Association of polygenic risk for attention-deficit/hyperactivity disorder with co-occurring traits and disorders

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Abstract

Background
A recent large-scale mega-genome-wide association study (GWAS) identified, for the first time, genetic variants at 12 loci significantly associated with attention-deficit/hyperactivity disorder (ADHD). In this study we use a powerful polygenic approach, with polygenic scores derived from the GWAS, to investigate the aetiological overlap between ADHD and frequently co-occurring traits and disorders.

Methods
Polygenic risk scores for ADHD derived from the mega-GWAS (20,183 cases, 35,191 controls) were computed in a large-scale adult population sample (N=135,726) recruited by the UK Biobank. Regression analyses were conducted to investigate whether polygenic risk for ADHD is associated with related traits and disorders in this population sample. The effects of sex were investigated via inclusion of an interaction term in the models.

Results
Polygenic risk for ADHD significantly and positively predicted body mass index (R²=0.45%;P=5x10⁻¹²⁹), neuroticism (R²=0.09%;P=2x10⁻²⁴), depression (R²=0.11%;P=2x10⁻¹³), anxiety (R²=0.06%;P=3x10⁻⁴), risk-taking (0.12%;P=9x10⁻²⁵), alcohol intake (R²=0.09%;P=8x10⁻²⁹), smoking (R²=0.33%;P=4x10⁻⁲¹), alcohol dependency (R²=0.21%;P=5x10⁻⁶), and negatively predicted verbal-numerical reasoning (R²=0.38%;P=5x10⁻³⁶). Polygenic risk scores did not significantly predict schizophrenia or bipolar disorder, although this may be due to the small number of diagnostic cases. We found no interaction effects between polygenic risk for ADHD and sex on any phenotypes.

Conclusions
Our findings suggest that common genetic variation underlying risk for clinically diagnosed ADHD also contributes to higher body mass index, neuroticism, anxiety and depressive disorders, alcohol and nicotine use, risk-taking and lower general cognitive ability in the general population. These findings suggest that the co-occurrence of several traits with ADHD is partly explained by the same common genetic variants.