



Application number/Title: 27121 - Imaging genetics on depressive and bipolar disorders

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Keywords provided by the Applicant PI to describe the research project:

Depression, bipolar disorder, MRI, genetics, environment

Application Lay Summary:

1a: The direct link between genotype and phenotype is hard to observe in complex mental illness such as depression and bipolar disorders. Yet the intermediate phenotypes such as brain imaging-derived phenotypes (BIDPs) could help clarify the underlying biology and assist in identifying genetically vulnerable variants. In the proposed study, we plan to find the common and specific risk profiles including BIDPs, genotypes and environmental factors, e.g., lifestyles and life events, contributing to major depression and bipolar disorder, and explore the causal relationships between the genotypes, phenotypes, environmental factors, and the disorders with advanced multivariate genotype-phenotype association analysis techniques.

1b: The proposed study will further the knowledge on the genetic and neurobiological mechanisms on depression and bipolar disorders and help to identify more reliable and meaningful genetic and neurobiological risks and how they interact with environment. Findings will help to improve the diagnosis of the disorders, identifying high-risk individuals, and establish disease prevention and treatment strategies, such as by introducing lifestyle choices that may overcome disease. The investigation of advanced methods on the imaging and genetic correlation analyses will improve the performance for dimension reduction and therefore facilitate the identification of the reliable relationships between BIDPs and the genotypes.

1c: MRI techniques and statistical analyses will be performed to identify BIDPs including brain structure, function, and network characteristics, and relationships with depressive and bipolar disorders. Genome-wide association

studies (GWAS) will be conducted to search for genetic variants associated with the disorders using the data from UK Biobank and Psychiatric Genomics Consortium. Associations between the genetic variants and the high-risk BIDPs will be examined with advanced dimension reduction techniques. The gene-environment interaction analyses on candidate genes and structural equation modeling will be conducted to explore the causal interactions between BIDPs, genetic variants, environmental factors, and disorder-related outcomes.

1d: These studies will make use of full cohort including the neuroimaging and genetic data. We also intend to determine incident mental health outcomes using the hospital inpatient records, so we are interested in requesting primary care records and adjudicated mental health outcome variables when available.