ASSOCIATION BETWEEN GENETIC RISK (PRS) AND AGE-SPECIFIC RISK OF MENTAL DISORDERS

MASTER THESIS IN BIOINFORMATICS

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June 2024

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Association between genetic risk (PRS) and age-specific risk of mental disorders, Master Thesis in Bioinformatics © June 2024

We found evidence of polygenic risk scores (PRS) being associated with the diagnosis of mental health disorders, with variations in the effect of PRS based on age of onset and gender. We analyzed major depressive disorder (MDD), bipolar disorder (BIP), schizophrenia spectrum (SCZ), autism spectrum disorder (ASD), and attention-deficit/ hyperactivity disorder (ADHD) in the iPSYCH cohort. Our results indicate that genetic risk is highest during late adolescence and early adulthood for MDD, SCZ, and BIP, peaking near the median age of onset for these disorders. Sex differences were evident, with males generally showing higher hazard ratios (HR) than females, even in disorders more prevalent in females, such as MDD; and especially relevant in schizophrenia where the estimates are 4 times higher for males. For ASD, PRS associations were strongest in early-diagnosed cases and exhibited significant gender differences, with females potentially requiring a higher genetic liability threshold for diagnosis. ADHD's high heritability is acknowledged, but the evolving diagnostic criteria limit conclusions on temporal trends in genetic influences.

PRS	Polygenic Risk Score
GWAS	Genome-Wide Association Studies
MDD	Major Depressive Disorders
SCZ	Schizophrenia
BIP	Bipolar Disorders
ADHD	Attention-Deficit/Hyperactivity Disorder
ASD	Autism Spectrum Disorders
AAO	Age At Onset
QC	Quality Control
PS	Population Structure
DST	Danmarks Statistik
SNP	Single Nucleotide Polymorphisms
MAF	Minor Allele Frequency
IPW	Inverse probability weighting
FPE	Female protective effect

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