Research progress in China on the assessment of cognitive function in schizophrenia

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Summary: Cognitive impairment – one of the core symptoms of schizophrenia – has become a focus of research about schizophrenia in China and elsewhere. The main reason for the interest in cognitive functioning is that the degree of cognitive impairment is associated both with the current severity of the illness and with the prognosis of the illness; cognitive functioning directly affects individuals’ ability to live independently and their occupational and social functioning. The first study on cognitive function in schizophrenia in China was conducted in the late 1970s; more recently there has been a resurgence of interest in the area because of new information that has emerged as neuroimaging technologies have improved. The current review summarizes studies on cognitive impairment in schizophrenia conducted in China and proposes directions for future research in this area.

1. Major cognitive impairments in individuals with schizophrenia

Kraepelin and Bleuler were the pioneers of studying cognitive impairment in schizophrenia. Kraepelin labeled schizophrenia ‘dementia praecox’ and described the three main characteristics of the disorder: early onset (in adolescence or young adulthood), chronic course of illness, and declining social functioning.[1-3] Although the positive symptoms of schizophrenia have been the focus of psychiatrists since the emergence of antipsychotic drugs in the 1950s, cognitive impairment in schizophrenia regained attention in the international scientific community in the 1990s.[2,4] In China, research on the cognitive functioning of patients with schizophrenia started in 1978, when Gong[5] reported impaired short-term memory among patients with schizophrenia using the free recall paradigm. In the same year, Zhu and colleagues[6] reported that ventricular expansion in patients with schizophrenia was significantly correlated with cognitive impairment. Since then, many studies about cognitive function in schizophrenia have emerged in China, most of which have focused on attention, learning and memory, working memory, executive functioning and social cognition.

1.1 Attention

Attention is the cognitive process that involves the selective focusing of awareness and processing of information. Several studies in China highlight a familial (i.e., genetic) relationship between attention deficits and schizophrenia. Liu and colleagues[7] found deficits in active attention (assessed using the backward masking test) among healthy siblings of individuals with schizophrenia that were intermediate between the deficits identified in individuals with schizophrenia and those in community members without siblings with schizophrenia. Similarly, studies using the Continuous Performance Test found decrements in sustained attention in the siblings and parents of individuals with schizophrenia that were intermediate in severity between those of individuals with schizophrenia and those in community members without first degree relatives with schizophrenia.[8,9] Other research has found that the severity of the attention deficit in schizophrenia is not related to executive functioning, disease classification, or to the positive, negative or general pathology scores of the Positive and Negative Syndrome Scale (PANSS).[10,11]

Researchers who use the physical line bisection test report that left-sided attentional bias is observed in individuals with schizophrenia, suggesting dysfunction in the left hemisphere that results in impairment in their dextral spatial attention.[12,13] Our group has conducted a series of studies[14-18] about the mechanism underlying attention deficit using inhibition of return (testing visual attention with visual stimuli) and P50 sensory gating (testing auditory attention with auditory stimuli). We have found that (a) inhibition of return in individuals

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in their first episode of schizophrenia was better than that in individuals with chronic schizophrenia (who had delayed inhibition of return); and (b) individuals with first-episode schizophrenia and those with chronic schizophrenia had deficiencies in P50 sensory gating that were of comparable magnitude. Thus, attention deficit in individuals with schizophrenia may be related to impaired inhibition and the deficit in visual attention in these individuals may be unrelated to the deficit in auditory attention.

1.2 Learning and memory
Learning is the process of obtaining new information that is then stored in memory. Learning and memory are interrelated, but most research in individuals with schizophrenia in China has focused on memory rather than on learning. Several studies have shown that immediate memory, short-term memory and long-term memory are all impaired in individuals with schizophrenia. Most of the studies focus on long-term memory which is either classified as explicit versus implicit memory (based on the degree of consciousness of the memory) or as episodic, emotional or semantic memory (based on the content of the memory). Explicit memory is more severely affected in schizophrenia than implicit memory. Explicit memory is associated with the negative (not positive) symptoms of schizophrenia while implicit memory is independent of both negative and positive symptoms.

The impairment of episodic memory in individuals with schizophrenia can have a variety of manifestations. Previous studies have shown that source memory, item memory and emotional memory are all impaired in patients with schizophrenia. Another type of episodic memory, prospective memory – which allows individuals to remember to perform a planned action or intention at the appropriate time – is also severely impaired among individuals with schizophrenia. The degree of impairment in prospective memory can be an important indicator of the prognosis of schizophrenia because remembering follow-up appointments, the time and dose of medication, work schedules, and so forth is beneficial for recovery.

1.3 Working memory
Working memory, which is similar to but distinct from short-term memory, consists of a central executive system and two subsystems – the visuospatial sketch pad and the phonological loop. Working memory is a platform for the storage and executive control of information used to direct activities and other advanced cognitive functions such as learning, understanding and reasoning. Working memory can be categorized as verbal working memory or visuospatial working memory.

Using digit span performance and space span performance, Wang and colleagues found that there were impairments in verbal and visuospatial working memory in individuals with schizophrenia both before and after the age of 45. To evaluate patients’ information storage capacity, the revised Sternberg item recognition task has been widely used in China; the results of these studies suggest that the capacity for storing spatial information and information of objects decreases in individuals with schizophrenia.[36,37] While their capacity for storing language-coded information still remains normal.[38,39] However, using the alphabet edition and digital edition of the n-back task, Chinese researchers found that executive control of language-coded information used to direct activities is decreased in individuals with schizophrenia.[40,41]

1.4 Executive function
Executive function is the self-monitoring and self-control of consciousness and behavior. It includes self-regulation, cognitive flexibility, planning, reaction inhibition, and so forth. Due to the complexity of executive function, there is no standard evaluation tool for it. The evaluation tools commonly used in China are the Wisconsin Card Sorting Test (WCST), the Stroop color words test and the Tower of London task. WCST, the most commonly used test in China for executive function, is considered a measure of prefrontal functions.

Significant impairments in executive function have been found in individuals with first-episode schizophrenia and in those with chronic schizophrenia, both when taking antipsychotic medication and when not taking medication.[10,42-44] Furthermore, parents and siblings of individuals with schizophrenia have also been found to have impairments in executive function.[44,45] Results of the Stroop color words test and the Tower of London task indicated impaired conflict suppression and problem solving in individuals with schizophrenia.[46-48]

Other researchers have assessed the relationship between psychiatric symptoms and executive functioning. Zhao and colleagues compared the WCST results of individuals with schizophrenia who do and do not experienced auditory hallucinations; they found no significant difference except in the number of WCST categories completed (i.e., the CC index). Two studies explored the relationship of homicidal or aggressive behaviors and executive function: Wang found that individuals with schizophrenia who had homicidal behaviors did worse in abstract conceptualization than those without homicidal behaviors; and Wang found that among males with schizophrenia those with a history of aggressive behavior had worse executive function than those without a history of aggressive behavior.

1.5 Social cognition
Social cognition is an advanced cognitive process which involves many components that help inform an individual’s social actions: interpreting facial expressions, understanding psychological states and personalities, interpreting gestures and facial expressions, evaluating
behaviors in social interactions and comprehending the characteristics of interpersonal relationships. Studies conducted by researchers in other countries show that individuals with schizophrenia have impairments in social cognition. Chinese researchers are just starting to pay attention to this topic. Zhu and colleagues\(^{[52]}\) explored social cue recognition in individuals with schizophrenia using the eye gaze discrimination task, eye basic emotion discrimination task and faux pas recognition task; they found that individuals with schizophrenia had impairments in social cue recognition, some of which led to impairments in their social functioning. Using the Chinese facial emotion test, Xia and colleagues\(^{[53]}\) found that individuals with schizophrenia had pervasive impairments in facial emotion recognition which were associated with their deficits in executive function.

2. Factors associated with cognitive function in schizophrenia

2.1 Age

Generally speaking, cognitive function improves as children develop and reaches a peak during early adulthood, after which it declines. It is still uncertain whether or not cognitive function in individuals with schizophrenia declines with age more quickly than in the general population. Most studies in China find that the cognitive function of elderly individuals is more impaired in persons with schizophrenia than in age-matched controls.\(^{[54-56]}\) Several follow-up studies and a study comparing elderly individuals with schizophrenia to those with Alzheimer’s disease found that the pattern of cognitive decline with age in schizophrenia started at a somewhat earlier age and was, unlike the decline in Alzheimer’s disease, largely limited to the types of cognitive functions that had been most affected by their schizophrenia illness at an earlier age.\(^{[57-59]}\)

2.2 Course of the disorder

There is much debate about whether or not the course of schizophrenia affects individuals’ cognitive function and, if it is related, how the trajectory of the illness is related to changes in cognitive function. In some long-term follow-up studies, individuals with schizophrenia were found to suffer from aggravated cognitive impairments (particularly in immediate memory and language function) if they had more frequent acute episodes of illness, a relationship that was more evident among individuals with an earlier age of onset of schizophrenia.\(^{[60-63]}\) In contrast, other studies have reported that the cognitive function of individuals with schizophrenia is not affected by the course of the disorder.\(^{[64,65]}\)

2.3 Psychiatric symptoms

Most studies concur that cognitive impairment in individuals with schizophrenia is associated with psychiatric symptoms, especially negative symptoms.\(^{[67,68,66-68]}\) Niu and colleagues\(^{[69]}\) followed a group of individuals with first-episode schizophrenia for three years and found that at the end of the first and second years of treatment patients’ cognitive impairment was strongly associated with the severity of both positive and negative symptoms; even at the end of the third year of treatment most of their cognitive function indicators were still related to some of the positive and negative symptoms. Their findings support the association between cognitive impairments and psychiatric symptoms in schizophrenia.

2.4 Other factors

Shang and colleagues\(^{[70]}\) reported that cognitive function was less impaired in males with schizophrenia than in their female counterparts. However, later studies failed to confirm this gender effect.\(^{[71,72]}\) Other investigators have reported that hospitalization\(^{[73,74]}\) the metabolic syndrome, diabetes,\(^{[75-78]}\) tardive dyskinesia\(^{[79,80]}\) and smoking\(^{[81,82]}\) may also affect cognitive function in persons with schizophrenia.

3. Biological basis of cognitive impairment in individuals with schizophrenia

3.1 Neurotransmitter and genetic research

Cognitive impairment in individuals with schizophrenia is associated with abnormalities of neurotransmitters, for instance the dysfunction of the serotonin system, degeneration of Y-gaba neurons, norepinephrine deficiency, hyperfunction of the dopamine system and hypofunction of excitatory amino acids.\(^{[83]}\) In addition, oxidative stress,\(^{[84,85]}\) interleukin\(^{[86]}\) and 4-hydroxy-3-methoxyphenylacetic\(^{[87]}\) have also been associated with the cognitive impairment of individuals with schizophrenia.

In recent years genetic studies have identified some genotypes that are correlated with cognitive function in individuals with schizophrenia, including dopamine genes, 5-HT genes, apolipoprotein E (ApoE), brain derived neurotrophic factor (BDNF) genes, and so forth.\(^{[88-93]}\) One study\(^{[94]}\) found that the severity of the cognitive impairment in individuals with schizophrenia and in their relatives increased as the degree of genetic loading increased, suggesting that cognitive impairment could be a potential endophenotype to detect generic vulnerability to schizophrenia.\(^{[95]}\) However, none of these findings were successfully replicated in different populations, so further studies are needed.

3.2 Electrophysiological and eye movement research

3.2.1 Evoked potentials and event-related potentials (ERP)

The sensory gating of the brain is usually viewed as an automatic pre-attentional suppression mechanism that reduces responses to meaningless stimuli. The P50 auditory-evoked potential sensory gating is widely used to identify deficits in schizophrenia. Some
studies reported P50 deficits in both first-episode individuals with schizophrenia and in those with chronic schizophrenia, deficits that do not improve with the use of antipsychotic medications. Surprisingly, the sensory gating malfunction identified as a reduction in P50 suppression was not correlated with the results of other neuropsychological indicators; this suggests that P50 sensory gating is the result of different cognitive processes than the other types of cognitive deficits seen in schizophrenia, but further studies are needed to explore this possibility.

The P300 component of the event-related potential (ERP) is associated with the cognitive process involved in selective attention and the mismatch negativity (MMN) component of ERP is associated with the automatic detection of deviated stimuli when not attending to the stimuli. Studies have shown that P300 and MMN could be used as objective indicators of cognitive impairment in individuals with schizophrenia, especially memory. The N400 component of ERP is an indicator of the ability to comprehend verbal material; studies finding positive effects of antipsychotic treatment on N400 suggest that N400 could be used as a state marker for schizophrenia. Error-related negativity (ERN) provides an opportunity to objectively observe how the brain processes the perception of errors; the latent period and amplitude of ERN are abnormal in individuals with first-episode schizophrenia, suggesting that they have defects in the functioning of the cognitive mechanism that monitors errors.

3.2.2 Eye movement
Studies in China have confirmed previous findings that impairments in executive functioning and other cognitive functions in persons with schizophrenia are associated with abnormal eye movements. It was also found that eye movements in individuals with schizophrenia can be affected by the course of the illness and by pharmacological treatment of the illness. Hence, detailed assessment of eye movement abnormalities could be a potential auxiliary diagnostic method for schizophrenia.

3.3 Functional neuroimaging research
Single Photon Emission Computed Tomography (SPECT), Positron Emission Tomography (PET) and functional Magnetic Resonance Imaging (fMRI) are the commonly used functional neuroimaging technologies. Functional neuroimaging research of individuals with schizophrenia started in the 1990s in China and fMRI technology became widely available in the early 2000s. To localize the encephalic region or neural network related to specific cognitive deficits, functional neuroimaging research compares the activation of certain brain regions when performing particular cognitive tasks to the resting-states of these regions. SPECT studies have detected regional cerebral blood flow (rCBF) abnormalities in the frontal and temporal lobes among patients with schizophrenia; for example, while performing the WCST task, the rCBF of the left frontal lobe increases among healthy controls but not among individuals with schizophrenia (one study found that the rCBF decreased during the WCST task among individuals with schizophrenia who had predominantly negative symptoms). PET has been less used in research about schizophrenia in China due to its high cost.

fMRI studies on schizophrenia in China have reported that: (a) during verbal fluency (VF) tasks the bilateral frontal gyrus, inferior frontal gyrus and anterior cingulate cortex are relatively inactive; (b) during the backward digit span tasks (BDST) the left frontal gyrus, left inferior frontal gyrus and bilateral posterior inferior parietal lobe are relatively inactive; and (c) the activity of some of the relatively inactive regions is increased after treatment with risperidone (for example, significantly improved activation of the left frontal gyrus and left inferior frontal gyrus during the BDST).

Other fMRI studies have focused on working memory. Yang and colleagues adopted the Sternberg’s Memory Scanning Test (MST) to investigate the neural mechanism of the encoding, maintenance and retrieval components of working memory (WM) and found that the executive brain regions of individuals with schizophrenia do not efficiently execute these core WM processes. Using n-back tasks, Wang and colleagues discovered that compared to healthy controls, in individuals with schizophrenia the volume of the prefrontal lobe being activated was smaller and the regions involved were more subcortical; moreover, the number of activated brain regions during the task were fewer and the size of the activated region was smaller in individuals with schizophrenia who performed poorly on the task than in individuals with schizophrenia who did not perform poorly. Zou and colleagues used facial recognition tasks to study WM and found that individuals with schizophrenia showed low activity in several cortical areas, particularly the fusiform gyrus.

4. Treatment of cognitive impairment in individuals with schizophrenia
4.1 Pharmacotherapy
4.1.1 Atypical Antipsychotics
The clinical use of the new types of antipsychotic medications once inspired hope. Studies in China and elsewhere reported that almost all of the new atypical antipsychotic drugs could significantly alleviate cognitive dysfunction in individuals with schizophrenia. However, in recent years – after the results of the influential Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study were published – both international and Chinese researchers have re-evaluated the effects of atypical antipsychotics on cognitive function and concluded that they have little to no effect
on these core symptoms of the disorder. Subsequently the Measurement And Treatment Research to Improve Cognition in Schizophrenia (MATRICS) trial has been funded by the NIMH with the specific purpose of developing two types of drugs for improving cognitive function in schizophrenia.[120]

4.1.2 Nootropics

Jie and colleagues[121] reported that the combination of risperidone and huperzine A could improve cognitive function in individuals with schizophrenia and suggested that the mechanism of action of huperzine A was via its ability to increase acetylcholine concentration in the central nervous system (CNS); the increased acetylcholine concentration enhances neuronal excitability and, thus, improves the learning and memory functions of the brain. Bai and colleagues[122] found that combining antipsychotics and aniracetam could mitigate the cognitive impairment of individuals with schizophrenia, especially their problems in memory processing.

4.2 Non-pharmacological treatments

4.2.1 Cognitive therapy

Several types of cognitive therapy have been used in the treatment of schizophrenia, including cognitive remediation therapy, cognitive rehabilitation therapy, and cognitive-behavioral therapy. These approaches combine cognitive restructuring and social skills training with the goal of improving patients’ cognitive function by teaching them information processing strategies for problem solving. One study reported that cognitive remediation therapy was able to improve memory, executive function and psychomotor speed in individuals with schizophrenia. In another study that compared the effectiveness of antipsychotic medication alone to that of combined treatment with medication and cognitive rehabilitation therapy, the latter intervention proved to have better outcomes.[123] Other reports suggest that cognitive-behavioral therapy improves the quality of life of individuals with schizophrenia. In addition, Naikan therapy and Morita therapy – which have some cognitive components – were also found to be effective in improving the social functioning, attention and a range of symptoms of interests in patients with schizophrenia.[126,127]

4.2.2 Repetitive transcranial magnetic stimulation (rTMS)

Transcranial magnetic stimulation (TMS) is a non-invasive method of brain stimulation that uses magnetic fields to stimulate nerve cells. Repetitive transcranial magnetic stimulation (rTMS), a variant of TMS, has been developed as an intervention for various psychiatric conditions that has been shown to be both safe and tolerable in routine clinical practice settings. rTMS helps to temporarily reinforce the functions of the cerebral cortex and neural networks by stimulating the brain regions that affect specific functions.

Liu and colleagues[128] found that rTMS could positively affect some aspects of cognitive impairment in patients with schizophrenia. Zheng and colleagues[129] found that compared to sham stimulation, 20 Hz rTMS could improve visuospatial working memory, 10 Hz rTMS could decrease negative symptoms, and that both 10 and 20 Hz rTMS could lessen general psychopathology symptoms. This suggests that different types of rTMS may have differential effects on cognitive function and psychotic symptoms in schizophrenia; the hope is that eventually it will be possible to individualize the rTMS stimulation parameters to meet the treatment goals of specific patients.

5. Summary and future directions

Research in China focusing on the cognitive function of individuals with schizophrenia began in the 1970s and has recently grown rapidly due to the development of functional imaging technologies in the mid and late 1990s. Several potential avenues for further research in China remain: (a) previous studies have demonstrated deterioration in overall cognitive functioning but more detailed studies are needed on specific cognitive functions such as information processing, selective attention, and working memory; (b) interdisciplinary research that combines the approaches of psychiatry, psychology and functional imaging are needed to clarify the underlying mechanisms of cognitive impairments in schizophrenia; (c) innovative treatment strategies including cognitive therapy, rTMS and so forth need to be developed and rigorously assessed; and (d) long-term panel studies of first-onset patients are needed to assess the natural history of cognitive functioning during the course of illness and the prognostic utility of cognitive tests.

Conflict of interest

All authors declare that they have no conflict of interest.

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References

1. Tandon R, Nasrallah HA, Keshavan MS. Schizophrenia, “just the facts” 4. Clinical features and conceptualization. Schizophr Res 2009; 110(1-3): 1-23.
2. Sharma T, Antonova L. Cognitive function in schizophrenia: deficits, functional consequences and future treatment. Psychiatr Clin North Am 2003; 26(1): 25-40.
4. Zhao JP, Yang DS. Progress in research on cognitive function in schizophrenia. *Chin J Psychiatry* 1998; 31(1): 58-59. (in Chinese)

5. Gong YX. Short-term memory of patients with schizophrenia using free recall. *New Medicine* 1978; 21: 227-230. (in Chinese)

6. Zhu XX, Song SY, Wan Y. Ventricular size and cognitive impairment in patients with chronic schizophrenia. *Foreign Medical Science: Section of Psychiatry* 1978; 3: 177-178. (in Chinese)

7. Liu ZN, Zhao JX, Tan WX. Attention function impairment in unaffected siblings of patients with schizophrenia. *Journal of Clinical Psychiatry* 2003; 13(2): 65-66. (in Chinese)

8. Wu TC, Li M, Gu XH, Chen Q, Jiang CX. Sustained attentional function in the parents of schizophrenic patients. *Journal of Clinical Psychiatry* 2006; 16(3): 139-141. (in Chinese)

9. Zhao JX, Liu ZN. Attention and executive function impairment in patients with schizophrenia and their unaffected siblings. *Chinese Journal of Psychiatry* 2003; 36(2): 85-87. (in Chinese)

10. Qi LG, Wu DH, Gao BL, Wu DL, Wang P, Liu F, et al. Wisconsin card sorting test and backward masking task in patients with acute-episode schizophrenia. *Journal of Psychiatry* 2010; 23(5): 336-337. (in Chinese)

11. Zhang WS, Wu DH, Gao BL, Cao CA, Piao SB, Yang KJ. Association analysis between the executive, attentional function and psychiatric symptoms in patients with schizophrenia. *Medical Journal of Chinese People's Health* 2009; 21(11): 1205-1209. (in Chinese)

12. Wang CY, Tian YH, Wang K, Dong Y, Jin SC. Dissociation between physical and mental number line bisection in schizophrenia. *Chinese Journal of Nervous and Mental Diseases* 2010; 36(4): 229-232. (in Chinese)

13. Chen JJ, Tian YH, Dong WW, Wang K, Jin SC. The study of emotional chimeric faces to attentional bias in schizophrenia. *Chinese Journal of Nervous and Mental Diseases* 2012; 38(4): 212-216. (in Chinese)

14. Wu Y, Xu YF, Wang Y, Zhuo KM, Yu YM, Hu Y, et al. Pilot study of time course of inhibition of return in acute schizophrenia. *Shanghai Archives of Psychiatry* 2007; 19(4): 197-202. (in Chinese)

15. Liu DT, Zhuo KM, Song ZH, Wu Y, Chen XS, Wang JJ, et al. Effect of risperidone on sensory gating P50 deficit in patients with schizophrenia. *Journal of Shanghai Jiaotong University (Medical Science)* 2010; 30(12): 1525-1529. (in Chinese)

16. Liu DT, Chen XS, Zhuo KM, Song ZH, Wu Y, Wang JJ, et al. Sensory gating P50 during the acute phase of schizophrenia in first-episode and in chronic patients. *Shanghai Archives of Psychiatry* 2010; 22(6): 339-342. (in Chinese)

17. Liu D, Fan X, Wang Y, Yang Z, Zhuo K, Song Z, et al. Deficient inhibition of return in chronic but not first-episode patients with schizophrenia. *Prog Neuropsychopharmacol Biol Psychiatry* 2010; 34: 961-967.

18. Wang YC, Li Y, Zhuo KM, Liao LW, Wang Y, Song ZH, et al. The effect of different task difficulty on time course of inhibition of return in patients with schizophrenia. *Journal of Psychiatry* 2012; 25(5): 321-325. (in Chinese)

19. Chu YH, Zhang XY, Li XY, Liu J, Yang WH. Comparative study on binomial forced-choice digit memory test in clinical application of schizophrenia. *China Journal of Health Psychology* 2010; 18(5): 518-519. (in Chinese)

20. Zhang LY, Gao BL, Pan DM, Liu XC, Cao LS, Huang JX. Study of memory structure in patients with schizophrenia. *Academic Journal of the Second Military Medical University* 1989; 10(4): 380-383. (in Chinese)

21. Wang YL, Liu GL, Luan QM. Study of memory ability in patients with schizophrenia. *China Journal of Health Psychology* 2000; 8(2): 216-217. (in Chinese)

22. Zheng JC, Lin ZY, Xu GA, Li YQ, Zhuang XJ. A clinical trial of the change of implicit memory in schizophrenia patients. *Journal of Clinical Pyschosomaitic Diseases* 2012; 18(2): 132-134. (in Chinese)

23. Lin XH, Lin SZ, Zheng JC, Lin ZY, Lin H. Memory impairment in schizophrenia. *Journal of Psychological Science* 2012; 35(2): 477-480. (in Chinese)

24. Zheng JC, Lin ZY, Xu GA, Li YQ, Zhuang XJ. Study on the features of memory in schizophrenia patients and its correlation between positive and negative symptoms. *Sichuan Mental Health* 2012; 25(1): 1-5. (in Chinese)

25. Jin SC, Wang K, Wang KY, Wang H. A study of item memory and source memory in schizophrenia. *Chinese Journal of Nervous and Mental Diseases* 2006; 32(2): 97-100. (in Chinese)

26. Jin SC, Wang KY, Wang K. A study of source of memory and item memory in first episode patients with schizophrenia. *Journal of Clinical Psychiatry* 2008; 18(4): 223-226. (in Chinese)

27. Zhu XZ, Wang K, Zhang L, Xu ZM, Qiu LS, Chen YB, et al. Emotional memory impairment in schizophrenia. *Chinese Journal of Nervous and Mental Diseases* 2009; 35(2): 74-78. (in Chinese)

28. Wang Y, Chan RC, Hong X, Ma Z, Yang T, Guo L, et al. Prospective memory in schizophrenia: further clarification of nature of impairment. *Schizophr Res* 2008; 105: 114-124.

29. Zhuo KM, Yang ZL, Song ZH, Wu Y, Ji CF, Shi SX, et al. Event-based prospective memory during acute phase schizophrenia. *Journal of Shanghai Jiaotong University (Medical Science)* 2011; 31(12): 1724-1728. (in Chinese)

30. Lui SS, Wang Y, Liu AC, Chui WW, GONG QY, Shum D, et al. Prospective memory in patients with first-onset schizophrenia and their non-psychotic siblings. *Neuropsychologia*, 2011; 49(8): 2217-2224.

31. Zhou FC, Xiang YT, Wang CY, Dickerson F, Au RW, Zhou JJ, et al. Characteristics and clinical correlates of prospective memory performance in first-episode schizophrenia. *Schizophr Res*, 2012; 135: 34-39.

32. Zhuo K, Lu Y, Yang Z, Fan X, Song Z, Liao L, et al. Prospective memory performance in patients with drug-naive, first-episode psychosis. *Schizophr Res* 2013; 143: 285-290.

33. Wu Q, Wang KY, Cheng Q, Li WF, Wang Y, Wu LM. Relationship between prospective memory and social functioning in patients with schizophrenia. *Chinese Journal of Behavioral Medicine and Brain Science* 2012; 21(2): 146-148. (in Chinese)

34. Liu DT, Jiang KD, Xu YF. Research on brain function in working memory. *Foreign Medical Science: Section of Psychiatry* 2003; 30(1): 52-55. (in Chinese)
35. Wang N, Yang FD, Li YL, Tan YL, Zhu FY, Tan SP, et al. Working memory change with age in patients with schizophrenia. *Chinese Mental Health Journal* 2011; 25(10): 760-764. (in Chinese)

36. Zhang L, Li ZA, Wang K. Impairment of working memory in patients with schizophrenia. *Journal of Psychiatry* 2010; 23(2): 98-100. (in Chinese)

37. Zou LQ, Yuan HS, Dong WT, Pei X, Xing W, Liu PC, et al. An fMRI study during a facial work memory of neuroleptic-naive schizophrenia. *Chinese Journal of Medical Imaging Technology* 2007; 23(8): 1134-1138. (in Chinese)

38. Tan SP, Zou YZ, Jin Z, Zhang L, Zeng YW, Zhou DF. Functional Magnetic Resonance Imaging Study of Working Memory in Patients with Schizophrenia. *Chinese Mental Health Journal* 2006; 20(12): 779-782. (in Chinese)

39. Yang GF, Zhang Q, Zhang YT, Shen JH, Zhang XJ, Chen QG. An fMRI study for different cognition components of working memory in schizophrenia patients. *Journal of China Clinic Medical Imaging* 2009; 20(10): 758-761. (in Chinese)

40. Jin SC, Wang K, Wang KY. A study of working memory in patients with schizophrenia. *Acta Universitatis Medicinalis Anhui* 2006; 41(6): 701-703. (in Chinese)

41. Wang X, Wang XS, Wang XY, Liu D, Chen B, Yao SQ. The dysfunction during a parametric N-back task in schizophrenia: an event-related potential study. *Chinese Journal of Clinical Psychology* 2010; 18(3): 269-273. (in Chinese)

42. An BF, Li Y, Wang CH. A study on the executive function of first episode paranoid schizophrenia. *Chinese Journal of Behavioral Medicine and Brain Science* 2006; 15(4): 340-341. (in Chinese)

43. Wu DH, Gao BL, Wu DL, Guo JH, Liao CP, Liu ZN. Comparison of Wisconsin card sorting test between neuroleptic-naive and short-term medicated onset schizophrenic patients. *Chinese Journal of Clinical Psychology* 2009; 17(2): 167-168. (in Chinese)

44. Yang L, Guan HY. Research on executive dysfunction in the first-episode schizophrenic patients and their biological parents. *Sichuan Mental Health* 2007; 20(3): 132-134. (in Chinese)

45. Fei JF, Lan GH. Executive function impairment in patients with schizophrenia and their unaffected siblings. *Suzhou University Journal of Medical Science* 2010; 30(1): 135-137. (in Chinese)

46. Zhang FF, Dong Y, Wang K, Zhan ZY, Zhang ZJ, Ji F, et al. An association study of empathy and executive function in schizophrenic patients. *Chinese Journal of Behavioral Medicine and Brain Science* 2010; 19(5): 408-411. (in Chinese)

47. Liu X, Wang HL, Liu LL, Fang Y, Wang GH, Wang XP. Executive Function and Its Relationship with Psychiatric Symptoms in Schizophrenia Patients. *Medical Journal of Wuhan University* 2010; 31(4): 538-540. (in Chinese)

48. Liu X, Wang HL, Fang Y, Liu LL, Wang XP, Liu ZC, et al. The executive function and learning ability in the patients with first-episode schizophrenia. *Chinese Journal of Psychiatry* 2011; 44(1): 32-35. (in Chinese)

49. Zhao B, Liu W, Huang CY, Li SC, Zhang LJ, Kang XM, et al. Study of cognitive function in first-episode schizophrenic patients with and without auditory hallucination. *Chinese Journal of Behavioral Medicine and Brain Science* 2010; 19(3): 226-227. (in Chinese)

50. Wang HX, Ma X, Zhen WF. Follow-up study on executive function of frontal lobe in schizophrenics with and without homicide behaviors. *Chinese Journal of Behavioral Medicine and Brain Science* 2010; 19(2): 136-139. (in Chinese)

51. Wang XR, Lin ZQ, Zhang HJ, Cao LP. Study on executive function of male schizophrenic patients with aggressive behavior. *Journal Of Clinical Psychiatry* 2012; 22(2): 82-84. (in Chinese)

52. Zhu CY, Wang K, Li XS, Jin SC, Feng ZH, Du J, Zhou SS. Neuropsychological study on impairments of social cognition in schizophrenia. *Acta Universitatis Medicinalis Anhui* 2006; 41(4): 471-474. (in Chinese)

53. Xia HT, Dong Y, Jin SC, Zhang ZJ, Wang K. Relationship between the recognition of facial expressions and executive function in patients with schizophrenia. *Journal Of Clinical Psychiatry* 2009; 19(5): 289-291. (in Chinese)

54. Zuo XG, Yang FD, Ji ZF. Clinical analysis of cognitive function in schizophrenic patients with age being more than 50 years old. *Journal of Clinical Psychiatry* 2001; 11(3): 132-133. (in Chinese)

55. Li X, Xiao SF, Lu Z. Cognitive function of elderly schizophrenics. *Shanghai Archives of Psychiatry* 2002; 14(2): 85-87. (in Chinese)

56. Ren YM, Lu SC, Sun AQ. Cognitive and social functioning in elderly patients with schizophrenia. *Journal of Psychiatry* 2008; 21(2): 133-134. (in Chinese)

57. Lv F, Yu XJ, Li XQ, Liu XP, Han BH, Zhu XP. Cognitive functioning in patients with schizophrenia under maintenance treatment: a nine year follow-up study. *Chinese Journal of Psychiatry* 2001; 34(3): 179. (in Chinese)

58. Luo LL, ShenY, Qi RB, Zhao LB. Five-year follow-up study of changes in cognitive functioning in elderly patients with schizophrenia. *Practical Geriatrics* 2008; 22(3): 235-236. (in Chinese)

59. Tang H. Levels and features of cognitive impairment in patients with senior schizophrenia and Alzheimer’s disease. *Chinese Journal Of Clinical Rehabilitation* 2003; 7(30): 4110-4111. (in Chinese)

60. Zhou YF, Zhao JP. Relationship of cognitive function impairment and illness duration in schizophrenia. *Journal of Clinical Psychiatry* 2001; 11(4): 201-202. (in Chinese)

61. Sheng JH, SongZH, Shi SX, Yuan YP. Memory function and its related factors in schizophrenia. *Journal of Psychiatry* 2007; 20(3): 132-134. (in Chinese)

62. He CC. Effects of illness duration on cognitive function in schizophrenic patients. *Medical Journal of Chinese People’s Health* 2009; 21(4): 345-346. (in Chinese)

63. Xing XP, Xu LQ, Lu WH, Lv QY, Xu QH, Yi ZH. A comparative study of cognitive functions between early-onset schizophrenia and non-early-onset schizophrenia. *Journal of Neuroscience and Mental Health* 2012; 12(1): 9-11. (in Chinese)

64. Liu N, Lu Z, Cai J, Li Y, Pan GH, Chen HY, et al. The analysis of clinical factors on cognitive function of stable patients with schizophrenia. *Shanghai Archives of Psychiatry* 2006; 18(6): 333-336. (in Chinese)

65. Chen Q, Wang Y, Huang Q, Dong F, Zhou FC, Wang CY. Factors influencing cognitive function in schizophrenic patients with a course of disease of less than 5 years. *Chinese Journal of Nervous and Mental Diseases* 2011; 37(4): 196-205. (in Chinese)
66. Sun ZM, Sun XL, Wang X, Liu ZY, Liu XH. A study of cognitive deficit and its correlation with mental symptoms. *Journal of Clinical Psychiatry* 2003; 13(1): 6-7. (in Chinese)

67. Niu YJ, Wu CJ, Ji ZF. Correlation of cognitive function and psychosis symptoms in patients with schizophrenia. *Journal of Clinical Psychiatry* 2007; 17(2): 110-111. (in Chinese)

68. Tian T, Zhang C, Xu H, Wang XL, Jiang KD. Study on the cognitive dysfunction in patients with first-episode schizophrenia. *Shanghai Archives of Psychiatry* 2009; 21(3): 140-142. (in Chinese)

69. Niu YJ, Phillips MR, Gu ZF, Zhang PY. Three-year follow-up of cognitive functions of first episode schizophrenic patients. *Chinese Mental Health Journal* 2003; 17(10): 708-710. (in Chinese)

70. Shang L, Li GW, Phillips MR, Zhang PY, Ji ZF. Comparison of cognitive function impairment between genders in patients with first-episode schizophrenia. *Chinese Journal of Nervous and Mental Diseases* 2000; 26(6): 360-362. (in Chinese)

71. Li YL, Chen DC, Wang N, Yang KB, Nie Y, Zhang XY, et al. Gender difference in clinical features and cognitive function of first-episode schizophrenics. *Journal of Neuroscience and Mental Health* 2009; 9(4): 281-284. (in Chinese)

72. Jie Y, Wang ZW. Differences of cognitive function between genders in patients with chronic schizophrenia. *Medical Journal of Chinese People's Health* 2011; 23(11): 1320-1324. (in Chinese)

73. Wu DC, Liu YZ, Lin HM, Zheng YS. Cognitive function of long-term inpatient and outpatient elderly schizophrenics. *Chinese Journal of Behavioral Medicine and Brain Science* 2005; 14(12): 1087-1088. (in Chinese)

74. Zhang HY, Zhan Y, Yang JH. The study of inpatient with schizophrenia and outpatient elderly schizophrenics. *Medical Journal of Chinese People's Health* 2011; 23(5): 613-615. (in Chinese)

75. Li QY, Bian QT, Zou YZ, Wang J, Zhang GH, Wang WS, et al. Cognitive change in schizophrenic patients with concomitant metabolism syndrome. *Chinese Journal of Behavioral Medicine and Brain Science* 2010; 19(4): 322-324. (in Chinese)

76. Li CH, Rao SZ, Shen WL, Zhan GL, Xu P, Zhang H, et al. Cognitive function of chronic schizophrenics with metabolic syndrome. *Journal of Neuroscience and Mental Health* 2011; 11(6): 586-588. (in Chinese)

77. Guo XF, Zhang ZC, Zhu WW, Lian N, Lv HL, Zhao JP. Cognitive functioning in schizophrenia with or without diabetes. *Journal of Central South University (Medical Science)* 2011; 36(8): 724-727. (in Chinese)

78. Chen JX, Wu SY, Peng HM, Chen XR, Lin R. The effects of diabetes mellitus on clinical symptoms and cognitive functions in aged patients with schizophrenia. *Hebei Medicine* 2012; 18(8): 1048-1051. (in Chinese)

79. Liu CW, Tan YL, Cao LY, Zou YZ, Su JM, Yao FX, et al. Comparison of cognitive state in schizophrenic patients with and without tardive dyskinesia. *Chinese Journal of Nervous and Mental Diseases* 2005; 31(5): 326-333. (in Chinese)

80. Hu WH, Jiang KD, Chen HF, Ding HR. Cognitive function in chronic schizophrenic patients with tardive dyskinesia. *Chinese Journal of Clinical Psychology* 2007; 15(5): 548-549. (in Chinese)

81. Chen DC, Zhang XY, Li YL, Wang N, Nie Y, Yang KB, et al. Association of smoking and psychiatric symptoms, clinical characteristics and cognitive function in first-episode schizophrenia patients. *Chinese Mental Health Journal* 2009; 23(1): 1-4. (in Chinese)

82. Zhang WY, Gu FH, Xuan CM, Han XD, Xie L, Ma JF. Serum level of neuron-specific enolase, cognitive function and clinical characteristics in first-episode smoking schizophrenics. *Journal of Psychiatry* 2010; 23(3): 204-207. (in Chinese)

83. Wei QW. Advances in neural biochemical studies of cognitive function impairment in patients with schizophrenia. *Sichuan Mental Health* 2012; 25(4): 247-250. (in Chinese)

84. Wang F, Jin KH, Ding BK, Liu Y, Peng M, Wang XM. Cognitive deficits and oxidative stress in schizophrenia: a preliminary study. *Chinese Journal of Psychiatry* 2002; 35: 7-10. (in Chinese)

85. Wen SL, Cheng MF, Wang HL, Yue JH, Wang HZ, Zhi Y, et al. A study on serum levels of albumins, uric acid, bilirubin and γ-glutamyl transpeptidase in schizophrenia patients. *Chinese Journal of Clinicians (Electronic Edition)* 2012; 6(19): 5922-5925. (in Chinese)

86. An BF, Liu XQ, Cheng JX. A comparative study of the correlation between cognitive impairment psychotic symptom and plasma IL-2 level in different subtype schizophrenia. *Sichuan Mental Health* 2004; 17(1): 7-10. (in Chinese)

87. Zhou YF, Zhao JP. A study on the relationship of negative schizophrenia cognitive function improvement with HVA and 5-HIAA. *Journal of Clinical Psychiatry* 2000; 10(3): 157-159. (in Chinese)

88. Ma XH, Wang Q, Sun XL, Li T, Deng W, Meng HQ, et al. Genetic study of neurocognitive function in first-episode schizophrenia. *Chinese Journal of Psychiatry* 2004; 37(3): 140-144. (in Chinese)

89. Jiang HY, Xu XF, Chen YQ, Liu H, Yang JZ. Association study between cognitive function in schizophrenics and catechol-O-methyltransferase gene polymorphism. *Chinese Journal of Behavioral Medicine and Brain Science* 2006; 15(12): 1090-1092. (in Chinese)

90. Zhang C, Li ZZ, Wu ZG, Chen J, Peng DH, Fang YR, Yu SY. Association study of dopamine D1 receptor gene and cognitive function of first-episode schizophrenic patients. *Chinese Journal of Behavioral Medicine and Brain Science* 2011; 20(3): 224-226. (in Chinese)

91. Dong CY, Yin Y, Tan LW, Liu Y. Cognitive function and platelet serotonin concentration in the first-degree relatives of schizophrenia. *Chinese Journal of Behavioral Medicine and Brain Science* 2006; 15(7): 604-606. (in Chinese)

92. Sheng JH, Zhang MD, Yu SY, Shi SX, Song ZH, Wang DX. Influence of apolipoprotein E gene on the clinical features of schizophrenia. *Journal of Clinical Psychiatry* 2008; 18(1): 4-6. (in Chinese)

93. Xu YQ, Ye CY, Shen YJ, Hu H, Lin ZG, Shi SX, et al. The role of serum brain-derived neurotrophic factor in symptoms and cognitive functioning of schizophrenia. *Chinese Journal of Nervous and Mental Diseases* 2011; 37(7): 425-427. (in Chinese)

94. Zhang ZK, Tan LW, Sun H. Effect of genetic loading on cognitive function in schizophrenia. *Chinese Journal of Psychiatry* 2010; 43(3): 146-150. (in Chinese)
95. Liu DT, Chen XS, Zhuo KM, Song ZH, Wu Y, Wang JJ, et al. Sensory gating P50 during the acute phase of schizophrenia in first-episode and in chronic patients. *Shanghai Archives of Psychiatry* 2010; **22**(6): 339-342. (in Chinese)
96. Liu DT, Zhuo KM, Song ZH, Wu Y, Chen XS, Wang JJ, et al. Effect of risperdone on sensory gating P50 deficit in patients with schizophrenia. *Journal of Shanghai Jiaotong University (Medical Science)* 2010; **30**(12): 1525-1529. (in Chinese)
97. Wang CQ, Hong XH, Kong FZ, Wan XN, Peng ZZ, Liang JH. Relationship between auditory sensory gating P50 and neuropsychological test in first-episode schizophrenics. *Journal of Shantou University Medical College* 2009; **22**(1): 29-31. (in Chinese)
98. Wang SX, Zhen WF, Ma X, Dou QS, Chen J, Cai CH. Correlation study on sensory gating P50 and Wisconsin card sorting test in schizophrenics with violent behaviors. *National Medical Journal of China* 2011; **91**(9): 582-585. (in Chinese)
99. Ji XW, Liu L, Zhang WW, Xue L. The correlation study of auditory sensory gating P50 and cognitive function in first-episode schizophrenics. *Journal of Clinical Psychosomatic Diseases* 2012; **18**(12): 12-14. (in Chinese)
100. Liu WB, Chen QZ, Yin HM, Zheng LL, Yu SH, Chen YP, et al. Event-related potentials P300 with memory function and psychopathology in first-episode paranoid schizophrenia. *Journal of Zhejiang University (Medical Sciences)* 2011; **40**(6): 647-652. (in Chinese)
101. Lou FY, Chen XS, Zhang MD, Liang JH, Chen C. Study on mismatch negativity of patient with schizophrenia. *Journal of Modern Electrophysiology* 2006; **13**(3): 131-134. (in Chinese)
102. Lv WQ, Mao Y, Chen JM, Chen C, Tang YX. Application of eletroencephalography mismatch negativity in patient with schizophrenia. *Shanghai Archives of Psychiatry* 2007; **19**(2): 92-94. (in Chinese)
103. Chen XS, Tang YX, Xiao ZP, Wang JJ, Zhang MD, Zhang ZF, et al. Study on neural generators of N400 in first episode schizophrenia. *Journal of Shanghai Jiaotong University (Medical Science)* 2009; **29**(11): 1351-1354. (in Chinese)
104. Zhou ZH, Yuan GZ, Tang BC, Zou HM, Wang Y, Chen ZH, et al. Effect of olanzapine on the N400 Chinese sentence task in schizophrenic teenagers with cognitive impairment. *Chinese Journal of Psychiatry* 2006; **39**(4): 256. (in Chinese)
105. Chen XS, Xu YF, Tang YX, Xiao ZP, Zhang MD, Wang JJ, et al. Changes of event related potential component N400 in first episode schizophrenia before and after risperidone treatment. *Journal of Shanghai Jiaotong University (Medical Science)* 2010; **30**(9): 1133-1137. (in Chinese)
106. Zheng CY, Chen XS, Tang YX, Xu YF, Zhang C, Zhang MD, et al. A preliminary study on error-monitoring function changes in first episode schizophrenia patients. *Chinese Journal of Psychiatry* 2012; **45**(5): 281-284. (in Chinese)
107. Song CS, Wang J, Zou YZ, Tan SP, Zhang JG, Li XL, et al. Relationship between exploratory eye movement and cognitive function in senile schizophrenic patients. *Chinese Journal of Behavioral Medicine and Brain Science* 2009; **18**(7): 618-620. (in Chinese)
108. Wang LL, Han YH, Zhu RS. Exploratory eye tracking movement in schizophrenic patients with different courses. *Chinese Mental Health Journal* 2003; **17**(10): 702-704. (in Chinese)
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中国精神分裂症认知功能的研究进展

摘要

认知功能障碍－精神分裂症的核心症状之一－已经成为国内外研究精神分裂症的热点。它不仅反映了疾病的严重程度，而且是精神分裂症功能预后的重要影响因素，因为认知功能损害的程度对患者的独立生活能力以及他们的就业和社会功能都会有影响。国内最早的精神分裂症认知功能研究可以追溯到上个世纪七十年代晚期。近年来，由于新的信息的出现，例如神经影像技术的进步，国内涌现了大量研究。本文在对国内既往研究进行综述的基础上提出了精神分裂症认知功能的未来研究方向。