

Evidence for shared genetic risk between schizophrenia and smoking behaviors: Findings from the Psychiatric Genomics Consortium.

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Objective: 17% of US adults and upwards of 60% of those with schizophrenia (SCZ) spectrum disorders smoke tobacco regularly, and several lines of evidence support a shared etiological basis for smoking and SCZ. The purpose of this study is to advance the understanding of the SCZ-smoking association by harnessing findings from genome-wide association studies (GWAS) to test for shared genetic liability.

Methods: We investigated the genetic relationship between SCZ and smoking using polygenic risk scores (PRS) constructed from results from the Tobacco and Genetics (TAG) GWAS meta-analyses of smoking behaviors. The availability of smoking behavior data in the PGC-SCZ facilitated analyses of smoking initiation (SI) and cigarettes-per-day (CPD), including association with TAG-based PRS, and exploratory SCZ case-only GWAS.

Results: PRS based on TAG results for SI significantly predicted SCZ case status in the full PGC cohort ($R^2=0.0015$, $P=8.11\times 10^{-15}$), as did scores based on results for CPD ($R^2=0.0005$, $P=4.18\times 10^{-6}$). These scores also significantly predicted SI ($R^2=0.0047$, $P=6.29\times 10^{-5}$) and CPD ($R^2=0.0007$, $P=0.0067$), respectively, among SCZ patients. In the replication phase of the cases-only GWAS of CPD, we identified a significant association upstream of *TMEM106B* on chromosome 7 (rs148253479; $P=3.18\times 10^{-8}$). Significant positive genetic correlations were found for SCZ and SI ($r_g=0.155$) and CPD ($r_g=0.085$), as well as SI in the general population and SI in SCZ ($r_g=0.624$).

Conclusion: We provide evidence of a partially shared genetic basis for SCZ and smoking behaviors. Preliminary case-only results highlight novel SCZ specific genetic liability for smoking quantity. Future research needs to address mechanisms underlying associations between these traits to aid both SCZ and smoking treatment and prevention efforts.