Polygenic risk scores for schizophrenia and bipolar disorder associate with addiction

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Addiction to tobacco, alcohol or drugs is frequently a comorbidity of other psychiatric disorders, including schizophrenia (SCZ) and bipolar disorder (BPD). The smoking rate among schizophrenia patients is high, and increased rates of addictions are observed among their first-degree relatives. The situation is similar for BPD, with over 40% comorbidity of substance use disorders and high smoking rates as well. These high comorbidities call for an explanation, but separating cause and consequence has remained a challenge, for example in the case of cannabis use and the onset of psychosis. The application of polygenic risk scores (PRS) to analyze the risks from an ensemble of common sequence variants of small effects can aid in elucidating whether comorbidity relationships reflect shared genetics. In particular, the PRS methodology can be applied to subjects who do not have the psychiatric disorders, providing separation of the effects of the diseases themselves from those of the underlying genetic risk factors. We used PGC-based PRSs for psychosis to predict smoking, and addiction to nicotine, alcohol or drugs in individuals not diagnosed with psychotic disorders. Using PRSs for 144,609 subjects, including 10,036 individuals treated for substance use disorders and 35,754 smokers, we found that addiction and smoking associate strongly with PGRs for SCZ and BPD. The associations are highly significant with p-values as low as 5.3×10^{-50} (SCZ PRS vs alcoholism). Using standardized scores for SCZ and BPD scaled to a unit increase doubling the risk of the corresponding disorder, the odds ratios (ORs) for alcohol and substance use disorders range from 1.19 to 1.31, for the SCZ-PRS, and from 1.07 to 1.29 for the BPD-PRS. These findings demonstrate a shared genetic aetiology in psychosis and addiction. Furthermore, analysis shows that the impact of the SCZ liability score on smoking behavior seems to be on the rise as the overall prevalence of smoking declines. The implication is that anti-smoking measures and smoking cessation programs may be ineffective in modifying the smoking behaviors of those among the population that have high psychosis PRSs.