Supplementary information of

**Psychiatric Disorders in China: Strengths and Challenges of Contemporary Research and Clinical Services**

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# Table S1 Reviews and meta-analyses on genetic research in the Chinese population

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| **Year** | **Authors** | **Title** | **Journal/Book** | **Disorders** | **Methods** | **Results** |
| 2020 | Ming et al. | Advances in the genetics of cognitive impairment in schizophrenia (in Chinese) | Chin J Behav Med Brain Sci | schizophrenia | review | -- |
| 2014 | Yang et al. | DNA methylation and depression (in Chinese) | Chin J Behav Med Brain Sci | major depressive disorder | review | -- |
| 2008 | Deng et al. | Progress in genetic studies of bipolar disorder (in Chinese) | Journal of Shantou University Medical College | bipolar disorder | review | -- |
| 2015 | Lu et al. | The Efficacies and Toxicities of Antidepressant Drugs in Clinics, Building the Relationship between Chemo-Genetics and Socio-Environments | Cent Nerv Syst Agents Med Chem | major depressive disorder | review | -- |
| 2014 | Gao et al. | Advances in molecular genetic studies of attention deficit hyperactivity disorder in China | Shanghai Arch Psychiatry | attention deficit hyperactivity disorder | review | -- |
| 2013 | Sun et al. | Advances in genetic studies of substance abuse in China | Shanghai Arch Psychiatry | substance abuse | review | -- |
| 2012 | Cui D, Jiang K. | Research in China on the molecular genetics of schizophrenia | Shanghai Arch Psychiatry | schizophrenia | review | -- |
| 2010 | Fu et al. | A selected review of recent biological psychiatric research in China (translated version) | East Asian Archives of Psychiatry | multiple psychiatric disorders | review | -- |
| 2008 | Li J. | Recent progress in the research field of neuropharmacology in China | Cellular and Molecular Neurobiology | multiple psychiatric disorders | review | -- |
| 2005 | Tosato et al. | Association between the neuregulin 1 gene and schizophrenia: A systematic review | Schizophrenia Bulletin | schizophrenia | review | -- |
| 2003 | Collier DA, Li T. | The genetics of schizophrenia: glutamate not dopamine? | Eur J Pharmacol | schizophrenia | review | -- |
| 2012 | Hung et al. | Monoamine oxidase A gene polymorphism and suicide: an association study and meta-analysis | J Affect Disord | suicide | Specific gene: MAOA-uVNTR | No significant association was identified between MAOA-uVNTR polymorphism and suicide attempts in Chinese Han people with psychiatric disorders, or using meta-analysis with previous studies of mixed ethnic groups |
| 2016 | Li et al. | Significant association of GRM7 and GRM8 genes with schizophrenia and major depressive disorder in the Han Chinese population | Eur Neuropsychopharmacol | schizophrenia and major depressive disorder | Specific gene: GRM7 and GRM8 | Significant associations were found between polymorphisms of GRM7, GRM8 and schizophrenia and depression in Chinese Han population. Gene–gene interaction analysis suggested interactive effects of these two genes for both disorders |
| 2016 | Zhang et al. | A comprehensive analysis of NDST3 for schizophrenia and bipolar disorder in Han Chinese | Transl Psychiatry | schizophrenia and bipolar disorder | Specific gene: NDST3 | Polymorphism of NDST3 (rs11098403) showed a significant association with schizophrenia, but not with bipolar disorder in Chinese Han population. The eQTL analysis further suggested that a nominal significant association between rs11098403 and NDST3 expression level in the hippocampus. |
| 2020 | Chen et al. | A comprehensive analysis of GSK3B variation for schizophrenia in Han Chinese individuals | Asian J Psychiatr | schizophrenia | Specific gene: GSK3B | GSK3B (rs3755557) polymorphism may confer susceptibility to schizophrenia and cognitive dysfunction in Han Chinese individuals. |
| 2018 | Guo et al. | Proline dehydrogenase gene (PRODH) polymorphisms and schizophrenia susceptibility: a meta-analysis | Metab Brain Dis | schizophrenia | Specific gene: PRODH | PRODH (rs372055) polymorphisms is associated with schizophrenia in Asian but not in Caucasian population |
| 2018 | Yang et al. | Genetic association and meta-analysis of a schizophrenia GWAS variant rs10489202 in East Asian populations | Transl Psychiatry | schizophrenia | Specific gene: MPC2 (rs10489202) | The rs10489202 polymorphisms is associated with schizophrenia in East Asian populations. The eQTL analysis also showed that rs10489202 variant is associated with the expression of TIPRL gene. |
| 2018 | Zhao et al. | Genetic Association of the Norepinephrine Transporter Gene G1287A Polymorphism with Risk of Schizophrenia: A Case-Control Study and Meta-Analysis | Genet Test Mol Biomarkers | schizophrenia | Specific gene: norepinephrine transporter G1287A | No association was found between G1287A polymorphisms and schizophrenia in Chinese Han population. |
| 2018 | Zhang et al. | Meta-analysis of GABRB2 polymorphisms and the risk of schizophrenia combined with GWAS data of the Han Chinese population and psychiatric genomics consortium | PLoS One | schizophrenia | Specific gene: GABRB2 | No association was found between GABRB2 polymorphisms and schizophrenia in the combined dataset of Chinese Han population and Psychiatric Genomics Consortium or in stratified ethinic subgroups. |
| 2017 | Li et al. | Association of NKAPL, TSPAN18, and MPC2 gene variants with schizophrenia based on new data and a meta-analysis in Han Chinese | Acta Neuropsychiatr | schizophrenia | Specific gene: NKAPL, TSPAN18, MPC2 | No significant associations were found between polymorphism of NKAPL (rs1635), TSPAN18 (rs11038167), and MPC2 (rs10489202) and schizophrenia risk in a combined sample of Chinese Zhuang and Han ethnicities. Meta-analysis suggested a significant association between MPC2 (rs10489202) and schizophrenia only in Han population |
| 2016 | Xiao X, Li M. | Replication of Han Chinese GWAS loci for schizophrenia via meta-analysis of four independent samples | Schizophr Res | schizophrenia | previous GWAS significant loci in Chinese Han population | Among nine GWAS significant loci reported in a previous study of Chinese Han population, one loci MPC2 (rs10489202) was significant in the independent replication sample. Only two SNPs achieved nominal significance in the PGC 2 samples |
| 2015 | Wang et al. | Further evidence supporting the association of NKAPL with schizophrenia | Neurosci Lett | schizophrenia | Specific gene: NKAPL | Significant associations were found between polymorphisms of NKAPL (rs1635) and schizophrenia in Chinese Han population. |
| 2015 | Zhang et al. | Lack of Association between the TSPAN18 Gene and Schizophrenia Based on New Data from Han Chinese and a Meta-Analysis | Int J Mol Sci | schizophrenia | Specific gene: TSPAN18 | No significant association was identified between TSPAN18 gene polymorphisms and schizophrenia in the Chinese Han patients |
| 2015 | Wang et al. | Meta-Analyses of Manganese Superoxide Dismutase Activity, Gene Ala-9Val Polymorphism, and the Risk of Schizophrenia | Medicine (Baltimore) | schizophrenia | Specific gene: MnSOD gene Ala-9Val | No significant association was identified between manganese superoxide dismutase (MnSOD) gene Ala-9Val and schizophrenia in meta-analysis of mixed ethnic groups. However, MnSOD activity of patients was significantly lower than that of controls in the chronic Chinese patients |
| 2014 | Ma et al. | Association of a miRNA-137 polymorphism with schizophrenia in a Southern Chinese Han population | Biomed Res Int | schizophrenia | Specific gene: miRNA-137 | Significant associations were found between miR-137 gene (rs1625579) polymorphisms and schizophrenia in a group of Southern Chinese Han population. Besides, miR-137 polymorphism also influences working memory performance of patients. |
| 2013 | Qin et al. | Lack of association between TNFα rs1800629 polymorphism and schizophrenia risk: a meta-analysis | Psychiatry Res | schizophrenia | Specific gene: TNFα-308G/A | No significant association was identified between TNFα-308G/A (rs1800629) and schizophrenia using meta-analysis of mixed ethnic groups. The negative results still hold in subgroup analyses by ethnicity and gender |
| 2013 | Ni et al. | T102C polymorphism of serotonin 2A type receptor gene confers susceptibility to (early onset) schizophrenia in Han Chinese: an association study and meta-analysis | Asia Pac Psychiatry | schizophrenia | Specific gene: HTR2A T102C | Significant associations were found between T102C polymorphism and schizophrenia in a group of early onset Chinese Han population. Meta-analysis with previous studies in Chinese Han population confirmed this finding. |
| 2012 | Yuan et al. | Effect of SOX10 gene polymorphism on early onset schizophrenia in Chinese Han population | Neurosci Lett | schizophrenia | Specific gene: SOX10 | Significant associations were found between SOX10 Gene (rs139887) polymorphism and schizophrenia in Chinese Han population. Subsequent analysis showed the association was significant only in males, but not in females. |
| 2012 | Yuan et al. | ANK3 as a risk gene for schizophrenia: new data in Han Chinese and meta analysis | Am J Med Genet B Neuropsychiatr Genet | schizophrenia | Specific gene: ANK3 | Signiant differences were found between Chines Han patients with schizophrenia and controls at the ANK3 Gene (rs10761482 and rs10994336). Further family-based analysis and meta-analysis confirmed the association of ANK3 Gene and schizophrenia. |
| 2009 | Che et al. | No relationship between 2',3'-cyclic nucleotide 3'-phosphodiesterase and schizophrenia in the Chinese Han population: an expression study and meta-analysis | BMC Med Genet | schizophrenia | Specific gene: CNP | No significant association was identified between CNP gene polymorphism and schizophrenia in Chinese Han population, or using meta-analysis with previous studies of mixed ethnic groups. |
| 2007 | Qian et al. | Brain-derived neurotrophic factor and risk of schizophrenia: an association study and meta-analysis | Biochem Biophys Res Commun | schizophrenia | Specific gene: BDNF | No significant association was identified between BDNF gene and schizophrenia in Chinese Han population, or using meta-analysis with previous studies of mixed ethnic groups. Yet, haplotype analysis revealed a common four-locus haplotype (A-274-C-T) is protective against schizophrenia. |
| 2006 | Guo et al. | RGS4 polymorphisms and risk of schizophrenia: an association study in Han Chinese plus meta-analysis | Neurosci Lett | schizophrenia | Specific gene: RGS4 | No significant association was identified between RGS4 gene and schizophrenia in Chinese Han population, or using meta-analysis with previous studies of mixed ethnic groups. |
| 2006 | Ma et al. | Further evidence for the association between G72/G30 genes and schizophrenia in two ethnically distinct populations | Mol Psychiatry | schizophrenia | Specific gene: G72/G30 | A significant association was found between G72/G30 Gene (rs779293) polymorphism and schizophrenia in Chinese Han population, and replicated in a Scottish sample. Meta-analysis indicated the association was significant in Asian populations, but not in European populations. |
| 2005 | Fan et al. | Catechol-O-methyltransferase gene Val/Met functional polymorphism and risk of schizophrenia: a large-scale association study plus meta-analysis | Biol Psychiatry | schizophrenia | Specific gene: COMT | A significant association was found between G72/G30 Gene (rs779293) polymorphism and schizophrenia in Chinese Han population, and replicated in a Scottish sample. Meta-analysis indicated the association was significant in Asian populations, but not in European populations. |
| 2002 | Lung et al. | Ethnic heterogeneity in allele variation in the DRD4 gene in schizophrenia | Schizophr Res | schizophrenia | Specific gene: DRD4 | No significant association was identified between DRD4 gene and schizophrenia using meta-analysis of mixed ethnic groups. Yet stratified analysis showed a significant association in Caucasian, but not in Asian population. |
| 2015 | Tang et al. | No association between wolframin gene H611R polymorphism and mood disorders: evidence from 2,570 subjects | Nord J Psychiatry | mood disorders | Specific gene: WFS1 gene H611R | No significant association was identified between WFS1 gene H611R and mood disorders using meta-analysis of mixed Caucasian and Asian populations. Further analyses by ethnic groups or by types of mood disorders also revealed negative results |
| 2012 | Zou et al. | Association of DRD2 gene polymorphisms with mood disorders: a meta-analysis | J Affect Disord | mood disorders | Specific gene: DRD2 | Meta-analysis of mixed Caucasian and Asian populations showed an association between DRD2 Gene (TaqI A1) with mood disorders. However, no associations were found in two other loci of DRD2 Gene (-141Cins/del, Ser311/Cys311) and mood disorders. |
| 2020 | Zhao et al. | The association between polymorphism of norepinephrine transporter G1287A and major depressive disorder, antidepressant response: a meta-analysis | Psychiatr Genet | major depressive disorder | Specific gene: norepinephrine transporter G1287A | G1287A polymorphisms is related to risk for major depressive disorder and antidepressant response in the Chinese Han population and Asian population |
| 2018 | Rui et al. | Meta-analysis on the Association Between Norepinephrine Transporter Gene rs2242446, rs5569 Polymorphisms and Risk of Major Depressive Disorder | Arch Med Res | major depressive disorder | Specific gene: norepinephrine transporter (NET) gene | NET (rs5569, but not rs2242446) polymorphism is significantly associated with MDD in the Asian population |
| 2018 | Tang et al. | SIRT1 rs3758391 and Major Depressive Disorder: New Data and Meta-Analysis | Neurosci Bull | major depressive disorder | Specific gene: SIRT1 | SIRT1 expression is significantly down-regulated in Chinese Han patients with major depressive disorder. The rs3758391 polymorphism is associated with SIRT1 expression level. |
| 2017 | Liu et al. | The gender-specific association of rs334558 in GSK3β with major depressive disorder | Medicine (Baltimore) | major depressive disorder | Specific gene: GSK3b | Meta-analysis of studies from Korea and China suggested that rs334558 polymorphism within the GSK3b promoter region was associated with risk for major depressive disorder. In a sample of Chinese patients, the association remained significant only in female patients. |
| 2016 | Jiang et al. | Association between MTHFR C677T polymorphism and depression: a meta-analysis in the Chinese population | Psychol Health Med | major depressive disorder | Specific gene: MTHFR C677T | Meta-analysis of Chinese Han population showed significant association between MTHFR C677T polymorphism and risk for major depressive disorder. Thus effect is stronger in North China than South China population |
| 2012 | Gao et al. | TPH2 gene polymorphisms and major depression--a meta-analysis | PLoS One | major depressive disorder | Specific gene: TPH2 | Significant associations were found between TPH2 Gene (rs4570625) polymorphism and major depressive disorder using meta-analysis of mixed ethnic groups of patients with major depressive disorder |
| 2016 | Gao et al. | TPH2 gene polymorphisms and bipolar disorder: A meta-analysis | Am J Med Genet B Neuropsychiatr Genet | bipolar disorder | Specific gene: TPH2 | Meta-analysis of mixed ethnic groups showed a significant association between TPH2 (rs4760820 and rs11178998) polymorphisms in association with bipolar disorder |
| 2014 | Chen et al. | Meta-analysis demonstrates lack of association of the GSK3B -50C/T polymorphism with risk of bipolar disorder | Mol Biol Rep | bipolar disorder | Specific gene: GSK3B-50C/T | No significant association was identified between GSK3B-50C/T (rs334558) and bipolar disorder using meta-analysis of mixed ethnic groups. Further analyses by ethnicity also showed negative results |

# Table S2 Reviews and meta-analyses on neuroimaging research in the Chinese population

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Year** | **Authors** | **Title** | **Journal/Book** | **Disorders** | **Methods** | **Results** |
| 2011 | Chen J., Shi S. | A review of neuroimaging studies of anxiety disorders in China | Neuropsychiatric Disease and Treatment | anxiety disorder | T1, rs-fMRI, DTI, PET, SPECT, MRS | Patients with general anxiety disorder (GAD) and/or panic disorder (PD) showed reduced regional cerebral blood flow (rCBF) in the frontal lobe and temporal lobe as well as abnormal activation in viewing emotional images.  Patients with obsessive-compulsive disorder (OCD) exhibited abnormal perfusion in several brain regions. Studies of PTSD indicate that the decreased hippocampal volume and NAA level in hippocampus. |
| 2020 | Wang et al | Large-scale network dysfunction in the acute state compared to the remitted state of bipolar disorder: A meta-analysis of resting-state functional connectivity | EBioMedicine | biploar disorder | rs-fMRI | Patients in acute state showed decreased connectivity within the affective network (AN) but not in the remitted state. Meanwhile, patients exhibited decreased connectivity within the default mode network in the acute state and increased connectivity in the remitted state. Different patterns of between-network dysconnectivity were also observed between the acute and remitted states. |
| 2018 | Tang et al. | Abnormal amygdala resting-state functional connectivity in adults and adolescents with major depressive disorder: A comparative meta-analysis | EBioMedicine | major depressive disorder | rs-fMRI | Adult patients with major depressive disorder (MDD) showed specific functional connectivity abnormalities between the amygdala and affective network (parahippocampus, ventromedial orbitofrontal cortex, insula and caudate), whereas adolescent patients with MDD have more apparent dysconnectivity between the amygdala and cognitive control network and default mode network |
| 2015 | Iwabuchi et al | Localized connectivity in depression: a meta-analysis of resting state functional imaging studies | Neurosci Biobehav Rev | major depressive disorder | rs-fMRI | Patients with depression had significantly increased ReHo in the medial superior frontal gyrus and left fusiform gyrus, as well as decreased ReHo in the left cerebellum, fusiform gyrus, left postcentral gyrus (BA4), left rolandic operculum (BA47), superior temporal gyrus, right cuneus (BA18), and rightinferior parietal gyrus (BA40). |
| 2014 | Yin Y, Yuan Y. | Neuroimaging studies of depressive disorders in China since 2000 | Shanghai Arch Psychiatry | major depressive disorder | T1, rs-fMRI, imaging-genetics |  |
| 2015 | Smith DF. | Systematic review of an emerging trend in china: resting-state functional connectivity in major depressive disorder | J Neuropsychiatry Clin Neurosci | major depressive disorder | rs-fMRI | Increasing number of neuroimaging studies from China focus on major depressive disorder, yet inconsistence exist between studies. Some studies chose to investigate patients with specific clinical characteristics, such as first-episode, treatment-naïve patients, treatment-resistant patients, elderly patients and patients with suicide attempts, traumatic experience or somatically disorders. |
| 2014 | Wei et al. | Review on Neuropsychological Mechanism and Cerebral Imageology Study of Executive Dysfunction of Depression Patients (in Chinese) | Journal of Zhejiang Chinese Medical University | major depressive disorder | fMRI, MRS | Patients with major depressive disorder exhibited deficits in excutive funtions measured by WCST and Stroop tasks, which are related to dysfunction in DLPFC, ACC and OFC. |
| 2016 | Liu et al. | Distinguishing role of brain imaging between unipolar depression and bipolar depression (in Chinese) | Chin J Behav Med&Brain Sci | mood disorder | T1, rs-fMRI, DTI | Patients with biplolar disorder exhibit more widespread neural abnormalities than patients with unipolar depression. |
| 2011 | McAlonan et al. | Is there an anatomical endophenotype for neurodevelopmental disorders? A review of dual disorder anatomical likelihood estimation (ALE) meta-analyses of grey matter volumes | Chinese Science Bulletin | multiple psychiatric disorders (schizophrenia, biploar disorder, autism) | T1 | The authors proposed an dual disorder anatomical likelihood estimation (ALE) meta-analyses method to explore shared structural abnormalities between schizophrenia and bipolar disorder and between schizophrenia and autism. |
| 2013 | Fan Q., Xiao Z. | Neuroimaging studies in patients with obsessive-compulsive disorder in China | Shanghai Archives of Psychiatry | obsessive-compulsive disorder | T1, rs-fMRI, DTI, PET, SPECT, MRS | Patients with obsessive-compulsive disorder (OCD) showed abnormalities grey and white matter in the prefrontal, corpus striatum and thalamus. PET, fMRI and MRS studies showed increased metabolism and activation in above regions, which were normalized after surgery treatment. |
| 2014 | Liu et al. | Advances in neuroimaging research of schizophrenia in China | Shanghai Arch Psychiatry | schizophrenia | T1, fMRI, DTI, MRS | -- |
| 2018 | Liu et al. | Research Progress in Biological Studies of Schizophrenia in China in 2017 | Shanghai Arch Psychiatry | schizophrenia | rs-fMRI, DTI, imaging genetics | -- |
| 2015 | Shen et al. | Brain structural imaging study in schizophrenia patients with violent aggressive behaviors (in Chinese) | Chin J Behav Med&Brain Sci | schizophrenia | T1 | Schizophrenia patients with aggressive behavior exhibit brain strucutral abnormalies in the frontal-temporal gyrus, hippocampus, amygdala, cerebellum and caudate nucleus |