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Detecting rGE Between Exposome Factors and Polygenic Risk Scores for Psychiatric and Substance Use Disorders in the Adolescent Brain Cognitive Development Study

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Although both genetic and environmental factors contribute to risk for psychiatric and substance use disorders (SUDs), research has often overlooked that genetic variation may shape the environment (i.e., gene-environment correlations; rGE). Most studies on rGE have only examined a single, self-reported, environmental context in relation to genetic risk for a given trait. However, relying on single assessments of genetic and environmental factors limits our ability to fully understand the risks underlying psychiatric and SUDs. Here, we explore rGE between multiple polygenic risk scores (PRS) for psychiatric and SUDs and the exposome—defined as a complex network of environmental influences generated using multi-level data (e.g., parent-reported, geocoded). Participants (N=10,492, M age=9.92, 53.3% male) were drawn from the Adolescent Brain Cognitive Development (ABCD) Study. Six specific exposome factors were examined: pregnancy/birth complications, positive day-to-day experiences, family values, household adversity, neighborhood poverty, and state-level conservatism/rurality. We created PRS using PRS-CSx for psychiatric and SUDs based on the largest GWAS from the Psychiatric Genomics Consortium. Regression analyses, adjusted for log income-to-need ratio, five genetic ancestry principal components, and False Discovery Rate correction, indicated that higher household adversity and fewer positive day-to-day experiences were significantly associated with higher PRS for psychiatric (e.g., anorexia and anxiety) and SUDs. In addition, birth/pregnancy complications were significantly associated with opioid use disorder PRS. These findings highlight the interdependence of exposome and PRS for psychiatric and SUDs, emphasizing the importance of considering multiple environmental exposures. Future genomic studies would benefit from addressing rGE as well as gene-environment interactions.