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Editorial comment

Shared genetic risk factors for psychiatric illness

Developments in genomic and statistical technologies have dramatically advanced our understanding of the role of genes in complex traits, including psychiatric disorders. Much of the focus has been on the identification of specific variants involved in disease, with more than 12 000 genome-wide significant associations reported in the past few years. Beyond associations between genetic variants and individual phenotypes, one of the most important interesting outcomes of the genomic revolution has been a striking recognition that the genes associated with one phenotype are often associated with additional phenotypes. For example, 44% of variants associated with one autoimmune disease are also associated with a second autoimmune disease (1). Relevant to psychiatric disorders, a recent Nature Genetics article from the Psychiatric Genomics Consortium (PGC) found evidence of substantial (20–40%) genetic overlap between schizophrenia (SZ), bipolar disorder (BD), major depression and attention-deficit hyperactivity disorder (2).

The article by Tesli and colleagues in this issue of the *Acta Psychiatrica Scandinavica* builds on this work to provide more granular understanding of the genetic relationship between psychosis spectrum disorders, through the construction of polygenic risk scores (3). Risk scores are built from the set of genetic risk alleles associated with a trait in genome-wide association studies (GWAS), weighted by the effect size of each risk allele. These scores can help us to identify the existence and extent of genotypic overlap between phenotypes. In the current study, Tesli and colleagues combined variants with an association $P < 0.05$ in the large PGC sample analyses to build SZ and BD risk scores. They then utilized independent patient samples to assess the predictive value of these risk scores in distinguishing patients across the full spectrum of psychotic diagnoses from control subjects. The authors find that both SZ and BD risk scores were associated with diagnoses across the psychosis spectrum, with the SZ risk score more strongly associated with schizophrenia, psychosis NOS, and schizoaffective disorder, and the BD risk score more strongly associated with bipolar I, bipolar II and bipolar disorder NOS. While these findings are not surprising, they provide further evidence of shared genes between psychiatric disorders and further evidence that psychotic disorders should be viewed on a continuum rather as diagnostically distinct entities. Much work remains to be done to identify the specific genes shared between diagnoses and to understand the function of these genes. However, this line of work provides a preview of how genetic advances could one day help us to develop diagnoses with greater biological validity and possibly, greater clinical utility.

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