·Editorial·

An update on research and approaches in biological psychiatry

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Many studies have shown that, in terms of global burden, mental disorders have exceeded diseases of the cardiovascular and respiratory systems as well as malignant tumors[1]. Nevertheless, the pathological mental activities caused by the millions of neurons in the human brain are far less clear than diseases of other organs and systems. This is not only due to the limited approaches to exploring the human brain, but also the multiple mechanisms by which human mental activities are regulated, including the internal and external physical and social environment. Therefore, our knowledge of mental disorders is still nowhere near the boundaries of truth, especially in the three most important aspects: pathogenesis, objective diagnosis, and effective therapy. For example, environment and heredity may be the most important factors in the pathogenesis of mental disorders, while the mechanism by which the environment impacts the brain and mental disorders remains unclear, and genetic studies have not yet provided definitive specific evidence[2-5]. On the other hand, from the aspect of clinical diagnostic biomarkers, although some operable diagnostic criteria and series of psychological assessment tools have been developed, we are still in urgent need of thorough research to find objective, quantifiable, simple, and convenient markers to facilitate early identification and decrease the misdiagnosis of mental disorders. Considering the topic of treatment, clinical studies have shown that, even when all the currently available treatment approaches are tried, the cure rates of mental disorders remain very low, and refractory mental disorders remain a troublesome clinical dilemma.

To achieve breakthroughs in the above problems, one of the core scientific issues is to seek and establish stable biomarkers from genes to clinical phenotypes. Only in this way can we carry out in-depth research on pathogenesis, establish objective diagnostic markers, and develop effective treatment approaches to mental disorder[6]. In recent years, the development of new techniques and methods in neuroscience seems promising for exploring the essence of mental disorders[7]. Also, in China, funds for research and productive teams in the core scientific issues have been increasing. For this issue, we invited scholars in the fields of clinical psychiatry and basic neuroscience research in China and the USA to present their research and opinions regarding genetics and neuroimaging in schizophrenia, bipolar disorder, major depressive disorder (MDD), and other major mental disorders.

In five studies of schizophrenia, Chen *et al.*[8], Liu *et al.*[9] and Duan *et al.*[10] review the current status and discuss updates in genetic studies of schizophrenia[8], with emphasis on the significance of circadian rhythm-related genes[9], the genetic regulation and perturbation of neurons derived from induced pluripotent stem cells, and genomic encoding[10]. Using mRNA expression measurements in postmortem temporal cortex from Han Chinese and linkage disequilibrium analysis, Sun *et al.*[11] demonstrate that *GNB1L* (guanine nucleotide-binding protein, beta-1-like) is regulated by a *cis*-acting variant within the 3'-region of the gene. And, in light of the mRNA expression results, they further re-analyze the data of previously published case-control studies and show that the *GNB1L* high-expression allele is the risk allele for schizophrenia and bipolar disorder in the Han Chinese population. In a molecular imaging study of schizophrenia, Li *et al.*[12] reveal that patients with schizophrenia show reduced grey matter volume (GMV) in

the cerebellum and the visual, medial temporal, parietal, and middle frontal cortex compared with healthy controls. Another finding of this study is an association between a Val108/158Met polymorphism of the COMT (catechol-O-methyltransferase) gene and the GMV of the superior frontal gyrus, and this effect is mainly due to the gene's effect on cortical thickness rather than cortical surface area. The authors also show that a diagnosis × genotype interaction has an effect on the GMV of the left precuneus.

By reviewing the studies of MDD-related biological mechanism, Cai et al.[13] deduce that brain-derived neurotrophic factor (BDNF) dysfunction and increased apoptosis may be the final common cascade for MDD, and therapeutic strategies aimed at enhancing the BDNF system may prove to be an effective approach to achieving a rapid antidepressant effect. Wang et al.[14] review studies comparing the effects of monoaminergic and glutamatergic antidepressants on neuronal plasticity, and infer that the pathogenesis of depression may involve maladaptive neuronal plasticity in glutamatergic circuits, which may serve as a new class of targets to produce rapid antidepressant effects. Cai et al.[15] compare the GMV in unipolar and bipolar depression by magnetic resonance imaging and voxel-based morphometry, and show that both forms of depression have decreased GMV in the right inferior frontal gyrus, while only bipolar depression shows reduction of GMV in the right middle cingulate gyrus, which, they conclude, may be specific to this disorder. In a study of functional connectivity of hippocampal subregions in remitted late-onset depression (rLOD), Wang et al.[16] show that rLOD patients have decreased connectivity between the left cornu ammonis and the bilateral posterior cingulate cortex/precuneus and increased connectivity between right hippocampal subregions and the frontal cortex compared with healthy controls. Further correlative analysis reveals that the abnormal functional connectivity is positively associated with the longitudinal changes in scores in the Symbol Digit Modalities and Digit Span Tests.

Another four studies are concerned with other aspects of mental disorders. Chen et al.[17] review studies of the structural and functional changes in the hippocampus in amnestic mild cognitive impairment (aMCI), and conclude that a combination of advanced multi-modal neuroimaging measures can provide more precise and sensitive

measurement of hippocampal changes than using only one of these measures. This may contribute to the exploration for biomarkers of the progression of aMCI to Alzheimer's disease. Peng et al.[18] investigate the point prevalence of the atypical features of 3 906 patients with bipolar disorder in 26 psychiatric services across China, and show that these features have potential impact on treatment practices for bipolar disorder in China. Zhang et al.[19] report on the application of Williams LifeSkills Training to improve trait anxiety, coping styles, and interpersonal support in Chinese male juvenile violent offenders, which may have significant practical value. Zhang et al. [20] also describe the mental health laws and regulations in different countries and districts, and outline their criteria and procedures for involuntary admission to psychiatric hospitals and to community services. This may help to standardize the legislation for involuntary disposition of patients with mental disorders in China and serve to improve mental-health care and treatment.

Although the studies in this issue are just a small part of the literature published by Chinese investigators in the field of biological psychiatry, we anticipate that our readers will be enlightened by these samples of current views.

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