

Shared Genetic Architecture Between Substance-Use and Psychiatric Disorders

David Peery

Different psychiatric and substance-use disorders often co-occur in the clinical setting. Uncovering common genetic and neurobiological mechanisms could lead to better treatments for individuals with these comorbidities. I begin this study with a broad look at the genetic correlations between several psychiatric and substance use disorder pairs and identify a few pairs with particularly high genetic correlations. In further analyses I focus on two specific pairs of psychiatric and substance-use disorders: schizophrenia versus nicotine addiction and major depressive disorder versus alcohol addiction. Beginning with GWAS data for the individual disorders, I map SNPs to genes using H-MAGMA, then use RRHO to find pleiotropic genes across disorder pairs. I then identify in which cell-subtypes these genes are most highly expressed using snRNA-seq data from post-mortem neurotypical donors. Because H-MAGMA identified more genes for both disorder pairs when using data from dopaminergic neuronal Hi-C, these neurons could play a more important role in these comorbidities. Additionally, from the expression data I identified specific neuronal subtypes in the nucleus accumbens that could be particularly relevant in these comorbidities.