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Major Depressive Disorder and Lifestyle: pleiotropic effects in bivariate genetic analyses of extended twin pedigrees

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ABSTRACT:

Major Depressive Disorder (MDD) is a prevalent, burdensome and heterogeneous disorder with a complex etiology of genetic and environmental determinants (Kendall et al., 2021). In recent years, evidence has accumulated with regard to the ubiquity of pleiotropy across the genome (Watanabe et al., 2019), and shared genetic etiology is thought to play a large role in the widespread comorbidity among psychiatric disorders and risk factors (van Rheenen, Pevrot, Schork, Lee, & Wray, 2019). The majority of recent methods investigate pleiotropy by estimating genetic correlation from Genome-Wide Association (GWA) summary statistics, but such estimates can also be derived from the known relatedness between genetic relatives. Here we conduct a series of bivariate genetic analyses in extended twin pedigree data on lifetime MDD and three indicators of lifestyle, namely smoking behavior, physical inactivity and Body-Mass Index, decomposing phenotypic variance and covariance into genetic and environmental components. We analyze lifetime MDD and lifestyle data in a large multigenerational dataset of *N* = 18,896 individuals, containing 4,882 families with two or more members and 8,677 twins, using the 'Mendel' software (Lange et al., 2013). Analysis of extended twin pedigree data allows for the estimation of genetic correlation for both additive and non-additive genetic effects, as well as shared environmental effects. Quantifying the relative contribution of genetic and environmental effects on MDD liability and comorbidity with risk factors benefits our understanding of its etiological architecture.

Citations

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