



## Characteristics and clinical correlates of prospective memory performance in first-episode schizophrenia

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### ABSTRACT

**Objective:** The aim of this study was to examine prospective memory (PM) and its socio-demographic, clinical, and neurocognitive correlates in first episode schizophrenia (FES).

**Methods:** Fifty-one FES patients and 42 healthy controls formed the study sample. Time- and event-based PM (TBPM and EBPM) performance were measured with the Chinese version of the Cambridge Prospective Memory Test (C-CAMPROMPT). A battery of neuropsychological tests was also administered. Patients' clinical symptoms were evaluated with the Positive and Negative Symptom Scale (PANSS).

**Results:** Patients performed significantly worse in both TBPM ( $8.7 \pm 5.3$  vs.  $14.8 \pm 3.5$ ) and EBPM ( $11.3 \pm 4.7$  vs.  $15.7 \pm 2.7$ ) than the controls. After controlling for age, gender, education level and neurocognitive test score, the difference in performance on the two types of PM tasks between patients and controls was no longer present. In multiple linear regression analyses, longer duration of untreated psychosis (DUP), lower scores of the Hopkins Verbal Learning Test-Revised (HVLT-R) and the categories completed of the Wisconsin Card Sorting Test (WCST-CC) and higher score of the Color Trails Test-2 (CTT-2) contributed to poorer TBPM performance, while lower score of HVLT-R, higher score of the perseverative errors of the Wisconsin Card Sorting Test (WCST-PE) and longer DUP contributed to worse performance on EBPM.

**Conclusions:** Both subtypes of PM are impaired in first-episode schizophrenia suggesting that PM deficits are an integral part of the cognitive dysfunction in the disease process.

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### 1. Introduction

Prospective memory (PM), defined as “remembering to do something at a particular moment in the future or the timely execution of a previously formed intention” (Kvavilashvili and Ellis, 1996), is gaining increased attention in research and clinical practice (Shum et al., 2004; Kliegel et al., 2007; McDaniel and Einstein, 2007; West,

2007). PM is considered to be different from, and more complex than, retrospective memory (RM).

Einstein and McDaniel (1990) identified two subtypes of PM: time- and event-based PM. Time-based PM (TBPM) involves remembering to carry out an intention at a specific time or after a certain time period. Event-based PM (EBPM) is defined as remembering to perform an intended action triggered by an external event.

To date, a number of studies have examined PM and its correlates in schizophrenia. Despite a wide range of methods used to assess PM, all studies have found that schizophrenia patients exhibit impairments in both PM subtypes. Executive functions, RM and learning seem to play important roles in PM (Kondel, 2002; Shum et al., 2004; Henry et al., 2007; Twamley et al., 2008; Xiang et al., 2010b). Yet, PM deficits in schizophrenia remain significant after controlling for these variables, which might suggest that impaired PM in

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schizophrenia is a primary rather than a secondary impairment (Henry et al., 2007; Wang et al., 2008b).

Most studies, however, have focused on chronically ill schizophrenia patients, which might have introduced bias caused by long-term treatment with psychotropic agents and electroconvulsive therapy (ECT). First-generation antipsychotic drugs (FGA) do not improve cognition and can have specific adverse effects on working memory, processing speed, motor skills, and other higher-order cognitive abilities (Kapur et al., 2001; Reilly et al., 2007). Although preclinical data have suggested that second-generation antipsychotics (SGA) could to some degree reduce cognitive impairment (Buchanan et al., 1994; Green et al., 1997), there is a growing body of evidence that both FGAs and SGAs can lead to cholinergic alterations in the brain areas traditionally involved in memory functioning (Mahadik et al., 1988; Squire, 1992; Terry et al., 2005, 2006a, 2006b). Cognitive deterioration in schizophrenia occurs mainly within the first 5–10 years after illness onset (Lieberman et al., 2001). In schizophrenia patients, multiple episodes are significantly associated with greater cognitive impairments, particularly of psychomotor speed, pattern memory, and executive functioning (Braw et al., 2008). By including only patients with first-episode schizophrenia (FES) in a study, it is possible to minimize the effects of the abovementioned confounding factors and help determine whether PM deficit is a consequence of the disease process itself.

Diffuse, non-localized neuropsychological deficits have been reported in studies of FES (Censits et al., 1997; Heinrichs and Zakzanis, 1998). The more specific cognitive deficits of FES include verbal learning and executive functioning (Saykin et al., 1991; Hutton et al., 1998). As noted above, learning and executive functioning are both closely related to PM (Henry et al., 2007; Twamley et al., 2008).

Given this background, the aims of the study were (1) to determine whether FES patients show impairment in the two types of PM (TBPM and EBPM) compared to healthy controls and (2) to clarify the relationships between PM and demographic and clinical variables, as these associations have not been examined in FES.

## 2. Methods

### 2.1. Participants

The study sample comprised 51 FES patients recruited in an 800-bed university-affiliated psychiatric hospital in Beijing and 42 healthy controls (HCs) matched by age (+/–2 years) and education (+/–2 years) recruited from the community through advertisements.

The inclusion criteria for patients included (1) diagnosis of schizophrenia according to DSM-IV (APA, 1994) established by administering the Structural Clinical Interview for DSM-IV (SCID-DSM-IV; First et al., 1996) augmented by a review of medical records; (2) first episode of the illness; (3) Chinese ethnicity; (4) age between 16 and 45 years; and (4) at least a primary level of education and the ability to understand the requirements of the study. The exclusion criteria were (1) a history of or current significant drug/alcohol abuse; (2) ECT in the past 12 months; and (3) a history of or current significant medical or neurological condition(s), including learning disability.

The study protocol was approved by the Clinical Research Ethics Committee of Beijing Anding Hospital. Written consent was obtained from each participant.

### 2.2. Assessment

#### 2.2.1. Positive and Negative Syndrome Scale (PANSS)

Psychiatric symptoms were assessed with the locally validated version of the Positive and Negative Syndrome Scale (PANSS; He and Zhang, 1997). The PANSS is a well-known instrument widely used in psychiatric research.

#### 2.2.2. Personal and Social Performance Scale (PSP)

Personal and social functioning was measured with the Personal and Social Performance Scale (PSP). The PSP is an interviewer-rated scale and was developed on the basis of the social functioning component of the DSM-IV social and occupational functioning assessment scale (SOFAS; Morosini et al., 2000). PSP scores range from 1 (extremely severe impairment with increased risk for survival) to 100 (excellent functioning). The PSP covers four main areas: socially useful activities including work and study, relationships, self-care, and disturbing and aggressive behavior.

#### 2.2.3. Prospective memory (PM)

PM was assessed with the locally validated, Chinese version of the Cambridge PM Test (C-CAMPROMPT; Lou et al., 2009). In this test, participants are asked to remember to carry out three time-based and three event-based tasks at different intervals, while performing a filler activity following both verbal and written instructions. The participants are allowed to spontaneously use strategies such as taking notes to help them to remember (Wilson et al., 2005). The C-CAMPROMPT generates scores on three TBPM and three EBPM tasks, each scoring a maximum of 6 with a sum score ranging from 0 to 36.

### 2.3. Other neurocognitive tests

#### 2.3.1. Hopkins Verbal Learning Test-Revised, Chinese version

The HVLT-R (Shi, 2005) is a list-learning verbal memory test consisting of 12 words. Participants are given 3 trials to learn the list of words and then asked to recall the list approximately 20–25 min later. In this study, the number of items from the learning trials correctly recalled was used to measure RM.

#### 2.3.2. Verbal Fluency Test, Chinese version (VFT)

In the VFT (Shi, 2005), participants are given four trials, each lasting 1 min. To assess fluency in Chinese language, they are asked to generate as many four-character Chinese idioms as possible beginning with the Chinese character “one” and “ten thousand”. To assess category fluency, they are also asked to generate words from the “animal” and “action” categories. The sum of words produced in the two-character and two-category trials is averaged separately to calculate an overall phrase and category verbal fluency performance, respectively.

#### 2.3.3. Color Trails Test (CTT)

The CTT (Spreen and Strauss, 1998), an analog of the Trials Making Test (TMT; Reitan, 1958), attempts to create a “culture-fair” version of the TMT by alternating between colors instead of letters and numbers. The CTT consists of two parts (CTT-1 and CTT-2). Part 1 requires the test taker to connect series of numbered circles arranged randomly on a sheet of paper using a pencil. In part 2, numbered circles are shown from 1 to 25 twice, the first time with a pink and the second time with a yellow background. Test takers are asked to connect the numbers from 1 to 25 alternating between the two colors. The time taken to complete part 2 (CTT-2) was used as an outcome variable in this study.

#### 2.3.4. Stroop Color Word Test (SCWT); Chinese version

The Chinese version of the SCWT (Shi, 2005) measures selective attention and cognitive flexibility. The classic card version was used in this study. Participants completed three parts for 45 s, each with five columns of 20 items. Part 1 involves reading a list of 100 words (e.g., the words “red”, “green” or “blue”) that are printed in black ink. Part 2 requires the participants to identify the color of the ink of a list of meaningless characters. The third task requires the participants to report the color of the ink in which the words “red”, “green” and “blue” are printed; the content of each word conflicts with the color of the ink with which it is printed. The score generated on this

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