M49. GENOME-WIDE POLYGENIC ATLAS OF THE PHENOME IN EMERGING ADULTHOOD: GENETIC OVERLAP OF RISK ACROSS FIVE ANCESTRIES

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Background Creating a network of the genetic relationships between multiple psychiatric and medical traits, during a critical developmental period, can enhance our understanding of risk for psychopathology. This study utilized genomic data from emerging adults (N = 5,947) to construct a comprehensive atlas of polygenic risk that indexes diverse psychiatric, behavioral and health outcomes.
Methods In addition to testing the GPSs prediction of the phenotypes (Moscati & Docherty, et al., this meeting), GPSs were also examined for associations with each other in this sample, across five ethnicities..Genome-wide association studies of 34 diverse phenotypes were used as as discovery samples to calculate genome-wide polygenic scores (GPS), and these scores were then used to predict over 50 phenotypes in the emerging adults. We computed partial correlations adjusted for ancestry principle components in order to estimate genetic relationships between the phenotypes, and corrected for multiple testing. Based on the cross-disorder psychiatric genomics findings to date, we hypothesized significant GPS associations between five major psychiatric disorders across each of the ancestry groups. We also attempted to replicate the associations reported in a previously derived atlas by Bulik-Sullivan and colleagues.
Results Several significant associations were observed in the European sample: SZ~BP ($\beta = 0.73$, $p = 2.7*10\text{-}67$), BP~MDD ($\beta = 0.23$, $p = 4.6*10\text{-}33$), and SZ~MDD ($\beta = 0.43$, $p = 7.2*10\text{-}21$). Significant associations were not observed for AUT~ADHD ($\beta = -0.005$, $p = 0.04$) or AUT~SZ ($\beta = 0.005$, $p = 0.19$). All of the GPS regression replications from the previous atlas were robustly significant and all were consistent with the sign of the previously published coefficients. Importantly, some unexpected but informative associations were observed: for example, significant positive associations of neuroticism GPS with GPSs for triglycerides and for coronary artery disease. We also present these regressions across the four additional ancestry groups, with a majority of the significant associations holding in these groups.
Discussion The findings here present a wide-ranging and nuanced picture of major dimensions of vulnerability to psychopathology at a genetic level. Overall, results reflect relationships between anxiety, depressive, and schizophrenia-spectrum disorders that are largely consistent with our current conceptualizations of diagnostic classification and confirm the important involvement of a network of medical and risk phenotypes in genetic predisposition to these disorders. Findings relating genetic risk for neuroticism with genetic risk for cardiovascular phenotypes may have important implications for psychiatry and public health.
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