phenotyped EF sample. Thus, using Psychiatric Genomics Consortium (PGC) data as our discovery set (Ns = 15,000–37,000), we computed polygenic risk scores for major depression, bipolar disorder, ADHD, autism, and schizophrenia in a sample of 36 participants from the Longitudinal Twin Study (LTS), and used them to predict individual differences in the activity of this frontoparietal network. Higher genetic risk for ADHD predicted more frontoparietal neural activation (i.e., a less efficient neural network) at an uncorrected p < .05. In general, the risk scores for the other disorders showed the same trend, however did not reach statistical significance. As this study had a small sample size, results must be interpreted carefully, and a replication with a larger sample and increased power is necessary.

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Prediction from polygenic scores based on GWA of neuroticism to psychiatric and lifestyle traits

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The first genetic variants associated with neuroticism were identified in a meta-analysis of genome-wide association (GWA) results based on 1000Genomes imputation in 63,661 participants from 29 discovery cohorts and 9786 participants from a replication cohort. Participants came from Europe, the United States or Australia (Van den Berg et al. Behav Genet 2014; de Moor et al. in press). Polygenic scores based on the meta-analysis of neuroticism in 27 cohorts (removing data from NTR and NESDA) significantly predicted neuroticism and MDD in NTR and NESDA. Here we extend the polygenic score prediction to other traits hypothesized to show genetic overlap with a higher neuroticism (anxiety, borderline personality disorder, migraine, smoking), with lower neuroticism (e.g., exercise) or to be independent of neuroticism (other NEO personality traits, alcohol use).

The intergenerational transmission of suicidal behavior: a children of twins and siblings study

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Prominent researchers have noted the need to better understand the intergenerational transmission of suicidal behavior, including suicide attempt and death by suicide (Brent & Melhem, 2008). Twin and extended family studies suggest that genetic factors partly account for the variability in suicidal behavior in the population (Brent & Melhem, 2008). Thus, studies that do not account for unmeasured genetic covariates are unable to draw strong causal inferences about the consequences of parental suicidal behavior. To address this limitation, we used Children of Twins and Siblings designs to test the genetic and environmental contributions to the intergenerational transmission of suicidal behavior.

We merged five longitudinal, population-based Swedish registers to generate a nationally representative sample of offspring born 1973–1998 (N = 2,022,665). We linked all cohort members to their parents and determined parent-sibling relationships (i.e., the first two adult siblings) via the Multi-Generation Register. We fit Cox proportional survival models and examined the risk for offspring suicidal behavior after parental suicidal behavior.

In the general population, offspring of parents who attempted or died by suicide were more likely to attempt or die by suicide (HR = 3.28). Controlling for offspring (i.e., sex and parity) and maternal and paternal covariates (i.e., educational attainment and country of origin) in the adjusted population model attenuated the risk for offspring suicidal behavior (HR = 2.94). In the cousin comparison models, children of half-siblings (HR = 2.46), full-siblings (HR = 2.97), DZ twins (HR = 3.14), and MZ twins (HR = 2.90) were at comparable risk for suicidal behavior.

The measured covariates in the adjusted model partially confounded the relationship between parental and offspring suicidal behavior; however, additionally controlling for unmeasured covariates in the cousin comparison models did not further attenuate the association. Similar risks across all cousin-comparison models suggested that environmental factors associated with parental suicidal behavior within extended families largely account for the intergenerational transmission of suicidal behavior.


Whole genome sequencing identifies balanced and complex de novo structural variation in autism

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Whole Genome Sequencing (WGS) provides a more complete ascertainment of de novo mutation compared to microarrays or targeted sequencing. WGS can identify copy number variants (CNVs) more than an order of magnitude smaller than microarrays, as well as balanced and complex structural variants (SVs). We investigated the contributions of de novo and inherited SVs to autism spectrum disorder (ASD) by WGS (30x) and custom mutation detection in 235 subjects, including 71 with ASD, 26 sibling controls and their parents. We integrated novel methodologies with existing algorithms to develop a comprehensive SV detection and genotyping pipeline. The final set of SVs consists of deletions, tandem duplications, inversions, mobile element insertions, and complex SV alleles. From this we identified de novo SVs ranging in size from 134 bp to over 5 Mb, including inversions, mobile element insertions, and complex SVs involving multiple SV types in a single event. Overall the structural mutation rate was 0.17/individual, and SV mutation was not elevated in ASD. However, SVs in ASD cases were larger and disrupted more genes than in controls. MEIs, complex, and balanced SVs likely explain a significant proportion of the missing heritability in autism spectrum disorder.