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TITLE: Shared genetic effects between schizophrenia and substance abuse: A multiplex extended pedigree study

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KEYWORDS: schizophrenia; substance abuse; genetic correlation; extended pedigree

ABSTRACT: Substance abuse is a serious public health issue and is increased among those with schizophrenia (28-47% versus 14.6% in the general population). In an attempt to better understand this comorbidity, the current study used an extended pedigree sample ascertained through schizophrenia probands (total sample N=1307, with N=790 relatives and N=517 unrelated controls) to examine the degree to which genetic effects influence shared liability for schizophrenia (N=123) and three different categorizations of DSM-IV substance use diagnoses: any substance dependence or abuse diagnosis (N=251), cannabis dependence or abuse (N=106) and alcohol dependence or abuse (N=179). We also assessed shared genetic effects between schizophrenia and two measures of nicotine use: binary "ever smoked daily" status (total available N=1082; smokers N=532) and a continuous measure of "pack years" (total available N=1047; pack years > 0 N=489). The univariate heritabilities of any

substance dependence/abuse diagnosis ($h^2=0.601$, $p=2.052e^{-8}$), cannabis dependence/abuse ($h^2=0.926$, $p=2.083e^{-9}$), and alcohol dependence/abuse ($h^2=0.434$, $p=1.00e^{-4}$), smoking status ($h^2=0.518$, $p=1.00e^{-7}$), and pack years ($h^2=0.873$, $p=1.360e^{-36}$) were all significant. The genetic correlations between schizophrenia and any substance dependence/abuse ($R_g=0.300$, $p=0.040$), schizophrenia and alcohol dependence/abuse ($R_g=0.389$, $p=0.024$), and schizophrenia and pack years of cigarette smoking ($R_g=0.458$, $p=0.006$) were significant; however, the genetic relationship between schizophrenia and cannabis dependence/abuse ($R_g=0.190$, $p=0.124$) and schizophrenia and smoker status ($R_g=0.197$, $p=0.167$) were not significant. Environmental correlations were all non-significant. Results indicate that genetic effects play a significant role in both unique and shared variance between schizophrenia and multiple measures of substance abuse. Future research will evaluate the genetic mediating effects of MRI brain structure volumes between schizophrenia and substance abuse.

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