 | 0.01 | .168 | [–0.004, 0.02] |

*Note*: MGPS = Multilocus genetic profile score; CM = Childhood maltreatment; IS = Interpersonal stress; AS = Academic stress; BP = Being punished; LO = Loss; ADS = Adjustment stress;

a The quadratic effects for genetic and environmental stress were not significant (–0.004 ≤ *b* ≤ 0.0001, *SE* ≤ 0.08, *p* > .604).

b The Bonferroni correction was used to control for multiple testing of three-way interactions: the significance threshold of *p* was .010 (.050/5 testing; five stress domains); the effect survived correction is displayed in bold.

**Table S10.** HLM predicting changes in depressive symptoms from three-way interactions between HPA-axis multilocus genetic score, exposure number of childhood maltreatment and recent stress

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Model |  |  | *b* | *SE* | *pa* | 95% CI of *b* |
| MGPS × CM × IS | .178 | .174 | 0.12 | 0.11 | .286 | [–0.10, 0.34] |
| MGPS × CM × AS | .171 | .174 | 0.06 | 0.12 | .616 | [–0.18, 0.30] |
| MGPS × CM × BP | .173 | .174 | 0.22 | 0.08 | **.006** | [0.06, 0.38] |
| MGPS × CM × LO | .170 | .174 | 0.12 | 0.13 | .333 | [–0.13, 0.38] |
| MGPS × CM × ADS | .174 | .174 | 0.14 | 0.18 | .441 | [–0.21, 0.48] |

*Note*: MGPS = Multilocus genetic profile score; CM = Childhood maltreatment; IS = Interpersonal stress; AS = Academic stress; BP = Being punished; LO = Loss; ADS = Adjustment stress;

a The Bonferroni correction was used to control for multiple testing of three-way interactions: the significance threshold of *p* was .010 (.050/5 testing; five stress domains); the effect survived correction is displayed in bold.

**Table S11.** HLM predicting changes in depressive symptoms from three-way interaction based on an approximation HPA-axis multilocus genetic score established in Di Iorio et al., 2017

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Model |  |  | *b* | *SE* | *pb* | 95% CI of *b* |
| MGPS × CM × IS | .242 | .253 | 0.006 | 0.004 | .117 | [–0.002, 0.014] |
| MGPS × CM × AS | .231 | .253 | 0.016 | 0.007 | .018 | [0.003, 0.029] |
| MGPS × CM × BP | .232 | .253 | 0.004 | 0.004 | .373 | [–0.004, 0.011] |
| MGPS × CM × LO | .228 | .253 | 0.005 | 0.006 | .398 | [–0.006, 0.016] |
| MGPS × CM × ADS | .243 | .253 | 0.015 | 0.007 | .027 | [0.002, 0.027] |

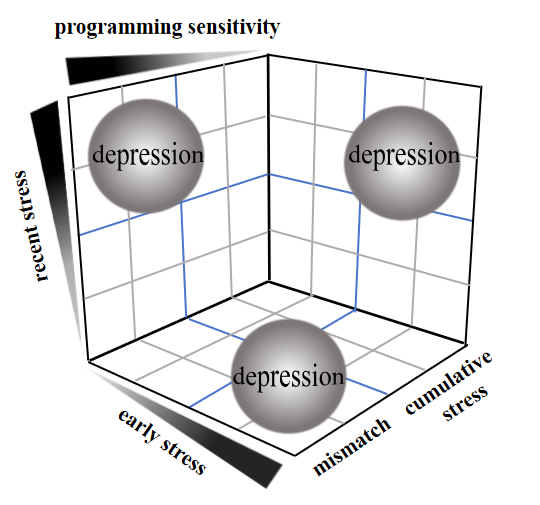
*Note*: MGPS = Multilocus genetic profile score; CM = Childhood maltreatment; IS = Interpersonal stress; AS = Academic stress; BP = Being punished; LO = Loss; ADS = Adjustment stress;

a The Bonferroni correction was used to control for multiple testing of three-way interactions: the significance threshold of *p* was .010 (.050/5 testing; five stress domains); the effect survived correction is displayed in bold.

**Table S12.** HLM predicting changes in depressive symptoms from three-way interactions between HPA-axis multilocus genetic score, childhood maltreatment and recent averaged noninterpersonal stress

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | | *b* | *SE* | *p* | 95% CI of *b* |
| Dep*t* intercept (β0*j*) | Intercept (γ00) | 17.52 | 2.16 | < .001 | [13.30, 21.75] |
| CM (γ01) | 0.31 | 0.02 | < .001 | [0.27, 0.35] |
| MGPS (γ02) | –0.25 | 0.17 | .151 | [–0.58, 0.09] |
| MGPS × CM (γ03) | 0.01 | 0.02 | .534 | [–0.03, 0.05] |
| sex (γ04) | 1.16 | 0.38 | .002 | [0.41, 1.90] |
| age (γ05) | –0.26 | 0.13 | .053 | [–0.51, 0.003] |
| Dep*t-*1 slope (β1*j*) | Intercept (γ10) | –0.21 | 0.01 | < .001 | [–0.24, –0.19] |
| CM (γ11) | 0.001 | 0.001 | .305 | [–0.001, 0.003] |
| MGPS (γ12) | –0.001 | 0.01 | .948 | [–0.02, 0.03] |
| MGPS × CM (γ13) | 0.001 | 0.001 | .153 | [0.00, 0.003] |
| NIS slope (β2*j*) | Intercept (γ20) | 1.79 | 0.23 | < .001 | [1.33, 2.24] |
| CM (γ21) | 0.03 | 0.02 | .206 | [–0.02, 0.07] |
| MGPS (γ22) | –0.38 | 0.21 | .074 | [–0.80, 0.04] |
| MGPS × CM (γ23) | 0.04 | 0.03 | .139 | [–0.01, 0.08] |
|  |  | .236 | | | |
|  |  | .253 | | | |

*Note*: MGPS = Multilocus genetic profile score; CM = Childhood maltreatment; NIS = noninterpersonal stress; aThe Bonferroni correction was used to control for multiple testing of three-way interactions: the significance threshold of *p* was .025 (.050/2 testing; two stress domains).



*Figure S1 The* *integrated model of cumulative stress and mismatch (Adapted from Nederhof & Schmidt, 2012).* The integrated model proposes that cumulative stress and mismatch hypotheses may depend on individuals’ programming sensitivity. That is, individuals with high programming sensitivity could benefit from a match of early and recent stress by adaptive programming (i.e., mismatch). In contrast, individuals with low programming sensitivity would be less likely to be adaptively programmed by early stress, resulting in continuous wear under the same situation (i.e., cumulative stress). In the current study, we aimed to test whether or not HPA-axis multilocus genetic variation reflecting programming sensitivity would moderate how childhood maltreatment interacts with recent stress in the prediction of prospective changes in adolescent depressive symptoms across two years.