Editorial

Special Issue "Deep Phenotyping of Psychiatric Diseases"

Chao Chen [1*], Elliot S. Gershon [2]

[1] State Key Laboratory of Medical Genetics, School of Life Science, Central South University, Changsha 410083, China;

[2] Department of Psychiatry and Behavioral Neuroscience, University of Chicago, 5841 S. Maryland Ave. MC 3077, Chicago, IL 60637, USA.

***Corresponding Author:** Chao Chen. Email: chenchao@sklmg.edu.cn.

Understanding of which phenotypic traits are relevant to a disease, and how to integrate them, is essential in "precision medicine for psychiatry" [1]. Analysis of multiple phenotypic measures such as brain imaging, cognition, neurophysiological, and behavioral traits, and examination of their genetic components, can serve to combine or subdivide diagnoses, or to predict treatment response.

The National Institute of Mental Health initiated Research Domain Criteria (RDoC) project in 2010 [2] integrates genomics, circuits, behavior and self-reports information aiming for better diagnosis of mental disorders. The goal of RDoC is to understand the nature of mental health and illness in terms of varying degrees of dysfunctions in general psychological/biological systems [3]. The RDoC framework focuses on dimensional psychological constructs that are relevant to human behavior and mental disorders. Constructs are grouped into higher level domains of human behavior and functioning and reflect psychological system of emotion, cognition, motivation, and social behavior. Methods used to investigate and understand constructs include molecular, genetic, neurocircuital and behavioral assessment.

The Bipolar and Schizophrenia Network for Intermediate Phenotypes (B-SNIP) consortium aims to systematically investigate shared phenotypic components of psychotic disorders, especially the phenotypes, genotypes and biomarkers of psychosis that may be related to disorders ranging from schizophrenia to bipolar disorder [4]. They use biomarkers as measures of physiological or cognitive traits, such as Electroencephalography (EEG), eye movement, brain Magnetic Resonance Imaging (MRI) measurements, to establish a pathway to biomarker-based classification in psychoses.

The Enhancing Neuroimaging and Genetics through Meta-Analysis (ENIGMA) network brings together researchers who are interested in cracking the genotype–phenotype relations in neurological and psychiatric disorders [5]. Their primary goal is to integrate genomics, neurology and psychiatry using MRI, fMRI, and genetic data in patient and control samples, and to contribute to understanding the structure

Journal of Psychiatry and Brain Science

http://jpbs.qingres.com

OPEN ACCESS

DOI: 10.20900/jpbs.20180006

Received: June 22, 2018

Accepted: June 22, 2018

Published: June 30, 2018

and function of the human brain. Working groups of ENIGMA Network include researchers in the field of bipolar, major depression, schizophrenia and many other psychiatric disorders. They develop new algorithms together for data analysis and provide information and methods for further replication.

Besides the studies mentioned above, there have been many other studies with deep phenotyping of psychiatric diseases. Although much progress has been made in the past few years, several important issues still need to be addressed:

1. Identification of new phenotypes not traditionally associated with diagnostic criteria. One promising extension of phenotyping is digital phenotyping. Digital phenotyping refers to direct measurements of behavior and physiological events from smartphone and wearable devices, to explore new aspects of behavior and physiology related to psychiatric diseases [6]. For example, GPS sensors can collect activity, location and social behavior data. Keyboard interaction can collect social media communications, and the microphone receiver can detect voices changes [7]. These and other types of digital data can be combined to attempt construction of valid new phenotypes for psychiatric diseases.

2. Explore efficient, inexpensive and accurate measurements. For psychiatry research, the device must be objective, passive and ubiquitous to capture behavioral and cognitive phenotypes [7]. The cost of the measurement is also vital for its application on larger population.

3. Develop new methods to integrate the results from multiple types of traits. For example, several methods have been developed to reveal casual relationships between phenotypes and disease based on genotype data. When genotypic data provides a molecular basis of a set of phenotypes, which are related to susceptibility to disease, the contribution of endophenotypic traits (subphenotypes) can potentially reveal the pathology and progress of psychiatric diseases. For example, mendelian randomization uses Genome-Wide Association summary data for thousands of phenotypes as instruments to make causal inferences [8]. The causal influence of the exposure can be inferred based on the model that one calculates the ratio between the SNP effect on the outcome over the SNP effect on the exposure [9]. Two-sample MR (2SMR) [10] can evaluate the SNP-exposure effects and the SNP-outcome effects obtained from separate studies. Other methods like causal inference test (CIT) [11] and network edge orienting (NEO) [12] can also make reliable conclusions about causality on large-omic datasets.

Furthermore, deep phenotyping combined with genomic analysis offers the opportunity to investigate the specificity and comorbidity of psychiatric diseases. Using a combination of deep phenotyping and cross-disorder genomics may help us to develop more precise diagnostic categories of psychiatric diseases, and to provide better treatment [13].

This issue aims to cover recent progress and trends in multiple related deep phenotyping studies. Research using various innovative technologies, such as web-based testing, smart phone sensor, and wearable devices is welcomed.

Especially, the following topics will be considered:

- Genetic basis of intermediate phenotypes and their relevance to disease;
- Novel technologies to measure and assess disease related phenotypes;
- Phenotypes for early diagnosis or disease prediction;
- New methods developed to interpret or integrate multi-omics data to reveal their unique or shared biological basis.

The novelty of each submitted paper will be considered as one of the acceptance criteria. Papers with conceptual advances, as well as advantages in clinical applications, are highly welcomed.

REFERENCES

1. Fernandes BS, Williams LM, Steiner J, Leboyer, M, Carvalho, AF, Berk, M. The new field of 'precision psychiatry'. BMC Med. 2017; 15: 80.
2. Insel T, Cuthbert B, Garvey M, Heinssen R, Pine DS, Quinn K, Sanislow C, Wang P. Research domain criteria (RDoC): Toward a new classification framework for research on mental disorders. Am J Psychiatry. 2010; 167(7): 748-751.
3. Research Domain Criteria (RDoC). Bethesda: NIMH. Available from https://www.nimh.nih.gov/research-priorities/rdoc/index.shtml
4. Tamminga CA, Ivleva EI, Keshavan MS, Pearlson GD, Clementz BA, Witte B, *et al*. Clinical phenotypes of psychosis in the Bipolar-Schizophrenia Network on Intermediate Phenotypes (B-SNIP). Am J Psychiatry. 2013; 170(11): 1263-1274.

5. Thompson PM1, Stein JL, Medland SE, Hibar DP, Vasquez AA, Renteria ME, *et al.* The ENIGMA Consortium: large-scale collaborative analyses of neuroimaging and genetic data. Brain Imaging Behav. 2014; 8(2): 153-182.
6. Jain SH, Powers BW, Hawkins JB, Brownstein JS. The digital phenotype. Nat Biotechnol. 2015; 33(5): 462-463.
7. Insel TR. Digital Phenotyping: Technology for a New Science of Behavior. JAMA. 2017; 318(13): 1215-1216.
8. Hemani G, Tilling K, Davey Smith G. Orienting the causal relationship between imprecisely measured traits using GWAS summary data. PLoS Genet. 2017; 13(11): e1007081.
9. Johnson T. Efficient calculation for multi-SNP genetic risk scores. 2012; Available from https://cran.r-project.org/web/packages/gtx/vignettes/ashg2012.pdf
10. Pierce BL, Burgess S. Efficient design for Mendelian randomization studies: subsample and 2-sample instrumental variable estimators. Am J Epidemiol. 2013; 178(7): 1177-1184.
11. Millstein J, Chen GK, Breton CV. cit: hypothesis testing software for mediation analysis in genomic applications. Bioinformatics. 2016; 32(15): 2364-2365.
12. Aten JE, Fuller TF, Lusis AJ, Horvath S. Using genetic markers to orient the edges in quantitative trait networks: the NEO software. BMC Syst Biol. 2008; 2: 34.
13. Clementz BA, Sweeney JA, Hamm JP, Ivleva EI, Ethridge LE, Pearlson GD, Keshavan MS, Tamminga CA. Identification of Distinct Psychosis Biotypes Using Brain-Based Biomarkers. Am J Psychiatry. 2016; 173(4): 373-384.