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Developmental cascades from polygenic and prenatal substance use to adolescent substance use: Leveraging severity and directionality of externalizing and internalizing problems to understand pubertal and harsh discipline-related risk

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ABSTRACT (current word count=247, max=250)

We tested a developmental cascade from puberty-related polygenic risk and prenatal substance use through pubertal timing and parenting to the severity and directionality (i.e., differentiation) of externalizing and internalizing problems to adolescent substance use in $n = 4504$ White boys, $n = 4287$ White girls from the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort. Puberty-related polygenic risk was calculated using summary statistics from the largest available GWAS on age at menarche. Prenatal substance use was a weighted severity score of smoking, alcohol, and cannabis use frequency maternally-reported prior to 18wk and at 32wk gestation. Parental harsh discipline was parent-reported at 9.5-11.5y. Pubertal timing was the age of reaching Tanner Stage 2 from repeated measures of parent- and youth-reports. Severity and directionality of internalizing and externalizing problems was parent-reported at 13y. Alcohol, smoking, and cannabis use were measured on continuums of substance-specific stages increasing in quantity and risk for dependence/abuse youth-reported at 18.5y. Results from path models found that girls' earlier pubic hair development timing mediated the PRS for puberty and differentiation towards internalizing symptoms. Limited associations of early pubertal timing with substance use outcomes were only observable via symptom directionality, differently for girls and boys. For boys, exposure to prenatal substance use predicted substance use via differentiation towards relatively more pure externalizing problems, but in girls associations were largely direct. Severity and especially differentiation towards externalizing problems were key intermediaries in developmental cascades from parental harsh discipline with substance use progressions for girls and boys.

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