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Examining the Effects of Prenatal Cannabis Exposure & Genetic Risk for Externalizing Traits on Executive Functioning and Behavioral Disinhibition in Early Adolescence

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Prenatal cannabis exposure (PCE) during critical periods may lead to disruptions in biological systems that have downstream consequences across development. Additionally, few studies account for familial confounding and genetic liability that could better explain disruptions to development. Data from the Adolescent Brain Cognitive Development (ABCD) study (release 5.0) was used to evaluate whether PCE, familial confounders, and genetic factors underlying externalizing traits were associated with executive functioning and behavioral disinhibition in early adolescence (9-13 years of age). One polygenic score (PGS) was developed using PRS-CS using non-substance use-related externalizing summary statistics from Brick et al. (preprint). The non-substance use externalizing PGS represents residual variance independent of the substance use related psychopathology after accounting for the correlation between internalizing and externalizing traits. In a model where PCE, propensity for PCE, and PGS was regressed on executive functioning, only the PGS was significantly associated with poorer executive function ($\beta = -0.06$, 95% Confidence Interval [-0.09, -0.03]). In comparison, PCE (0.05 [0.01, 0.09]), propensity for PCE (0.19 [0.12, 0.23]), and externalizing PGS (0.03 [0.01, 0.06]) were all significantly associated with greater behavioral disinhibition. These associations indicate that parsed genetic risk for externalizing behaviors may interfere with the ability of children to perform tasks that require executive functioning. Additionally, PCE, along with its associated propensity and parsed genetic risk for externalizing behaviors, all appear to be linked to behavioral disinhibition. The underlying mechanism of these factors on behavioral disinhibition, however, is not fully understood and should be explored in future research.