

Principal Investigator

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Funding

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Summary of research

Cognitive function, Psychiatry, Comorbidity, pathway, GxE

Application Lay Summary:

1a: The main goal of our study is to quantify and understand the role of genetic variants, the environment (including lifestyle), and their interaction on outcomes related to cognitive health. In doing so we will combine expertise of statistical genetics, medical genetics, bioinformatics and functional genomics. We are specifically interested in the following health-relevant outcomes from the U.K. Biobank data: cognitive function (incl. normal function and dementia), mental health (incl. depression, neuroticism, personality, smoking, and alcohol drinking), and brain MRI.

1b: Our research will contribute to quantifying and understanding how several risk factors (e.g. lifestyle, environment, genes), both separately and in combination, influence cognitive health as well as the comorbidities between different cognitive health outcomes.

1c: Our study will consist of a combination of methods, including:

- Genome-wide association studies (GWAS) that aim to identify individual genetic variants associated with a particular outcome.
- Comorbidity analyses, using e.g. meta-analytic techniques, LD score regression or BOLD-GREML methods to quantify the extent of genetic overlap between particular outcomes
- Gene-set analyses (e.g. using MAGMA and INRICH tools) and bioinformatic secondary analyses to understand genetic findings in terms of their biological function
- Heterogeneity analyses to determine genetic subgroups of individuals
- Annotation of genetic findings using external information from e.g. expression or quantitative proteomics data
- Gene-by-environment correlation and interaction analyses to quantify the relevance of the interplay between genes and environment (including lifestyle) on outcomes related to cognitive health

1d: We aim to use all available observations in the UKB that are currently released and will be released in the future, and that have been successfully genotyped and have measures of relevant outcomes