A genome-wide association study of shared risk across psychiatric disorders implicates gene regulation during fetal neurodevelopment

There is mounting evidence that seemingly diverse psychiatric disorders share genetic etiology, but the biological substrates mediating this overlap are not well characterized. Here we leverage the unique Integrative Psychiatric Research Consortium (iPSYCH) study, a nationally representative cohort ascertained through clinical psychiatric diagnoses indicated in Danish national health registers. We confirm previous reports of individual and cross-disorder single-nucleotide polymorphism heritability for major psychiatric disorders and perform a cross-disorder genome-wide association study. We identify four novel genome-wide significant loci encompassing variants predicted to regulate genes expressed in radial glia and interneurons in the developing neocortex during mid-gestation. This epoch is supported by partitioning cross-disorder single-nucleotide polymorphism heritability, which is enriched at regulatory chromatin active during fetal neurodevelopment. These findings suggest that dysregulation of genes that direct neurodevelopment by common genetic variants may result in general liability for many later psychiatric outcomes.

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