Contents lists available at SciVerse ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Prospective memory performance in patients with drug-naïve, first-episode psychosis

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ARTICLE INFO

ABSTRACT

Schizophrenia is associated with an impairment of prospective memory (PM) which refers to the ability to remember to carry out an intended action in the future. However, most of these studies were limited to chronic samples. The current study examined the event-based PM and time-based PM using a dual-task paradigm in 22 drug-naïve, first-episode psychosis (FEP) patients and 23 healthy controls. Results indicated that FEP patients performed significantly poorer than healthy controls in both event-based and time-based PM. However, the significant difference in time-based PM disappeared after controlling for working memory. Correlation analysis indicated that both types of PM did not correlate with positive symptoms or negative symptoms, duration of illness, or duration of untreated psychosis. However, time-based PM was correlated with the general psychopathology subscale of the PANSS. Taken together, these findings suggest that PM deficits are present in drug-naïve FEP patients; impairment of event-based PM appears to occur independently, whereas time-based PM impairment may be, in part, a secondary consequence of a working memory deficit.

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1. Introduction

Neurocognitive deficits are key features of schizophrenia (Elvevag and Goldberg, 2000; Keshavan et al., 2008) and are a critical determinant of quality of life and functional outcome (Green et al., 2000; Kurtz et al., 2005; Matza et al., 2006; Kurtz et al., 2008). Substantial evidence also suggests that patients with schizophrenia have deficits in a diverse array of cognitive domains, including working memory, language function, executive function, episodic memory, processing speed, attention, inhibition and sensory processing (Chan et al., 2004; Fioravanti et al., 2005; Chan et al., 2006b; Reichenberg and Harvey, 2007; Mesholam-Gately et al., 2009). Within the context of generalized cognitive deficit, it has been suggested that the most severe impairments are episodic memory and executive control processes (Chan et al., 2004, 2006a, 2006b; Reichenberg and Harvey, 2007).

Prospective memory (PM) is a unique form of episodic memory and has been gaining increasing attention due to its theoretical and functional implications (Kliegel et al., 2008). PM by definition is the ability to remember to carry out an intended action in the future (Kliegel et al., 2008). According to the nature of the cue associated with the future intention, three subtypes of PM have been identified (Shum et al., 2004). The event-based PM refers to remembering to execute an intention when an event/cue appears (e.g., remembering to give a document to a colleague when attending the seminar chaired by that colleague). The time-based PM refers to remembering to execute an intention at a specific time or after a period of time (e.g., remembering to turn up for a medical appointment at 3:00 pm on Monday). The activity-based PM refers to remembering to execute an intention after completion of an activity (e.g., remembering to go shopping after finishing homework) (Wang et al., 2010). Moreover, PM can be divided into different phases of cognitive processing, comprising intention formation, intention retention, intention initiation and intention execution (Kliegel et al., 2011). Accordingly, some cognitive resources such as planning, storage, monitoring and switching of inhibition are required during the PM process (Kliegel et al., 2011). The study of PM is both clinically and theoretically important for patients with schizophrenia, for PM has been implicated in many everyday life activities; it is proposed that PM is mostly mediated by the frontal and medial temporal systems (Kliegel et al., 2011; McDaniel and Einstein, 2011), and dysfunction of the prefrontal cortex and the medial temporal cortex might be especially important for

patients with schizophrenia (Antonova et al., 2004; Minzenberg et al., 2009).

Growing evidence has consistently identified PM deficits in schizophrenia patients (Elvevag et al., 2003; Shum et al., 2004; Henry et al., 2007; Altgassen et al., 2008; Chan et al., 2008; Ungvari et al., 2008; Wang et al., 2008a, 2008b). A recent meta-analysis found moderate to large effect sizes for PM deficits in patients with schizophrenia (Wang et al., 2009). Three types of PM were all significantly impaired in schizophrenia, with time-based PM being more impaired than event-based PM. Because it is commonly acknowledged that PM is a complex cognitive function involving multiple processes and cognitive variables, some researchers have tried to elucidate the components of PM impairment in patients with schizophrenia by controlling for other cognitive functions such as working memory, executive function and IQ. The results indicate that PM deficits in schizophrenia patients might be due to the impairment of the cue detection and intention retrieval stage (Woods et al., 2007; Wang et al., 2008a). Results of some studies also indicate that PM deficits are a primary impairment rather than a secondary consequence of other cognitive impairments (Henry et al., 2007; Woods et al., 2007; Wang et al., 2008a) whereas other studies found PM deficits to be associated with other cognitive deficits such as impaired retrospective memory (Xiang et al., 2010; Zhou et al., 2012).

However, most of these studies were limited to patients with a long duration of illness and the findings may have been confounded by medication effects and illness duration. There are only two studies identified from the literature that have specifically examined PM performance in patients with first-episode schizophrenia (Lui et al., 2011; Zhou et al., 2012). Lui et al. (2011) found that patients with first-episode schizophrenia performed poorly in both event-based PM and time-based PM as compared to healthy controls. However, when other cognitive functions were controlled, the significant group difference in time-based PM disappeared and the effect size of event-based PM was reduced from large to moderate. Zhou et al. (2012) replicated a similar finding of PM deficits in patients with first-episode schizophrenia using an ecologically-valid test of PM. Once again, when age, gender, education, and other neurocognitive tests were controlled, the event-based PM and time-based PM differences between groups disappeared. Despite the fact that these two studies recruited first-episode schizophrenia patients, most of their subjects were receiving atypical antipsychotic medication. It is still not clearly known whether PM deficits observed in patients with schizophrenia are the effect of the illness or a result of medication. A recent meta-analysis indicated that PM may have an inverse relationship with antipsychotic medication dosage (Wang et al., 2009). Therefore it is important to rule out the potential medication effect upon PM performance in patients with schizophrenia.

This study aimed to clarify these confounding factors by examining a first-episode drug-naïve sample with a relatively short illness duration. In the present study, only event-based PM and time-based PM based on a modified PM paradigm were evaluated. Activity-based PM was not included because a meta-analysis suggested that impairments of time-based PM and event-based PM in schizophrenia have larger mean effect sizes than activity-based PM (Wang et al., 2009). Moreover, the task for activity-based PM is different from the tasks for time-based PM and event-based PM (Wang et al., 2008b, 2009; Lui et al., 2011). We hypothesized that event-based PM and time-based PM in patients with first-episode psychosis (FEP) are both impaired. We also hypothesized that other cognitive domains, such as working memory, have differential effects on event-based and time-based PM in FEP patients.

2. Methods

2.1. Participants

This study was conducted at the Shanghai Mental Health Center. Those first episode psychosis patients with significant symptoms but in relatively stable clinical condition (e.g., be quiet and cooperative without obviously aggressive behavior or suicidal attempt) are admitted to the First Episode Psychosis Specialty Unit; psychotic patients in unstable clinical condition (e.g., risk to himself or herself, or others) are admitted to other units (ICU ward). Potential drug-naïve research subjects were recruited from the First Episode Psychosis Specialty Unit if their treating clinicians determined that they were capable of providing informed consent, met inclusionary and exclusionary criteria and were clinically stable enough to complete the testing procedure which took no more than 40 min. Twenty-two patients were enrolled; 15 were male and 7 female, the mean age was 26.6 years old, the mean education level was 12.6 years, and the mean duration of illness was 6.1 months. All patients were diagnosed with schizophrenia or schizophreniform disorder; 17 patients with schizophreniform disorder and 5 patients with schizophrenia. All subjects diagnosed with schizophreniform disorder at the time of study enrollment were subsequently diagnosed with schizophrenia after 6 months of illness duration.

A diagnosis of schizophrenia or schizophreniform disorder was confirmed by a research psychiatrist (D.L.) using MINI plus v 5.0 (Sheehan et al., 1998). Exclusion criteria for the study included: (1) inability to provide informed consent, (2) current substance abuse, (3) personality disorders, (4) mental retardation, (5) significant medical conditions including severe cardiovascular, hepatic, renal disease, and (6) pregnancy or breastfeeding.

Twenty-three healthy controls were recruited from the local community; 16 were male and 7 were female; the mean age was 26.8 years old; the mean education level was 13.6 years. All subjects completed the structured clinical interview performed by a research psychiatrist (D.L.) using MINI plus v 5.0. Those with other Axis I mental disorders, neurological diseases, or positive family history of mental illness were excluded.

Clinical symptoms were assessed using the Positive and Negative Symptom Scale (PANSS) (Kay et al., 1987, 1989); and the Clinical Global Impressions-severity scale (CGI) (Guy and Bonato, 1976). This study was approved by the Institutional Review Board of Shanghai Mental Health Center. Written informed consent was obtained from all participants.

2.2. Measures

2.2.1. Prospective memory tasks

Event-based PM and time-based PM computerized tasks were designed based on the dual-task paradigm of Einstein and McDaniel (1990). Compared to the traditional dual task paradigm, a different task design was adopted in our study. In the same session, participants were required to complete an event-based PM task and time-based PM task while simultaneously performing an on-going task.

The ongoing task was a simple category task: a noun was presented in green letters above the center of the screen, while 4 different words indicating the category were shown at the bottom of the screen (i.e. commodity, animal, plant and people). The participants were asked to respond by categorizing the noun by clicking on the appropriate category button, for example, commodity for fan and animal for elephant. Each session comprised 4 blocks and each block contained 50 trials. The task used 100 nouns which were selected from a text book and reading material used in Chinese primary schools (Shanghai Educational Publishing House). Each category contained 25 words; 50 words were randomly selected for block 1, and the remaining 50 words were included in the 2nd block. The selection of words for blocks 3 and 4 used the same procedure. There was a 1 minute time interval between each block during which short stories were presented.

The event-based PM task required participants to suspend the ongoing task and switch to the PM task by pressing the spacebar when the word was presented in blue (target cue). A method of