

## Review Article

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# Psychiatric disorders in China: strengths and challenges of contemporary research and clinical services

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## Abstract

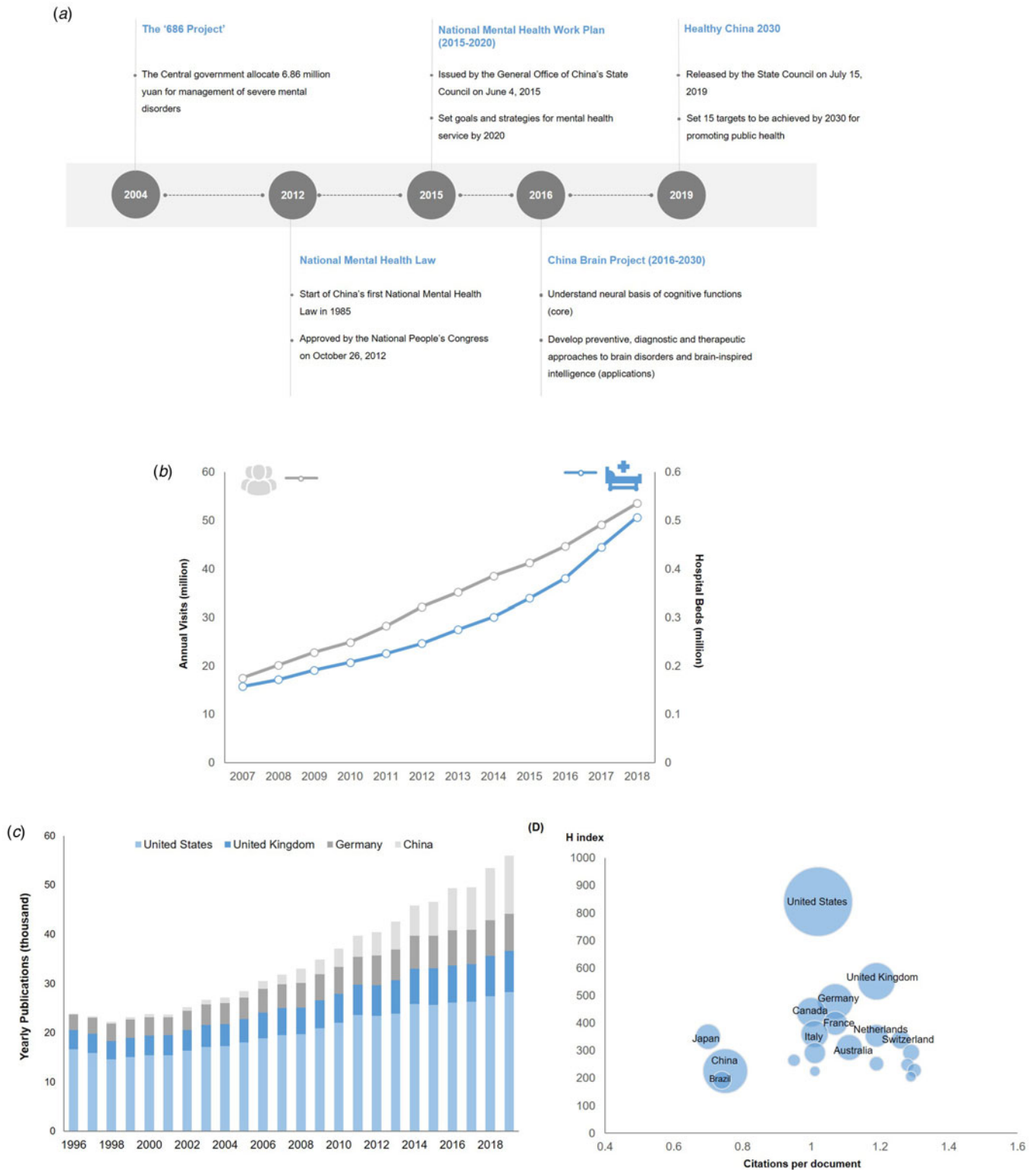
China accounts for 17% of the global disease burden attributable to mental, neurological and substance use disorders. As a country undergoing profound societal change, China faces growing challenges to reduce the disease burden caused by psychiatric disorders. In this review, we aim to present an overview of progress in neuroscience research and clinical services for psychiatric disorders in China during the past three decades, analysing contributing factors and potential challenges to the field development. We first review studies in the epidemiological, genetic and neuroimaging fields as examples to illustrate a growing contribution of studies from China to the neuroscience research. Next, we introduce large-scale, open-access imaging genetic cohorts and recently initiated brain banks in China as platforms to study healthy brain functions and brain disorders. Then, we show progress in clinical services, including an integration of hospital and community-based healthcare systems and early intervention schemes. We finally discuss opportunities and existing challenges: achievements in research and clinical services are indispensable to the growing funding investment and continued engagement in international collaborations. The unique aspect of traditional Chinese medicine may provide insights to develop a novel treatment for psychiatric disorders. Yet obstacles still remain to promote research quality and to provide ubiquitous clinical services to vulnerable populations. Taken together, we expect to see a sustained advancement in psychiatric research and healthcare system in China. These achievements will contribute to the global efforts to realize good physical, mental and social well-being for all individuals.

## Introduction

Psychiatric or mental disorders are the leading cause of disease burden calculated by years lived with disability, and affected 970.8 million people worldwide (GBD, 2017). Psychiatric disorders have been a rising concern for China, accompanying its rapid economic growth, profound societal changes and expansion in the ageing population in the past few decades. A recent nationwide epidemiological study reported a 16.6% lifetime prevalence of mental disorders in adulthood in China (Huang et al., 2019b). The disease burden of mental, neurological and substance use disorders in China accounted for 17% of the global disease burden in 2013, constituting 10% of its national disease burden (Charlson, Baxter, Cheng, Shidhaye, & Whiteford, 2016).

Over the last two decades, the Chinese government has initiated a series of work plans to promote healthcare for mental disorders and to facilitate understanding of underlying mechanisms through neuroscience research (Fig. 1a). In 2005, the government launched a national public health programme to integrate community and hospital services for severe mental disorders, later referred to as the ‘686 Project’ (Ma, 2012). In 2012, the first

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**Fig. 1.** (a) Milestones of mental health services and research in China in the past three decades. (b) Mental health clinics annual visits and facilities increase from 2007 to 2018. Data from the China Health Statistical Yearbook (National Health Commission, 2019). (c) Number of papers published in international peer-reviewed journals in the neuroscience field for four countries (USA, China, UK and Germany) from 1996 to 2019. (d) Number of papers published in neuroscience field (circle size) in top 20 countries with the highest H index (y-axis) in 2019. Data of (c-d) are from <https://www.scimagojr.com/>.

National Mental Health Law (Chen et al., 2012) was endorsed by the National People's Congress which stipulates the rights of people with mental disorders and duties of healthcare providers at the

legislative level (Shao, Wang, & Xie, 2015; Xiang, Yu, Ungvari, Lee, & Chiu, 2012). The National Mental Health Work Plans (2002–2010, 2015–2020) set principals and priorities of mental

health work (Health, Affairs, & Security, 2003; Xiong & Phillips, 2016). In 2016, the government announced the Outline of the Healthy China 2030 Initiative, in which promoting psychological well-being is one of the 15 targets to be achieved within the next decade (Chen, Li, & Harmer, 2019; The State Council, 2019).

With the implementation of these regulations and initiatives, profound changes have occurred in psychiatric research and clinical services. On the clinical side, China has achieved significant progress in making healthcare services accessible and affordable to a great number of patients. A nationwide management system for severe mental disorders was established (Liang, Mays, & Hwang, 2018; Luo, Law, Lin, Yao, & Wang, 2017; Ma, 2012). The number of annual visits to psychiatric clinics grew from 17.52 to 53.52 million from 2007 to 2018, and the number of hospital beds in psychiatry department increased from 0.16 to 0.51 million during the same period (National Health Commission, 2019) (Fig. 1b). Psychiatric health care professionals will reach 4.5 per 100 000 people by 2030 (The State Council, 2019).

Research into psychiatric disorders is an integral part of brain projects across the world. For example, the second phase of the NIH BRAIN initiative proposed the goal to understand brain disorders through understanding the basic mechanisms underlying the function of the healthy brain. The China Brain Project, entitled 'Brain Science and Brain-Inspired Intelligence', is a 15-year research plan (2016–2030) with a core theme and two principal areas of applications. The purpose of the China Brain Project is to enhance the understanding of neural circuit mechanisms of cognition, and based on this foundation, to further develop preventive, diagnostic and therapeutic approaches to brain disorders and to advance brain-inspired intelligence technologies (Poo *et al.*, 2016). Two national brain research centres in Beijing and Shanghai and several local research centres have been established with the launch of the China Brain Project. Neuroscience research has witnessed a rapid growth in the past three decades. Annual publication numbers in neuroscience from China increased exponentially from 227 in 1996 to 11 849 in 2019, ranking the second after the USA (SCImago, *n.d.*) (Fig. 1c). However, in terms of citation per document and *H* index, China is still lagging behind among the top 20 countries with the highest *H* index (SCImago, *n.d.*) (Fig. 1d).

The landscape of Chinese psychiatric research together with the healthcare system underwent unprecedented changes in the last few decades (Liu *et al.*, 2011). Such progress is indispensable to the development of global mental healthcare and research (Collins *et al.*, 2011). As China makes one-seventh of the world's population, its ability to provide high-quality clinical services is part of the global efforts to achieve universal coverage for mental disorders (World Health Organization, 2013). Meanwhile, Chinese researchers are making a growing contribution to the neuroscience community. A number of reviews and commentaries have described achievements and challenges in mental health in China from different perspectives (Liu *et al.*, 2011; Que, Lu, & Shi, 2019; Shi, 2019; Wang *et al.*, 2019a, b, c, d). Yet, this review aims to provide an overall depiction of psychiatric research and healthcare system in China in the last three decades. We first present psychiatric studies from China with different research technologies, and then present a list of ongoing large-scale, open-access research cohorts and brain banks. Next, we look into transformations occurring in the healthcare system. Finally, we discuss the challenges to and potential opportunities for improving neuroscience research and clinical services in China. Understanding the progress and existing challenges will help to:

- (1) provide a basis for policy makers devising work plans that allocate resources to areas where the largest gaps remain and
- (2) facilitate collaborations among mental health professionals between China and the rest of the world.

### Specific research topics

We begin with reviewing several aspects of research topics on psychiatric disorders, focusing on human research. The national and major cross-provincial epidemiological studies were retrieved from a reference search. For genetic and neuroimaging research, we systematically searched PubMed, Scopus and Chinese National Knowledge Infrastructure (CNKI) databases for reviews and meta-analyses that were conducted on Chinese populations from January 2000 to April 2021 (Fig. 2). Online Supplementary Tables S1 and S2 listed the included reviews and meta-analyses of genetic and neuroimaging studies. In addition, we discuss some representative studies published in recent years that were not covered by reviews and meta-analyses, as examples of research from China that contribute to the field knowledge.

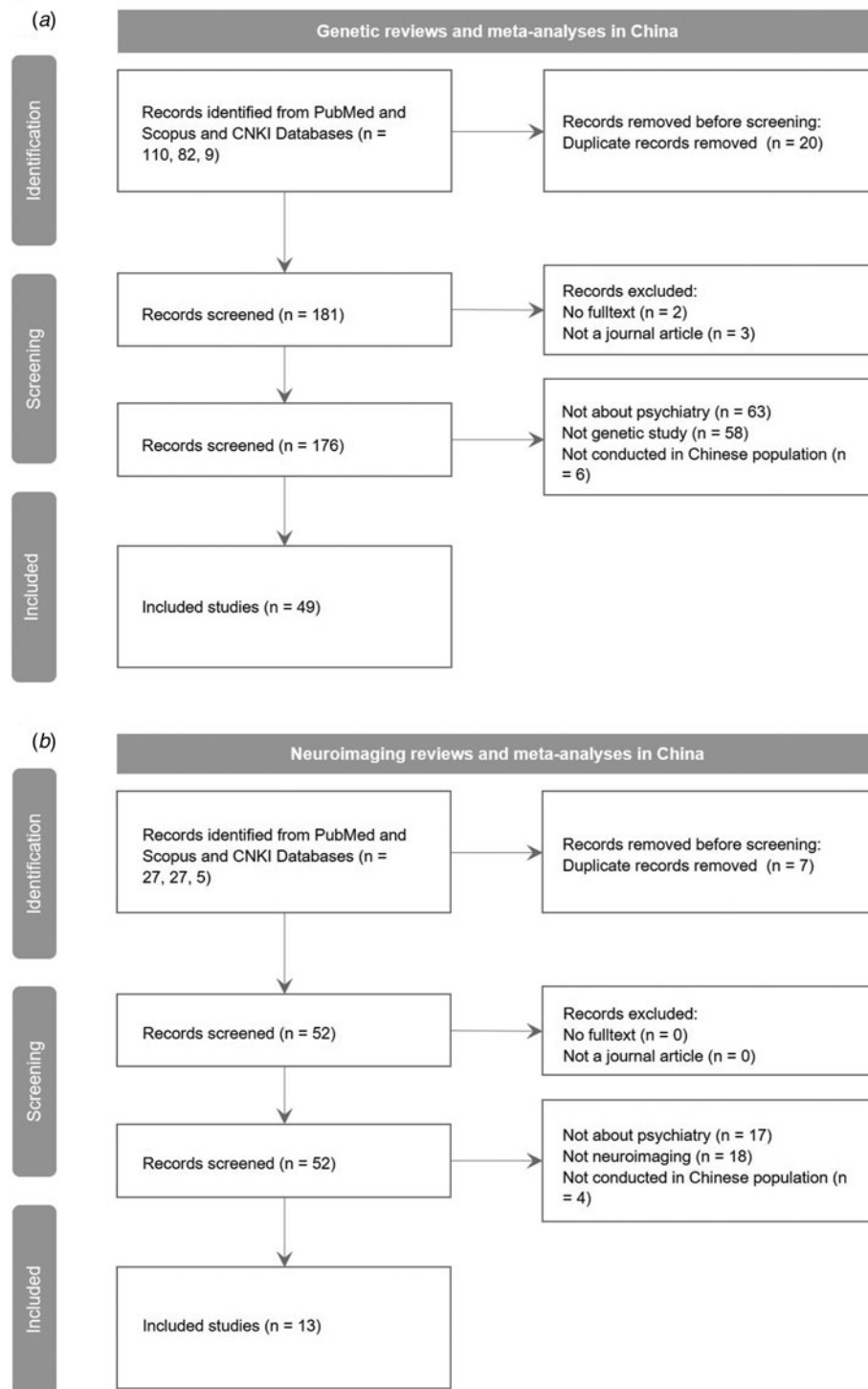
### Epidemiological studies

The China Mental Health Survey (CMHS) is the first nationally representative epidemiological survey of neuropsychiatric disorders and health services use (Huang *et al.*, 2016). According to this study, the prevalence of mental disorders in adulthood is 16.6% during the lifetime and 9.3% in the 12 months before the interview (Huang *et al.*, 2019b). The most prevalent psychiatric diagnosis was anxiety disorder, with a lifetime prevalence of 7.6% and a 12-month prevalence of 5.0% (Fig. 3a). The prevalence of mental disorders was slightly lower than that was reported in 2009, which found that the 1-month prevalence of any mental disorder was 17.5% (Phillips *et al.*, 2009) and higher than an earlier epidemiological study conducted in Beijing and Shanghai with a 12-month prevalence of 7.0% (Shen *et al.*, 2006). Despite disparities in the sampled population, diagnostic criteria, instruments used and assessed disorders between studies, the occurrence of mental disorders may have become more prevalent in China (Huang *et al.*, 2019b).

### Genetic research

In total, 201 records for genetic research were identified from PubMed, Scopus and CNKI databases. After duplication removal and screening for exclusion criteria, 49 reviews and meta-analyses were included (Fig. 2 and online Supplementary Table S1), among which 10 are reviews and 39 are meta-analyses of specific genetic variants and risk for psychiatric disorders in Chinese populations. Schizophrenia is the most commonly studied disease (25/49), followed by affective disorders (14/49), two autism spectrum disorders, two attention deficit hyperactivity disorder (ADHD), one substance abuse, one suicide and four multiple disorders.

Findings from candidate gene associations and genome-wide association study (GWAS) in Chinese populations were summarized in three reviews (Collier & Li, 2003; Cui & Jiang, 2012; Yue, Yu, & Zhang, 2017). Among the 22 meta-analyses of candidate genes and schizophrenia, 10 reported significant associations between risk genes and schizophrenia in Chinese populations, seven reported no significant relationship while five indicated mixed results (online Supplementary Table S1). A recent Chinese GWAS for schizophrenia (7699 cases and 18 327

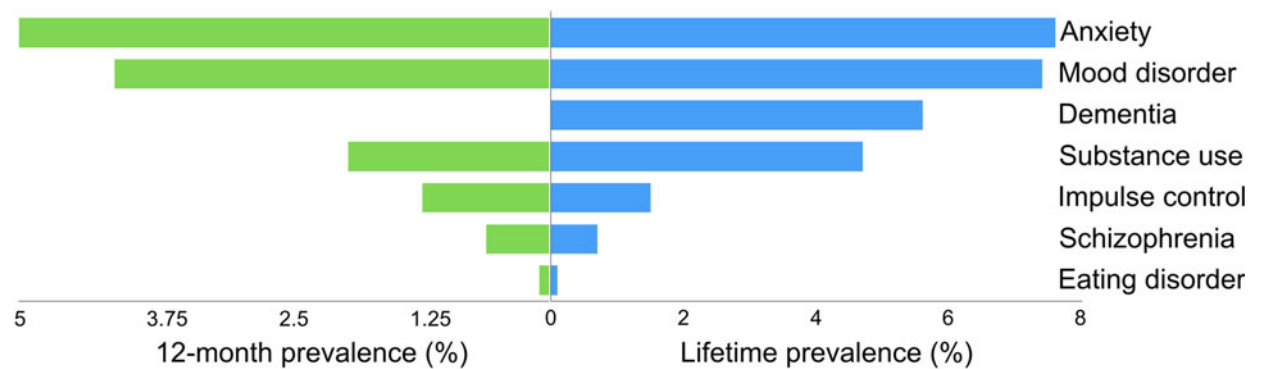
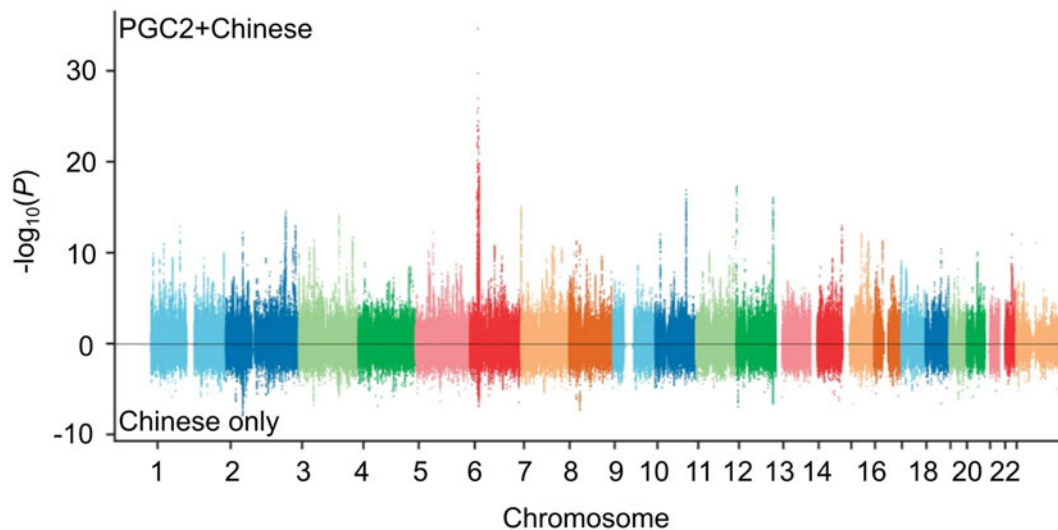
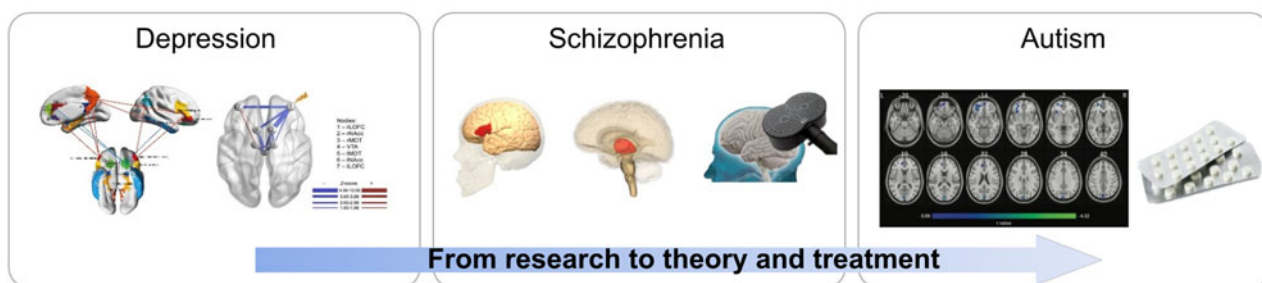


**Fig. 2.** Reviews and meta-analyses on (a) genetic research and (b) neuroimaging research in China systematically retrieved from PubMed, Scopus and CNKI databases. The search terms were: ['mental disorder' OR psychiatr\* OR schizophrenia OR 'affective disorder' OR depressi\* OR 'bipolar disorder' OR 'anxiety disorder' OR autism OR ADHD OR 'obsessive compulsive disorder' OR 'drug abuse' OR 'substance abuse'] AND [China [Title/Abstract]] AND ['genetic' OR 'GWAS' OR 'methylation' OR 'gene expression'] for genetic research; ['mental disorder' OR psychiatr\* OR schizophrenia OR 'affective disorder' OR depressi\* OR 'bipolar disorder' OR 'anxiety disorder' OR autism OR ADHD OR 'obsessive compulsive disorder' OR 'drug abuse' OR 'substance abuse'] AND [China[Title/Abstract]] AND ['neuroimaging' OR 'brain imaging' OR 'magnetic resonance imaging' OR MRI OR 'positron emission tomography' OR PET] for neuroimaging research. Limited to publication type: Meta-Analysis, Review and Systematic Review. Exclusion criteria include no-fulltext, not a journal article, not about genetic/neuroimaging research, not about psychiatric disorders or not conducted in Chinese populations.

controls) identified seven genome-wide significant loci (Fig. 3b), and among the 108 loci identified from the Psychiatry Genomics Consortium (PGC2) cohort, 98 loci were overrepresented in Chinese cases (Li et al., 2017a, b). A trans-ancestry meta-analysis of East Asian and European ancestries identified 208 significant associations in 176 genetic loci (53 novel) (Lam et al., 2019). Pharmacogenomic studies from China identified five genome-wide significant loci, *MEGF10*, *SLC1A1*, *PCDH7*, *CNTNAP5* and *TNFK*, that may contribute to individual therapeutic effects of antipsychotic treatment (Yu et al., 2018).

Another study showed that rare damaging variants in glutamatergic neurotransmission are enriched in patients less responsive to antipsychotic treatment (Wang et al., 2018).

For affective disorders, positive findings were reported in eight out of 11 meta-analyses of candidate genes and affective disorders (major depression and bipolar disorder), two reported negative results and one with mixed finding. Two reviews examined genetic variants and methylation in relation to affective disorders (Deng, Liu, He, Liu, & Zhang, 2008; Yang et al., 2014). Another review summarized findings of efficacies and toxicities of

(a) **Epidemiological studies**(b) **Genetic research**(c) **Neuroimaging studies**

**Fig. 3.** Representative studies and research applications in psychiatric disorders. (a) Lifetime and 12-month prevalence of mental disorders in adulthood reported by Huang *et al.* (2016). (b) Genome-wide associations in the Chinese schizophrenia cases (lower) and in the combined sample (upper) of the Psychiatry Genomics Consortium (PGC2) and Chinese populations (43 175 cases; 65 166 controls) (Li *et al.*, 2017a, 2017b). (c) Implications to disease neuropathology and clinical application from neuroimaging studies of major depressive disorder (Cheng *et al.*, 2016), schizophrenia (Du *et al.*, 2021) and autism (Dai *et al.*, 2021). Figures reproduced with permission.

antidepressant drugs (Lu, Lu, Zhu, & Che, 2015). For ADHD, a review implicated several candidate genes that may involve in the disease pathology, yet GWAS for ADHD in Chinese

populations failed to identify any significant SNPs, and only found an increased burden of copy number variants in ADHD cases (Yang *et al.*, 2013a). For autism spectrum disorders, a

study investigated *de novo* (DN) mutations in 189 risk genes in 1543 Chinese patients, and reported ~4% of patients carry a DN mutation in one of the 29 autism candidate genes (Wang et al., 2016a, b). In a follow-up study, the authors found that transmission of deleterious mutations is primarily associated with DN mutations (Guo et al., 2018). Yang et al. (2013a, b) analysed two independent GWAS for alcohol consumption and found common variants at 12q24 that may contribute to drinking in Chinese Han population.

Genetic studies in Chinese populations can expand the ethnic diversity of neuroscience research findings. According to the GWAS catalogue, although European descent accounts for only 16% of the world's population, it represents approximately 79% of participants in GWAS (Martin et al., 2019). Therefore, research into non-European ethnic groups will inform common and unique genetic predispositions across populations.

### Neuroimaging studies

*In vivo* neuroimaging techniques such as magnetic resonance imaging (MRI) and positron emission tomography provided an unprecedented amount of information about macro-scale brain structure, function and metabolism. Application of neuroimaging techniques in psychiatric disorders has led to a better understanding of complex brain abnormalities in patients with psychiatric disorders, and facilitated psychoradiology as an emerging subspecialty of radiology (Gong, Kendrick, & Lu, 2021; Gong, Lui, & Sweeney, 2016; Huang, Gong, Sweeney, & Biswal, 2019a; Kressel, 2017; Lui et al., 2009; Lui, Zhou, Sweeney, & Gong, 2016; Port, 2018). We identified 13 neuroimaging reviews and meta-analyses of psychiatric disorders from PubMed, Scopus and CNKI databases that were conducted in Chinese populations (Fig. 2 and online Supplementary Table S2).

Among the 13 included reviews and meta-analyses, seven were about affective disorders. Many studies focused on functional connectivity abnormalities in patients with specific clinical characteristics (Smith, 2015). For example, Tang et al. (2018a, b) identified different patterns of amygdala-based functional connectivity from studies using adult and adolescent patients with major depressive disorder. Wang et al. (2020a, b) summarized large-scale brain network dysfunctions in the acute state and remitted state of bipolar disorder. Liu and Yao (2016) reviewed neuroimaging studies comparing patients with unipolar depression and bipolar disorder. Studies of first-episode, medication-naïve patients are particularly relevant to investigate primary neural abnormalities in disease pathology. For example, a study comparing first-episode, medication-naïve patients with current or remitted depression showed that both groups have abnormal activation in the ventromedial prefrontal cortex and precuneus during a stress task, whereas only remitted patients exhibited increased activations in the dorsolateral prefrontal cortex and bilateral striatum (Ming et al., 2017). A follow-up study showed that both groups exhibited abnormalities in cortical morphology in the left precentral gyrus and left superior frontal gyrus (Xiong et al., 2019). These findings are in accordance with the psychoradiology hypothesis proposed by Gong et al., i.e. brain structural alterations lead to clinical symptoms through impacting on widely distributed functional connectivity (Canario, Chen, & Biswal, 2021; Schranke, Ruhé, & Reneman, 2020).

Findings from neuroimaging studies may implicate potential target brain regions for treatment. For example, Cheng et al. (2016) pinpointed dysconnectivity in two separable reward and

non-reward neural circuits in patients with major depressive disorder using a brain-wide association study approach (Cheng et al., 2015). An independent study later showed that transcranial magnetic stimulation to the non-reward circuit achieved symptom remission in 59.5% of patients previously resistant to treatment (Feffer et al., 2018) (Fig. 3c). Gong et al. (2011) differentiated patients with refractory and non-refractory depressive disorder based on grey and white matter volume, suggesting that brain deficits in distributed regions could predict the clinical outcome of depression.

For schizophrenia, two reviews summarized detailed lists of neuroimaging studies of schizophrenia in Chinese populations (Liu, Xu, & Jiang, 2014, 2018). Some recent studies showed that different functional dysconnectivity patterns exist in first-episode and chronic patients (Li et al., 2017a; Wang et al., 2019b). Dysconnectivity in the early stage of illness mainly involves the inferior frontal gyrus, which correlates with the polygenic risk score of language-related FOXP2 genes, supporting the notion that the genesis of schizophrenia is related to language-related anomalies (Crow, 1997; Du et al., 2021) (Fig. 3c). Sun et al. (2015) found two subtypes of first-episode, medication-naïve patients with schizophrenia using hierarchical clustering on diffusion tensor imaging data. Based on a unique sample of untreated schizophrenia with varying illness durations, Zhang et al. (2015) showed accelerated age-related cortical thinning in the prefrontal and temporal areas in patients. Using machine learning techniques, Li et al. (2020) developed a new hypothesis-driven neuroimaging biomarker for schizophrenia identification, prognosis and subtyping based on striatal functional abnormalities.

Another two reviews summarized neuroimaging abnormalities in patients with anxiety disorders (Chen & Shi, 2011) and obsessive-compulsive disorder (Fan & Xiao, 2013). Neuroimaging studies also implicated the underlying neural circuitry of reinforcement-related processing in relation to alcohol abuse (Jia et al., 2020, 2021), and implicated the therapeutic effect of bumetanide in reducing symptoms of children with autism spectrum disorder (Dai et al., 2021). Taken together, many neuroimaging studies from China investigated patients with specific clinical characteristics, aiming to disentangle complex neuropathology of psychiatric disorders and to provide potential target brain areas for treatment.

### Research cohorts and brain banks

#### Large-scale, open-access imaging genetic cohorts

To identify reproducible and representative findings with small effect sizes, it is important to establish large-scale, multi-centre research cohorts (Button et al., 2013; Poldrack et al., 2017; Schnack & Kahn, 2016). Several open-access cohorts with healthy participants have been established in China (Table 1). The Chinese Imaging Genetics (CHIMGEN) study is an imaging genetic study cohort which collected a full set of genomic, neuroimaging, environmental and behavioural data from 7000 healthy Chinese Han participants between 18 and 30 years old (Xu et al., 2020). The Chinese Color Nest Project (CCNP) aims to delineate a normative trajectory of brain development across the lifespan (Yang, Kang, Li, Li, & Zhao, 2017a, b). A neuroimaging data sharing platform – Brain Imaging Sharing Initiative (BISI, <http://bisi.org.cn>) was recently established, including repeated scans of healthy subjects (Liu et al., 2017; Zuo et al., 2014) and healthy subjects with rumination states (Chen et al., 2020).

**Table 1.** Large-scale, open-access research cohorts of healthy participants and patients with psychiatric disorders<sup>a</sup>

Project	Healthy subjects	Patients	Age range	Neuroimaging	Neurocognitive battery	Blood	Environmental variables	Gut microbiota	DOI
<i>Patients with psychiatric disorders</i>									
Zhangjiang International Brain BioBank (ZIB)	7500	4400 (schizophrenia, major depressive disorder, autism, stroke, neurodegenerative disorders)	6–80	Yes	Yes	Yes	Yes	Yes	Ongoing project
REST-meta-MDD consortium	1128	1300 major depressive disorder	18–65	Yes	Unknown	Unknown	Unknown	Unknown	<a href="http://rfmri.org/REST-meta-MDD">http://rfmri.org/REST-meta-MDD</a>
<i>Healthy participants</i>									
Chinese Imaging Genetics (CHIMGEN)	7000	–	18–30	Yes	Yes	Yes	Yes	Unknown	10.1038/s41380-019-0627-6
Chinese Color Nest Project (CCNP)	240 adults, 480 children, 480 elderly people	–	6–84	Yes	Yes	No	Unknown	Unknown	10.1360/N972017-00362
Consortium for Reliability and Reproducibility (CoRR)	1692	–	6–88	Yes	No	No	No	Unknown	10.1038/sdata.2014.49
Southwest University Longitudinal Imaging Multimodal (SLIM) study	580	–	17–27	Yes	Yes	Yes	Yes	Unknown	10.1038/sdata.2017.17
Rumination fMRI Dataset	42	–	18–35	Yes	No	No	No	No	10.1016/j.neuroimage.2020.117185
Chinese Human Connectome Project (CHCP)	250	–	19–37	Yes	Unknown	Unknown	Unknown	Unknown	10.1016/j.neuroimage.2019.116318.
Chinese paediatric population (CHN-PD)	328	–	6–12	Yes	Yes	Unknown	Unknown	Unknown	10.1016/j.neuroimage.2019.01.006

<sup>a</sup>Accessibility to the dataset is subjected to regulations on scientific data of China ([http://www.gov.cn/zhengce/content/2018-04/02/content\\_5279272.htm](http://www.gov.cn/zhengce/content/2018-04/02/content_5279272.htm)) and individual cohort consortium.

Efforts to establish patient cohorts were also initiated (Table 1). One ongoing imaging genetic cohort is the Zhangjiang International Brain BioBank (ZIB) based at Fudan University. Participants in the ZIB constitute six cohorts, including patients with schizophrenia, major depressive disorder, autism spectrum disorder, stroke, neurodegenerative disorders and healthy university students. To date, 2143 subjects took part in the study and completed 1866 brain scans, 1491 blood samples, 2143 sets of behavioural questionnaires, 1143 sets of neurocognitive batteries and 619 gut microbiota samples. The ZIB aims to reach 12 000 participants by 2023, making it the world's largest Chinese population dataset for neuropsychiatric research. Another project, the REST-meta-MDD consortium collated resting-state functional MRI data from 1300 patients with major depressive disorder and 1128 healthy controls from 25 sites across China (Yan et al., 2019).

### Brain banks

Brain banks are invaluable resources to investigate neurological and psychiatric disorders. Researchers can perform histological, genetic sequencing and molecular profiling studies based on post-mortem brain tissues, yielding pathological information that is otherwise difficult to obtain (Kretschmar, 2009). There are hundreds of brain banks worldwide, including the BrainNet Europe (<https://www.brainnet-europe.org>), Australian Brain Bank Network (<http://www.austbrainbank.org.au/index.html>), US NIH NeuroBioBank (<https://neurobiobank.nih.gov>) and UK Brain Banks Network (<https://brainbanknetwork.ac.uk/>), etc. The China Brain Bank Consortium was set up in 2016, and released the Standardized Operational Protocol for brain tissue acquisition, processing and preservation (Qiu et al., 2019). Over the years, dozens of brain banks have been established in China (Wang et al., 2019a, b, c, d). Xiangya Hospital of Central South University started the first brain bank in China in 2004 (Cao et al., 2020). Two national human brain banks, one in Zhejiang University collected about 200 human brain samples with healthy and neuropsychiatric disorders. The other national brain bank based in Peking Union Medical College has received 181 healthy samples, samples from 34 donors with dementia and 38 donors with other brain disorders by 2019 (Zhang et al., 2018a, b). The Shanghai brain bank has collected about 50 postmortem brain samples in the past 3 years (Li et al., 2021).

Although initiation of large-scale research cohorts and brain banks started relatively late in China, they will constitute important platforms for neuroscience research in the near future. Datasets from China will facilitate international collaborations and increase both ethnic diversity and sample sizes of healthy participants and patients with varying kinds of brain disorders (Poo et al., 2016).

### Healthcare systems

#### Integrated hospital and community-based healthcare systems

Mental healthcare service is undergoing a transition from hospital-centred service mode to an integration of hospital and community-based service mode worldwide (Liang et al., 2018; Luo et al., 2017). Community-based treatment has been shown to reduce the number of relapses and chances of re-admission to hospitals (Luo et al., 2019). The community mental healthcare system in China is developed with the launch of a public health

project, the 'Central Government Support for the Local Management and Treatment of Severe Mental Illnesses' in 2004. The project allocated 6.86 million Chinese yuan (\$829 000 in 2004 US dollars) to nationwide mental health service centres for the management of patients with severe mental disorders, and was thus referred to as the '686 Project' (Ma, 2012). The amount of funding quickly reached 473.39 million yuan in 2014 (accumulated funding: 943.41 million yuan) (Liang et al., 2018). The goal of '686 Project' was to provide free standardized antipsychotics and community-based follow-up visits to patients with severe mental disorders, as well as to build a team of specialists consisting of psychiatrists, nurses, psychologists and social workers to support patients and their families (Ma et al., 2011). The '686 Project' is a demonstration of a government-led, community-based integrated mental health service model in China.

With the implementation of the nationwide community-based healthcare system, a National Information System for Psychosis was established in 2011, to provide a reference for policy making and services delivering (Wu et al., 2017). According to this system, there are 6 million patients with psychosis (0.43% of the population) registered to the system by the end of 2018. Among the registered patients, 81.30% were under medications, and 80.60% of patients were in stable stages. Mean untreated periods of schizophrenia, delusional psychosis, schizoaffective disorder and bipolar disorder were 3.54, 4.61, 2.73 and 3.18 years, respectively (Wang et al., 2020a, b). The registration and management rate of psychosis patients have been increasing since 2014.

#### Early identification and prevention schemes

Another focus of mental healthcare is prevention and early treatment of psychiatric disorders (Beddington et al., 2008). For psychosis, many studies investigated neural and cognitive deficits in subjects with subclinical psychotic symptoms or with familial risk for psychosis (Cannon et al., 2016; Cornblatt et al., 2003; Fusar-Poli et al., 2013) to identify early pathological changes and targets for prediction and intervention (Addington et al., 2015; Simon et al., 2007). The Shanghai Mental Health Center launched the Shanghai At Risk for Psychosis (SHARP) programme, which recruited 517 individuals at clinical high risk for psychosis (Zhang et al., 2020a, b). The authors showed that 24% of high-risk individuals converted to psychosis in 2 years (Zhang et al., 2021), with a higher conversion rate in a subgroup of high-risk individuals with extensive negative symptoms and cognitive deficits (Zhang et al., 2020a, b). Individual risk for transition to psychosis can be predicted using clinical symptoms and cognitive functioning scores with good discriminative power (area under the curve of ROC = 0.78) (Zhang et al., 2018a, b, 2021).

### Strengths and challenges for mental health research and services

#### Growing funding investment and interdisciplinary research centres

Brain science and brain-inspired technology have been raised to the national strategic level in the 13th Five-Year Plan for Science and Innovation (The State Council, 2016). The increasing rate of gross domestic spending on research and development (R&D) in China is quickly catching up with the USA (Organisation for Economic Co-operation and Development, 2020). During 2011–2015, the National Key Basic Research



Program of China (973 Program) funded 50 neuroscience projects, amounting to one billion Chinese yuan (approximately 0.15 billion US dollars) (Wang *et al.*, 2016a, b). To promote research translation and application to clinical services, China has set up 50 National Clinical Research Centres as collaborative research networks between hospitals, research institutes and universities since 2013 (Ministry of Science and Technology, 2013). Three National Clinical Research Centres for mental disorders were founded.

### *International collaborations*

Investment in research funding can drive an increase in the number of publications, yet the impact of research is more closely related to the extent of international cooperation (Wagner & Jonkers, 2017). The current outbreak of coronavirus disease 2019 (COVID-19) demonstrates the vital importance of sharing scientific information and initiating concerted plans across countries to combat the pandemic (Rourke, Eccleston-Turner, Phelan, & Gostin, 2020), including its effects on mental health (Vatansever, Wang, & Sahakian, 2021). Research collaborations in China are growing at a rapid speed: the number of international co-authorship publications rose from 16 000 in 2006 to 71 000 in 2015 (Zhou *et al.*, 2019). The National Natural Science Foundation of China (NSFC), the main governmental funding agency, funded 1140 International (Regional) Cooperation and Exchange Programs in 2019, amounting to 1 billion Chinese yuan (0.15 billion US dollars) (Tian *et al.*, 2020). International collaborations on research and clinical services are both active; for example, the Institute of Science and Technology for Brain-inspired Intelligence (ISTBI) of Fudan University established long-term collaborations with research teams from the University of Cambridge, the University of Oxford, King's College London and the University of Sydney. The Shanghai Institute of Mental Health formed partnerships with leading psychiatric hospitals such as the Massachusetts General Hospital and the Maudsley Hospital to collaborate on research and training projects (Barako, Li, & Yeung, 2019). Among the top 10 research institutes in China, international collaborations account for 30–45% of all research output (Springer Nature, 2020).

### *Insights from traditional Chinese medicine*

Traditional Chinese medicine (TCM) is an integral part of healthcare system in China. According to the National Bureau of Statistics, China has 4221 TCM hospitals in 2019, consisting of 12.3% of the medical service capacity (National Bureau of Statistics, 2019). Consultation to TCM is high among patients with mental disorders, because of its general acceptance, low stigmatization, perceived low costs and less side effects (Thirthalli *et al.*, 2016). TCM has different forms including herbal medicine, acupuncture, moxibustion and qigong, etc. The therapeutic effect often relies on polypharmacological interactions of the ingredients and the philosophy of taking mind and body as a whole. Based on previous reviews and meta-analyses (Thirthalli *et al.*, 2016; Ulett, Han, & Han, 1998; Wang *et al.*, 2019a, b, c, d), studies showed promising effects of TCM, such as acupuncture and Chinese herbs, in alleviating psychiatric symptoms, although high-quality studies are needed to confirm the conclusion. The potential efficacy of TCM can be understood by analysing bioactive compounds of herbal medicines. For example, a study analysed 15

herbal medicines targeting neurodegenerative disorders and found a large overlap of chemical compounds between herbal medicines and standard treatment of neurodegenerative disorders (Tang, Ye, Feng, & Quinn, 2016). The discovery of artemisinin extracted from Chinese medicine to treat malaria is a good example that investigation into TCM with known efficacy may be a promising strategy to develop novel treatment against mental disorders (Tu, 2016).

### *Promoting research quality and open science*

Although China has been the second most prolific country in yearly neuroscience publications (Fig. 1c), Chinese researchers still face the challenge to promote research quality and increase the level of transparency. The growth of high-impact publications is slower than the rise of overall publication numbers (Leydesdorff, Wagner, & Bornmann, 2014). The quality of randomized controlled trials is also of concern in clinical studies, especially those published in domestic journals (Tong, Li, Ogawa, Watanabe, & Furukawa, 2018). In order to respond to these challenges, the government has been reforming the academic evaluation system that placed much emphasis on the number of publications (Qiu, 2010), and has announced strict regulations against academic fraud (Normile, 2017). Meanwhile, to promote open research, China initiated the construction of national data sharing platforms since 2001 (Chen & Li, 2020), and established 20 National Scientific Data Centres and 30 Biological Materials Resource Banks by 2019 (Ministry of Science and Technology, 2019). If effectively implemented, these measures and resources will improve research quality in China over the long term.

### *More equitable distribution of healthcare resources*

Although mental healthcare expenditure in underdeveloped areas is increasing every year since the implementation of the '686 Project', there is still a large disparity in terms of medical resources between urban and rural areas (Liang *et al.*, 2018). Highly trained professionals and financial support are heavily centred in Southeast provincial hospitals, whereas township and rural area clinics – the primary healthcare system, often lack professionals and facilities to provide high-quality medical services.

Another challenge is insufficient research and clinics for specific subgroups of population. For example, due to rapid urbanization and internal migration, China has approximately 68.8 million left-behind children, and 54.9 million are in rural areas (Duan, Lai, & Qin, 2017). Left-behind children have a higher risk for emotional and behavioural difficulties and are more likely to encounter school bullying (Fellmeth *et al.*, 2018; Tang *et al.*, 2018a, b). Another group of people in need of more healthcare resources is China's 55 ethnic minorities, constituting 8.5% of the national population. Many minority groups live in traditional rural areas where healthcare services are insufficient. They are also vulnerable to the adverse effects of rapid social and economic changes (Yang *et al.*, 2017a, b).

### *Reducing stigma and raising public awareness of mental disorders*

Stigmatization and discrimination against mental disorders are common impediments that prevent individuals seeking help from professionals (Patel *et al.*, 2016). This may be particularly prominent in China, as the collectivism culture may aggravate

the self-stigmatization of patients and their family members (Yang & Kleinman, 2008). The consultation rate in the Psychiatry Department is low in China. An early epidemiological study conducted in Beijing and Shanghai from 2001 to 2002 reported that only 3.4% of psychiatric patients sought treatment in the previous 12 months (Shen et al., 2006). In another study performed during 2001–2005, 8% of patients with mental disorders ever sought professional help, and only 5% had ever seen a mental health care professional (Phillips et al., 2009). Delayed treatment could result in prolonged illness and worse prognosis, as indicated by studies examining the effects of the duration of untreated psychosis (Allott et al., 2018; Marshall et al., 2005).

Mental health literacy is defined as 'knowledge and beliefs about mental disorders which aid their recognition, management or prevention' (Jorm, 2000). Better mental health literacy can increase the rate of detection and treatment of psychiatric disorders and promote help-seeking behaviours. A study showed that compared with Australian people, Chinese people (sampled from Shanghai, Hong Kong, Taiwan and Australia) generally had a lower level of recognition of depression (12.1–24.4% *v.* 73.9%) and early schizophrenia (6.0–21.2% *v.* 37.90%) (Wong et al., 2017). To increase mental health literacy and reduce stigmatization against psychiatric disorders, more efforts should be spent on educational campaigns and psychological interventions for the general public and patients with mental disorders (Xu, Huang, Kösters, & Rüsche, 2017; Xu, Rüsche, Huang, & Kösters, 2017).

## Conclusions

In summary, significant progress has been made in research and healthcare for psychiatric disorders in China. Specifically, a nationwide epidemiological survey suggested a lifetime prevalence of 16.6% for mental disorders. Genetic and neuroimaging studies in Chinese populations expanded the ethnic diversity of neuroscience research and elucidate neuropathological changes in patients with specific clinical characteristics. Ongoing efforts are devoted to establish large-scale research cohorts and brain banks in Chinese populations. Regarding clinical services, community-based healthcare is being integrated into hospital-centred healthcare systems to provide continuous support to patients. Early prevention and intervention is a new focus in mental healthcare. These achievements in research and clinical services are indispensable to growing funding investment and continued engagement in international collaborations. Knowledge from TCM may provide insights into drug development for psychiatric disorders. Meanwhile, we acknowledge existing challenges such as efforts are still needed to improve research quality and to equally distribute healthcare resources. With ongoing efforts, we expect to see continued improvement in research and clinical services for psychiatric disorders. These achievements will contribute to global efforts to understand the neurobiological basis of psychiatric disorders and to devise novel, more effective treatments, so that all individuals can reach their potentials and flourish in society.

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