



Application number/Title: 19542 - Identifying multi-level biomarkers and disease mechanisms for major mental disorders

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Funding body: National Natural Science Foundation of China

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

Wholebrain analysis, Nonlinear GWAS, biomarkers, networks

Application Lay Summary:

- 1a: 1. What is the primary change of the brain (including functional connectivity, gray matter volume and fiber integrity) for major psychiatric disorders?
2. Are these changes caused by genetic variants, or environmental factors, or

both? Are there interactions between them?

3. What are the main neurotransmitter dysfunctions for various mental disorders? What brain regions are influenced by these neurotransmitter dysfunctions?

1b: Our proposal meets the purpose of Biobank by two important goals raised: 1. Identification of sensitive neuro- and genetic biomarkers is expected to help early diagnosis of major mental disorders and 2. The association between neuroimaging changes, genetic variants and various phenotypes may help target neurotransmitters crucial for drug development and treatment of the mental disorders.

1c: First we will look for changes in multimodal neuroimaging data and identify brain regions with significant alteration. A GWAS analysis is then carried out to find SNPs that is potentially responsible for these changes. Both neuroimaging changes and genetic variants will be correlated with various behavior phenotypes so that a closed loop among neuroimaging alterations, genetic variants, and behavior phenotypes will be identified which may help understand the etiology of the mental disorders being investigated.

1d: As we are using whole brain association analysis and GWAS analysis with tens of thousands of variables, we would use the whole cohort data, including data now being available and future data when available.