Time-based but not event-based prospective memory remains impaired one year after the onset of schizophrenia: A prospective study

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ABSTRACT

Background: Prospective memory (PM) deficits have been consistently found in people with schizophrenia. Although there is evidence to suggest that PM deficits may be putative markers for schizophrenia, no longitudinal study has investigated the persistence of PM deficits.
Aims: We examined whether PM deficits persist after the onset of schizophrenia, and compared the trajectories of time- and event-based PM performance 12 months after illness onset. We also examined whether the association between PM and clinical symptoms changes over time 12 months after illness onset.
Method: We recruited 58 individuals with first-episode schizophrenia for a 12-month follow-up study. Comparison participants were 37 healthy individuals who were matched in terms of demographics and intelligence with the patient group. PM functions and clinical symptoms were measured at baseline, the sixth month, and the twelfth month, using a computerized PM task and the Positive and Negative Syndrome Scale.
Results: People with schizophrenia showed a gradual improvement in both time- and event-based PM 12 months after illness onset. However, compared to event-based PM, deficit in time-based PM persisted and was relatively stable. At baseline, PM functions were not associated with clinical symptoms. However, an association between time-based PM and PANSS positive and general symptoms emerged 12 months after the onset of schizophrenia.
Conclusion: People with first-episode schizophrenia exhibit persistent time-based PM deficit. Our findings support that PM deficit, in particular, time-based deficit, may be a putative neuropsychological marker of schizophrenia.

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1. Introduction

Prospective memory (PM) is defined as the ability to remember to carry out a delayed intention in the future (Einstein & McDaniel, 1990; Kvavilashvili & Ellis, 1996), and is typically classified into time-based (i.e., intended actions are appropriately carried out at a certain time) and event-based (i.e., intended actions are appropriately carried out at the occurrence of a certain event).

PM could be assessed using different experimental paradigms, which typically involve a dual-task design (Einstein & McDaniel, 1996), in which participants are asked to encode and maintain an intention to carry out a PM task, while they are continuously engaged in an ongoing task. In a dual-task paradigm, participants have to execute the PM task at a certain time or on the appearance of certain PM cues.

The majority of previous PM studies in people with schizophrenia used this kind of well-controlled, dual-task PM paradigms (Elvevag et al., 2003; Shum et al., 2004; Wood et al., 2007; Altgassen et al., 2008; Twamley et al., 2008; Wang et al., 2008a; Wang et al., 2008b; Chan et al., 2008; Ungvari et al., 2008; Zhuo et al., 2013; Lui et al., 2014). Other studies (Henry et al., 2007; Zhou et al., 2012) used ecologically-valid paradigms, such as the Virtual Week Task and the Cambridge PM Task, which are not as well controlled as the dual-task paradigms but had the advantage of simulating real-life situations and allowing participants to adopt strategies, such as taking notes as reminders, to facilitate PM performance.

PM ability has consistently been shown to be impaired in people with schizophrenia in both the chronic stage (Elvevag et al., 2003; Shum et al., 2004; Henry et al., 2007; Wood et al., 2007; Twamley et al., 2008; Wang et al., 2008a; Wang et al., 2008b; Chan et al., 2008; Altgassen et al., 2008; Ungvari et al., 2008) and at illness onset (Zhou et al., 2012; Zhuo et al., 2013; Lui et al., 2014). Individuals with self-reported schizotypal features (Wang et al., 2008a) and unaffected

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relatives of people with schizophrenia (Wang et al., 2010) have also been found to have PM deficits. Taken together, evidence suggests that PM deficits in people with schizophrenia are characterized by disease association, state-independence (present in both the first episode and chronic stage), familial association, and association with high risk populations. Therefore, PM deficits appear to have met several of the criteria of an endophenotype proposed by Gottesman & Gould (2003). However, most previous studies are cross-sectional in design and the longitudinal stability of PM impairment has rarely been studied in schizophrenia spectrum disorders. To date, only one longitudinal study had examined PM ability in people with psychiatric disorders; Wang et al. (2011) tested individuals with self-reported schizotypal features and found moderate test–retest correlations of 0.62 and 0.55 for event-based and time-based PM respectively. These results suggest a relatively stable PM deficit in these individuals. Because longitudinal stability is an important criterion for a trait marker or an endophenotype, and given the paucity of evidence in this area, a longitudinal study is indicated to ascertain whether PM deficits persist in people with first-episode schizophrenia.

In this study, we aimed to address three issues: (1) whether PM deficits persist after the onset of schizophrenia; (2) the twelve-month trajectory of performance of different PM types (time- and event-based) 12 months after the onset of schizophrenia; and (3) whether the association between clinical symptoms and different PM deficits in schizophrenia change over time. We had the following hypotheses: (1) based on a previous study (Wang et al., 2011) in participants with self-reported schizotypal features, we hypothesized that PM deficits persist longitudinally after a 12-month period; (2) given that individuals with schizophrenia in different stages showed deficits in both types of PM, we hypothesized that there would be no difference in trajectory between different types of PM deficits; and (3) we hypothesized that PM is correlated with clinical symptoms at the three assessment time points.

2. Method

2.1. Participants

We recruited 58 individuals with DSM-IV diagnosis of first-episode schizophrenia from the outpatient clinic of the joint research-based first-episode psychosis program (Lui et al., 2011a) between Castle Peak Hospital of Hong Kong and the Key Laboratory of Mental Health, Institute of Psychology, the Chinese Academy of Sciences in Beijing led by the two senior authors (RCKC and EFCC). Psychiatric diagnoses of the participants were ascertained using the Structured Clinical Interview for DSM-IV Axis I diagnoses (First et al., 1996) by experienced psychiatrists, supplemented by information from medical records obtained in frequent follow-ups (average interval 4–8 weeks). All participants with schizophrenia recruited in this study were clinically stable to undertake neuropsychological assessment. We recruited 37 demographically matched healthy individuals from the neighboring community as controls. These individuals were screened by a qualified psychiatrist using structured interviews to ascertain that none of them had any lifetime or family history of psychosis. Inclusion criteria for participants with schizophrenia included: (1) clinically-stable mental condition as assessed by their treating psychiatrists; and (2) absence of adjustments of antipsychotic medications in the past one month prior to the assessments. Exclusion criteria for both the schizophrenia participants and controls included: (1) life-time history of substance abuse, (2) history of electroconvulsive therapy in the past six months, (3) history of neurological disorders, (4) history of head injury with loss of consciousness for more than 30 min, and (5) mental retardation. All participants were Chinese in ethnicity. This study was approved by the Institutional Review Board of the Institute of Psychology, the Chinese Academy of Sciences and Castle Peak Hospital.

All participants provided written informed consent before the assessment.

2.2. Measures

2.2.1. Prospective memory

We used a validated dual-task laboratory paradigm to measure PM (Einstein & McDaniel, 1996). This paradigm has been described in detail elsewhere (Wang et al.; 2008a; Lui et al., 2011b). Although the original paradigm comprised four conditions, only two (viz., semantic time- and event-based) were used in this study, because an earlier study from our group (Chan et al., 2013) showed that these conditions were more sensitive than the remaining ones (viz., perceptual time- and event-based) in detecting PM deficits in people with schizophrenia.

In the event-based condition, a series of four-character phrases in Chinese was presented at the centre of the computer screen at a rate of one phrase every 4 s. Participants were asked to judge whether the phrases were idioms or not by pressing two pre-specified response buttons. At the same time, participants were also instructed before the start of this task to press another pre-specified button when they saw the appearance of an animal character (e.g., monkey) in the phrases (i.e., the PM task). The time-limit for execution of a correct response in this condition was approximately 4 s. There were five PM targets embedded in the ongoing lexical-decision task in the event-based condition, and each PM cue was presented approximately (and irregularly) 60 s after another.

In the time-based PM condition, the same lexical-decision task was used as the ongoing task. However, participants were required to monitor the passage of time and to press a pre-specified button when the digital clock situated near the keyboard reached a full minute (e.g., 12:00). The time-limit for execution of a correct response in this condition was 10 s. As in the event-based condition, there were a total of five opportunities for participants to respond to the PM task, once for each one-minute interval.

Each condition lasted for approximately six minutes. After the participants completed both conditions, we also asked them to recall the instructions provided in the beginning of the session. The time- and event-based PM scores were calculated by dividing the total number of correctly executed PM tasks (event-based PM: pressing a pre-specified button when animal characters appeared on the screen; time-based PM: pressing a pre-specified button as the clock reached a full minute) by the total number of expected PM responses (i.e., five).

2.2.2. IQ and clinical symptoms assessment

Participants' intelligence was estimated using a prorating method based on the Arithmetic, Similarities and Digit Span subscales of the Chinese version of the Wechsler Adult Intelligence Scale-Revised (Gong, 1992). Clinical symptoms of the participants with schizophrenia were rated by trained psychiatrists using the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987).

2.2.3. Time-points for sequential assessment

Participants with schizophrenia completed three time points of assessment using the PM task and PANSS rating (at baseline, 6-month, and 12-month), while healthy controls were only assessed once using the same assessment instrument at baseline.

2.2.4. Statistical analysis

Demographics of the two groups were compared using ANOVAs for parametric data (i.e., age) and Chi-square tests for non-parametric data (i.e., gender and handedness). We used three MANOVAs and six follow-up ANOVAs to compare the time- and event-based PM scores (baseline, 6-month, 12-month) in participants with schizophrenia with PM scores (baseline) of the comparison group. The 12-month longitudinal stability of PM in participants with schizophrenia (n = 58)