Application number/Title: 13310 - Impact of genetic and environmental associations on neuropsychiatric disorders and associated phenotypes

Applicant PI: Dr James Walters

Application Institution: Cardiff University, Cardiff, UK

Keywords provided by the Applicant PI to describe the research project: environment, genetics, mental-disorders, neuropsychiatry, outcomes

Application Lay Summary:

Neuropsychiatric disorders often have a profound impact on individuals, their families and wider society. Four of the six leading causes of years lived with disability are due to neuropsychiatric disorders (depression, alcohol-use disorders, schizophrenia and bipolar disorder). Developing effective treatments for neuropsychiatric disorders is one of the most important challenges facing medicine but in recent decades few novel medications have emerged. This is attributed, at least in part, to a lack of knowledge of the biological underpinnings of these conditions. However, thanks to large-scale genomic studies, the last 5-10 years has seen genetic research deliver results that are beginning to address these knowledge gaps at an accelerating rate.

This project aims to improve our knowledge and understanding of the genetic and environmental causes of neuropsychiatric disorders such as schizophrenia, bipolar disorder, depression, Alzheimer's disease and ADHD. We will also investigate the interplay between these factors and examine their effects in people with psychiatric disease and in the wider UK Biobank sample. We will also assess how genetic and environmental factors contribute to traits that are related to psychiatric disorders such as cognition, behavior, brain imaging and physical health measures. Finally, we aim to characterise the various consequences, such as social and health outcomes, of having a psychiatric disorder or related trait.

To investigate the genetic causes of neuropsychiatric disease, we will characterise the impact of both common genetic changes (differences in genetic sequence that are found in more than 1% of individuals) and rare genetic changes (found in less than 1% of individuals). The environmental factors we propose to investigate include early life factors, psychosocial factors, trauma, home environment, drug
use, smoking, education and functional outcome markers such as employment. We will also investigate physical illness in neuropsychiatric disorders and related traits such as diabetes, epilepsy, heart disease, respiratory disease and stroke.

These analyses will be conducted over an initial three-year period. The results of this project will give insights into the genetic and environmental causes of these conditions. This knowledge will ultimately lead to better classification and diagnosis, improved forecasting of clinical needs and will help identify novel targets for drug discovery. Furthermore, by exploring factors related to resilience to developing mental health conditions, the project has the potential to inform intervention strategies for those at high risk of neuropsychiatric disorders.