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Prospective memory in non-psychotic first-degree relatives of patients with schizophrenia

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ABSTRACT

Although a number of studies have found prospective memory (PM) impairment in patients with schizophrenia, very little is known about the PM performance in non-psychotic relatives of these patients. The current study aimed to explore the PM performance in non-psychotic first-degree relatives of these patients. Two groups of participants (26 non-psychotic first-degree relatives of schizophrenia patients and 26 healthy comparison participants) were administered three PM tasks (time-, event-, and activity-based) and a set of neurocognitive tests. Results showed that the relatives performed significantly worse than the comparisons on most indices of the PM tasks, with a similar pattern of impairment found in other neurocognitive measures. Together with findings from previous studies, results of the current study suggest that PM may be a potential endophenotype for schizophrenia.

1. Introduction

Studies suggest that schizophrenia may be heritable (Kendler and Diehl, 1993). First-degree non-psychotic relatives of schizophrenia patients have been reported to have a higher rate in developing psychosis than the general population (Gottesman, 1991, 1993). Neurocognitive disorder, as one of the core deficits in schizophrenia, is also heritable. First-degree non-psychotic relatives of schizophrenia patients have also been found to show similar but milder degree neurocognitive impairments (Cannon et al., 2000; Gottesman and Shields, 1982; Kendler and Diehl, 1993; Tuulio-Henriksson et al., 2002).

Results of meta-analyses (Heinrichs and Zakzanis, 1998) indicate that schizophrenia patients have a wide range of neurocognitive disorders. Among them, memory impairment is one that has been studied extensively (Aleman et al., 1999; Lee and Park, 2005; Pelletier et al., 2005; Piskulic et al., 2007). This type of impairment is also evident in first-degree non-psychotic relatives of schizophrenia (Sitskoorn et al., 2004; Szokr et al., 2005; Trandafir et al., 2006; Whyte et al., 2005). However, all of these studies were limited to the study of retrospective memory (RM) rather than prospective memory (PM).

PM refers to the ability to remember to carry out an intended action in the future (Brandimonte et al., 1996). It is considered important for daily living. Everyday functionings such as remembering to turn up for an appointment and make a phone call at the right time, all require good working of PM. In addition, failures of PM such as forgetting to take medication or forgetting to turn off the oven after cooking could have dire consequences (Shum et al., 2001).

PM can be divided into three types according to the nature of the cues associated with the planned delayed intention (Einstein and McDaniel, 1990; Kvavilashvili and Ellis, 1996). Time-based PM refers to remembering to execute an intention at a specific time or after a period of time (e.g., remember to attend a meeting at 10:00am on Tuesday); event-based PM refers to remembering to execute an intention when an event/cue appears (e.g., remember to give a message to a friend upon his/her

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appearance); and activity-based PM refers to remembering to execute an intention after completion of an activity (e.g., remember to answer an email after lunch).

Among the studies that examined PM in individuals with schizophrenia, their findings consistently showed that these patients are impaired on PM, irrespective of subtypes (Chan et al., 2008b; Elvevag et al., 2003; Henry et al., 2007; Kondel, 2002; Kumar et al., 2005, 2008; Shum et al., 2004; Twamley et al., 2008; Wang et al., 2008a,b; Woods et al., 2007). Furthermore, some of these studies have found that PM impairment in these patients persist even after controlling for other neurocognitive disorders, suggesting that PM impairment is a primary rather than secondary deficit of schizophrenia (Henry et al., 2007; Wang et al., 2008a). In terms of the nature of impairment, some of these studies suggest that the PM impairments in these patients mainly occur at the cue detection and intention retrieval stages (Wang et al., 2008a; Woods et al., 2007), and others suggest that subjective PM complaints may be dissociated from objective PM performances (Chan et al., 2008b).

We know about the cognitive profiles of first-degree relatives of schizophrenia patients on verbal and visual memory, working memory, attention, and executive functions. Basically, this group of individuals has been found to perform significantly more poorly than matched controls on these functions but their level of performance was not as severe as patients with schizophrenia. However, the performance of PM in this population has not been studied yet. This study will provide information on the PM performance in this group of individuals. By studying PM in relatives of schizophrenia patients, we can identify whether PM would be an endophenotypic marker of schizophrenia and can lead to further genetic studies. In addition, we can provide cognitive remediation therapy to improve the PM difficulties in this high risk group. The present study, therefore, aimed to explore the PM performance in these relatives. We hypothesized that the relatives would perform significantly more poorly than the comparison group.

2. Methods

2.1. Participants

Twenty-six first-degree non-psychotic relatives (14 parents and 12 siblings) of schizophrenia patients were recruited, one relative from each patient. All the patients fulfilled the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV; American Psychiatric Association, 1994) diagnostic criteria for schizophrenia based on diagnostic interviewing (using the Structural Clinical Interview for DSM-IV and medical record reviews). These relatives were recruited from two regional psychiatric hospitals in China (Mental Health Center of Shantou University & Beijing Anding Hospital of Capital Medical University). Relatives were interviewed by psychiatrists to ensure that they did not have psychiatric illness, history of neurological illness, or drug/alcohol dependence. None of the participants reported had human immunodeficiency syndrome (HIV) infection.

Twenty-six healthy participants were also recruited as comparison group from three universities and the general community. A semi-structured interview was conducted by a trained research assistant to ensure that none of the comparison group had any family history of psychiatric illness, suffered from neurological illness, or had alcohol/drug dependence.

Intellectual functioning was estimated using the four-subtest (viz., information, arithmetic, similarity, and digit span) short-form of the Chinese version of the Wechsler Adult Intelligence Scale—Revised (WAIS-R)(Gong, 1992). Handedness was assessed by the Annett Handedness Scale (Spreen and Strauss, 1991). Demographic information of the participants is shown in Table 1. Age, education, and gender ratio were not significantly different between the two groups but intelligence quotient (IQ) was [$F(1,50) = 6.23$, $P = 0.016$]. The present study was approved by the ethics committees of the corresponding institutions. Written informed consent was obtained from each participant.

Table 1
Demographic and clinical data of participants.

	Relative ($N = 26$)		Control ($N = 26$)		$F(1,50)$/ $\chi^2(1)$	P
	Mean	S.D.	Mean	S.D.		
Male: female	18:8		18:8		0	1
Right handed percentage	92		96		1.33	0.513
Age (years)	50.02	13.66	43.38	11.54	3.58	0.064
Education (years)	11.71	2.92	11.15	2.98	0.47	0.498
IQ	108.42	12.93	98.31	16.13	6.23	0.016

Gender and handedness used χ^2 test.

2.2. Measures

2.2.1. PM tasks

Detailed description of the three PM tasks used in this study has been included in our previous studies (Chan et al., 2008b; Wang et al., 2008a,b). Briefly, there were two versions of the task (i.e., semantic and perceptual) in order to control for semantic memory. In the semantic event-based PM (se_ev) session, a four-character phrase (in Chinese) was presented in the center of the screen and the participants were asked to judge whether the phrases were idioms or not. They were asked to press the "J" key to answer affirmatively and the "F" key to answer negatively (this was defined as the ongoing task). If there was an animal character in the phrase (e.g., horse), they were asked to press the spacebar (this was defined as the PM task). A total of five animal characters appeared during the session and the time interval between the appearances of each animal character was approximately 1 min. The participants were told that the two tasks (ongoing task and PM) were of the same importance. There were 88 ongoing task trials and five PM task trials in this session.

The semantic time-based PM (se_ti) session is basically the same as the semantic event-based PM one except that a clock was placed at the upper right part of the keyboard. The participants were asked to monitor the time throughout the testing session. Each time the clock reached the full minute (e.g., 12:23:00, the last two digits are 00), they were asked to press the spacebar (PM task). This session lasted for about 5 1/2 min. Unlike the semantic event-based session, no animal characters were included in the four-character phrases of this task. There were 90 ongoing task trials and five PM task trials in this session.

The perceptual event-based PM (pe_ev) session is similar to the semantic event-based one except that the ongoing task involved judging whether a perceptually degraded digit appeared in the center of the screen was a 0. The participants were asked to press "J" if it was the case and "F" if it was not. On occasions that there was a down arrow under the perceptually degraded digit, the participants were asked to press the spacebar regardless whether the digit was 0 or not, and this was defined as the PM task. There were 122 ongoing task trials and five PM task trials in this session.

The perceptual time-based PM (pe_ti) session is the same as the perceptual event-based one except that a clock was placed at the upper right part of the keyboard and participants were asked to monitor the clock and press the spacebar at each 1 min interval. No down arrows was included in any of the trials. There were 135 ongoing task trials and five PM task trials in this session.

At the end of each of the above four sessions, participants would see the phrase "Thank you for your participation! Bye" on the screen and they were instructed to press the "Enter" key upon seeing this phrase. This was defined as the activity-based PM task. The activity-based PM performance was the proportion of time the participants pressing the "Enter" key in all four sessions. For all the time-, event-, and activity-based PM performances, accuracy of PM was recorded.

2.2.2. Other neurocognitive tests

A set of neurocognitive tests was also administered to all participants. Details of these tests have also been described elsewhere (Chan et al., submitted; Wang et al., 2008a,b). In brief, verbal and visual memory were assessed by the logical memory and visual reproduction subtests of the Chinese version (Gong et al., 1989) of the Wechsler Memory Scale—Revised (Wechsler, 1987); working memory was assessed by the Chinese version of the Letter–Number Span Test (Chan et al., 2008a) and the 2-back part of the *n*-back task (Callicott et al., 1998), for Letter–Number Span, the total correct number and longest passed item were recorded, for 2-back task, the accuracy and reaction time for correct responses were recorded; sustained attention was evaluated by the Sustained Attention Response to Task (SART) (Robertson et al., 1997), the correct press rate and commission error rate were recorded; executive function was evaluated by the modified Wisconsin Card Sorting Test (WCST) (Nelson, 1976) and the animal name semantic verbal fluency task (Spreen and Strauss, 1998), for WCST, categories achieved and perseverative errors were recorded, for verbal fluency task, correct items were recorded.

2.3. Procedure

All participants were given a general introduction to the study as well as an opportunity to ask questions about the study. They then signed an informed consent form before testing began. IQ subtests were administered between PM practice and formal testing as a delay activity. The four PM tasks were given in the following randomly generated order for all participants: se_ti, pe_ev, se_ev and pe_ti. Then the neurocognitive tests were administered in a random order.

2.4. Data analysis

Se_ev and pe_ev PM task performances were averaged to generate an event-based PM score. Se_ti and pe_ti PM task performances were averaged to generate a time-based PM score. Event-based, time-based, and activity-based PM scores were converted to standardized scores (using save standardized values as variables in SPSS 13.0). These scores were then added up to give a summary PM score Z_PM.