A Genome-Wide Association Meta-Analysis of Attention-Deficit/Hyperactivity Disorder Symptoms in Population-Based Paediatric Cohorts

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Abstract

Objective

To elucidate the influence of common genetic variants on childhood attention-deficit/hyperactivity disorder (ADHD) symptoms, to identify genetic variants that explain its high heritability, and to investigate the genetic overlap of ADHD symptom scores with ADHD diagnosis.

Method

Within the EArly Genetics and Lifecourse Epidemiology (EAGLE) consortium, genome-wide single nucleotide polymorphisms (SNPs) and ADHD symptom scores were available for 17,666 children (<13 years) from nine population-based cohorts. SNP-based heritability was estimated in data from the three largest cohorts. Meta-analysis based on genome-wide association (GWA) analyses with SNPs was followed by gene-based association tests, and the overlap in results with a meta-analysis in the Psychiatric Genomics Consortium (PGC) case-control ADHD study was investigated.

Results

SNP-based heritability ranged from 5% to 34%, indicating that variation in common genetic variants influences ADHD symptom scores. The meta-analysis did not detect genome-wide significant SNPs, but three genes, lying close to each other with SNPs in high linkage disequilibrium (LD), showed a gene-wide significant association (p values between 1.46×10⁻⁶ and 2.66×10⁻⁶). One gene, WASL, is involved in neuronal development. Both SNP- and gene-based analyses indicated overlap with the PGC meta-analysis results with the genetic correlation estimated at 0.96.

Conclusion

The SNP-based heritability for ADHD symptom scores indicates a polygenic architecture and genes involved in neurite outgrowth are possibly involved. Continuous and dichotomous measures of ADHD appear to assess a genetically common phenotype. A next step is to combine data from population-based and case-control cohorts in genetic association studies to increase sample size and improve statistical power for identifying genetic variants.