

Examining Additive Genetic Variation in the Relationship between Early Life Stress Exposure and Trait-Level Latent Depressive Symptoms



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BACKGROUND

- Additive genetic variation and environmental stress are thought to jointly shape depression risk, via the HPA axis and serotonin (5HT) system¹
- Past work largely focuses on 5HT or HPA additive genetic scores (multilocus genetic profile scores; MGPS) in interactions with recent life stress, rather than early life stress (ELS)¹
- However, theory and evidence suggest that ELS exposure can neurobiologically alter stress-responsive systems and influence protracted depression in adulthood¹
- Interactive effects may be reflected in *trait* levels of depressive symptoms, though this is untested.
- We examined whether MGPS in the HPA axis or 5HT system moderate ELS exposure on trait depression symptoms in emerging adulthood. We also ran post-hoc tests on whether type or timing of ELS drives effects.
- Consistent with differential susceptibility theory¹, we hypothesized that individuals with *high* levels of MGPS would exhibit higher levels of trait depressive symptoms if exposed to higher levels of ELS, but would show *low* levels of trait depressive symptoms if exposed to lower ELS.

| Demographics | N = 403 | Demographics | N = 403 |
|-----------------------------|---------------|------------------------|---------|
| Gender | | Race/Ethnicity | |
| Male | 30.6% | White | 48.4% |
| Female | 69.4% | Black | 13.2% |
| Mean Age at baseline | 16.1 (.44) | Hispanic/Latine | 14.1% |
| Socioeconomic Status | 48.63 (12.27) | Asian/Pacific Islander | 5.2% |
| CTI severity | 2.01 (1.03) | Multiracial | 13.4% |
| HPA MGPS | 3.45 (1.53) | Other | 6.2% |
| 5HT MGPS | 6.49 (1.25) | | |

Table 1. Demographic and baseline characteristics of sample.

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METHOD

- Participants (N=403) are from the Youth Emotion Project, a longitudinal study of risk for emotional disorders that oversampled for neuroticism in high school juniors
- Participants provided DNA for genotyping, and completed self-report depression measures (the Mood and Anxiety Symptoms Questionnaire and the Inventory to Diagnose Depression).
- Participants completed the childhood trauma interview (CTI) over the phone retrospectively.
- MGPS were computed from coded genetic variants from the HPA axis and 5HT system, respectively.
- Analyses included: 1) measurement invariance of waves, 2) latent Trait State Occasion modeling, and 3) longitudinal SEM. Post-hoc tests were completed.
- Benjamini-Hochberg procedure was implemented to correct for multiple testing.

RESULTS

- Measurement invariance testing supported inclusion of 4 waves of data, spanning ages 17-21, representing emerging adulthood
- Neither HPA or 5HT MGPS profile interacted with ELS exposure to predict trait depression ($p\text{-adj.}'s > .05$)
- ELS exposure positively predicted trait depression across models ($B = 0.349, p\text{-adj} = .020$)
- ELS in adolescence ($B = 0.181\text{--}.206, p\text{-adj} = .034\text{--}.039$), and “threat-based” ELS ($B = .251\text{--}.256, p\text{-adj} = .020\text{--}.024$) predicted trait depression.
- Post-hoc tests showed a 5HT MGPS interacted with threat-based adversity ($0.154, p\text{-adj} = 0.039$)
- At -1 SD of adolescent adversity, a 5HT MGPS marginally and negatively predicted trait depression ($B = -0.048, p = .056$).
- At +1 SD of adolescent adversity, a 5HT MGPS positively predicted trait depression ($B = 0.061, p = .047$). Results did not survive additional post-hoc sensitivity tests

RESULTS CONTINUED

- Gender interacted with ELS predicting trait depression ($B's = -0.199 \text{ -- } -0.193, p\text{-adj} = .033\text{--}.034$). Post-hoc tests showed the magnitude of the effect was greater for female compared to male participants.
- 48.3% of depression was explained by trait variance



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CONCLUSION

- Early (ELS) predicted enduring, trait depression in emerging adulthood, though hypothesized pGxE effects did not emerge
- Findings refine that ELS may not be a candidate environment by which stress predicts later depression in emerging adults
- ELS occurring during adolescence (ages 9–16), rather than childhood—drove effects on trait depression.
- Threat-based adversity predicted trait depression over and above deprivation-based adversity
- Findings suggest that the timing and dimension of early adversity, rather than cumulative exposure alone, may be key for understanding enduring depression risk

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