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TITLE: Investigating the specificity of the genetic associations between smoking behaviours and psychiatric traits and disorders with genomic structural equation modelling

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KEYWORDS: Psychotic experiences; schizophrenia; depression; bipolar disorder; Genomic SEM

ABSTRACT:

Background: The phenotypic association between cigarette smoking and major psychiatric disorders is well established. Psychiatric traits in the general population such as psychotic experiences are also associated with smoking, even after accounting for co-occurring risks such as cannabis and alcohol use. We aimed to investigate whether genetic overlap between smoking and psychiatric traits and disorders exists beyond genetic influences shared with confounding variables.

Methods: Bivariate genetic correlations between smoking behaviours (cigarettes per day, smoking status, age of smoking initiation and smoking cessation) and psychiatric disorders (schizophrenia, major depression and bipolar disorder) and with psychotic experiences in adolescents and adults were computed in LD score regression. Fully saturated genomic multiple regression models were specified in Genomic SEM to estimate genetic associations between smoking and psychiatric traits and disorders conditional on genome-wide genetic influences on confounders (cannabis and alcohol use, risk taking and insomnia).

Findings: Significant bivariate genetic correlations were found between smoking and psychotic experiences in adulthood (r_g = .33 - .40) as well as between smoking and psychiatric disorders (r_g = -.08 - .38). Genomic SEM indicated that genetic associations (conditional on covarying genetic influences on the confounders) remained between most smoking behaviours and schizophrenia and depression (b_g = .14 - .40) but not between smoking and bipolar disorder or most psychotic experiences.

Conclusions: Our results suggest that pleiotropy between cigarette smoking and some psychiatric disorders likely reflect shared biological pathways whereas pleiotropy between smoking and psychotic experiences may be attributable to genetic influences of co-occurring risk factors.