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TITLE: Interplay between genetic risk and the parent environment in adolescence and substance use in young adulthood: a TRAILS study

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ABSTRACT:

**Background** During adolescence, many youth start using tobacco, alcohol and cannabis, a pattern that can persist into adulthood and can have deleterious health consequences. Genetic vulnerability, parent factors during adolescence, and interaction (GxE) and correlation (rGE) between these factors can contribute to the development of substance use.

**Methods** Using 11-year prospective data from the TRacking Adolescent Individuals’ Lives Survey (TRAILS, N=1,649) we modelled latent parent characteristics (ages 11-16; involvement, substance use, and parent-child relationship) in adolescents to predict young adult substance use (age 22). Based on recent GWAS, polygenic scores (PGS) were created with GCTA-SBLUP for smoking, alcohol use, and cannabis use. Using Structural Equation Modelling we modelled direct, GxE, and rGE effects of parent factors and PGS on young adult smoking, alcohol use, and cannabis initiation.

**Results** High PGS, low parental involvement, high parental substance use, and low quality parent-child relationship predicted smoking. There was GxE such that the PGS amplified the effect of parental substance use. There was positive rGE between all parent factors and the PGS. Alcohol use was not predicted by genetic or parent factors, nor by interplay between those. Cannabis initiation was predicted by high PGS and parental substance use, but there was no evidence for GxE or rGE.

**Discussion** We found evidence for the contribution of genetic risk and parent factors to smoking and cannabis initiation, and complex interplay between those for smoking. Our method is promising for disentangling genetic nurturing and other complex interplay phenomena between genes and the environment.

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