



Do Patients with Schizophrenia and Healthy Elderly People show Similar Patterns of Prospective Memory Performance?

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Abstract

Schizophrenia and normal aging have both been associated with structural and physiological changes in the prefrontal and temporal cortex and impairments in prospective memory (PM). This study aimed to compare PM performance in patients with schizophrenia, healthy older, and healthy younger individuals. Computerized event- and time-based PM tasks were administered to 30 patients with schizophrenia, 30 healthy older adults, and 30 healthy younger adults. The healthy older adults and patients with schizophrenia demonstrated deficits in time-based PM when compared with the healthy younger adults. However, only healthy older adults were found to be impaired in event-based PM when compared with the healthy younger adults. These findings suggest that patients with schizophrenia show a similar pattern of performance on one type but not another type of PM and provide only partial support for the accelerated aging hypothesis of schizophrenia.

Keywords: Schizophrenia; Normal aging; Prospective memory

Introduction

Aging is associated with changes in the prefrontal and temporal cortex. These changes include structural (Moscovitch & Winocur, 1995; Raz, Gunning-Dixon, Head, Dupuis, & Acker, 1998; Resnick, Pham, Kraut, Zonderman, & Davatzikos, 2003; Tisserand *et al.*, 2002; West, 1996), neurochemical (Volkow *et al.*, 1996, 1998), and physiological (Logan, Sanders, Snyder, Morris, & Buckner, 2002; Rypma & D'Esposito, 2000; Rypma, Prabhakaran, Desmond, & Gabrieli, 2001). A wide range of cognitive functions including information processing speed and memory has been found to decline with age (Fabiani & Friedman, 1996; Finkel, Reynolds, McArdle, & Pedersen, 2007; Old & Naveh-Benjamin, 2008; Royall, Espino, Polk, Palmer, & Markides, 2004; Singer, Verhaeghen, Ghisletta, Lindenberger, & Baltes, 2003). Previous studies on aging of memory have focused on retrospective memory, the ability to recollect past events (for reviews, *see* Cirillo & Seidman, 2003; Heinrichs & Zakzanis, 1998). In recent years, research in this area has examined the effect of aging on another kind

of memory, namely, prospective memory (PM; Brandimonte, Einstein, & McDaniel, 1996; Einstein & McDaniel, 1990; Kliegel, McDaniel, & Einstein, 2008; Woods et al., 2009, 2010).

PM involves the ability to remember to perform an intended action at some appropriate time in the future (Ellis, 1996). Conventionally, PM is divided into time- and event-based subtypes. Whereas time-based PM requires a person to remember to perform an action at a certain time (e.g., at 2 p.m.) or after a specified time duration (e.g., in 15 min), event-based PM requires the person to remember to perform an action when a particular event occurs in the environment (Einstein & McDaniel, 1990). Brain lesion (Burgess, Veitch, Costello, & Shallice, 2000) and imaging studies (Burgess, Quayle, & Frith, 2001; Burgess, Scott, & Frith, 2003; Okuda et al., 1998, 2007; Simons, Scholvinck, Gilbert, Frith, & Burgess, 2006) have found that the prefrontal cortex (particularly Brodmann's area 10) and the temporal lobes were involved in both time- and event-based PM task performance.

There is evidence to suggest that PM performances decline with age (Henry, MacLeod, Phillips, & Crawford, 2004; Uttl, 2008). Although time-based PM has been consistently reported to be impaired in older adults, some studies did not find age-related decline in event-based PM (Einstein & McDaniel, 1990). This is likely to be due to the nature of event cue (focal vs. non-focal) used in different studies. When the cue is focal to the ongoing task and when the ongoing task involves processing the defining features of the PM cue, the PM cues may be sufficiently processed to enable the automatic retrieval of the delayed intention. When the cue is non-focal to the ongoing task and when it is not part of the information being processed during the ongoing task, more strategic effort is required to monitor the cue in order to realize the delayed intention (Einstein & McDaniel, 2005; Kliegel, Jager, & Phillips, 2008). Older participants performed as well as younger participants in focal cued event-based PM but worse in non-focal cued event-based PM tasks (Kliegel et al., 2008).

Schizophrenia, a major psychiatric disease once described as “dementia praecox” (Kraepelin, 1971), is also associated with a wide range of cognitive impairments (e.g., information processing speed, episodic memory; Bowie & Harvey, 2006; Heinrichs & Zakzanis, 1998; Tang et al., 2009). Given that the early-life manifestation of cognitive impairments in schizophrenia resembles the characteristics of age-related changes, it has been argued that these two conditions may share vulnerability in some common neurobiological substrates (Harvey, Reichenberg, & Bowie, 2006). This argument is supported by the fact that PM (Chan et al., 2008; Henry, Rendell, Kliegel, & Altgassen, 2007; Kondel, 2002; Shum, Ungvari, Tang, & Leung, 2004; Wang, Chan, Hong, et al., 2008; Wang, Chan, Yu, et al., 2008; Wang et al., 2009), frontal and temporal lobes (Callicott et al., 2000; Goldman-Rakic, 1999), and frontal-lobe-related connections (Andreasen et al., 1999; Chan, Di, McAlonan, & Gong, *in press*; Di, Chan, & Gong, 2009; Friston & Frith, 1995) are also impaired in patients with schizophrenia. In addition, patients with schizophrenia and older individuals have been found to have similar brain abnormalities, that is, compared with younger individuals, they both had significant volume reductions in the superior frontal gyrus and orbitofrontal regions but the two groups were not found to be different (Convit et al., 2001). It has, therefore, been suggested that schizophrenia may seem like a syndrome of accelerated aging (Kirkpatrick, Messias, Harvey, Fernandex-Egea, & Bowie, 2008).

The main purpose of the current study was to compare PM performance in patients with schizophrenia, healthy older adults, and healthy younger adults. It was predicted that compared with healthy younger adults, patients with schizophrenia and healthy older adults would show a similar pattern of PM deficits. It is advantageous to test this hypothesis using PM tasks because they involve both prefrontal and temporal lobe processes.

Method

Participants

Thirty patients with schizophrenia (25 inpatients and 5 outpatients), diagnosed based on the Structural Clinical Interview for DSM-IV (American Psychiatric Association, 1994), were recruited from the Institute of Mental Health at Peking University, Beijing Anding Hospital, Capital Medical University, and Mental Health Center of Shantou University. Sixteen of them were diagnosed as the paranoid subtype, 12 undifferentiated subtype, and 2 residual subtype. Twelve were acute cases and 18 were chronic cases. Patients with a history of neurological disease or drug/alcohol abuse/dependence were excluded. Clinical symptoms of the patients were rated using the Positive and Negative Symptom Scale (PANSS; Kay, Fiszbein, & Opler, 1987) by trained psychiatrists. All patients were on typical or atypical antipsychotic medications at the time of the study and 93% of them were taking atypical medication and 7% typical medication. Eight patients were taking other medications such as Atenolol and Artane.

Thirty healthy older (60 years old or older) and 30 healthy younger adults (younger than 60 years old) were also recruited from the community and the above universities for this study. They were interviewed semi-structurally and all met the following criteria: no history of neurological disease or psychiatric disease, no first-degree relative with psychiatric disease,

no drug/alcohol abuse/dependence, and no physical or somatic disease. The healthy older adults all had a Mini-Mental State Examination score above the cutoff of 24 (Zhang, 1993).

Demographical information of the three groups of participants is summarized in Table 1. The gender ratio was significantly different among groups ($\chi^2 = 16.94, p < .001$), but the gender difference in PM performance was not significant ($p > .05$). Thus, gender was not included as an independent variable in subsequent analyses. Not surprisingly, age was significantly different among groups, $F(2,87) = 331.89, p < .001$. Further analysis showed that the healthy older adults were significantly older than patients with schizophrenia ($p < .001$), patients with schizophrenia and healthy younger adults were not significantly different ($p > .05$). Years of education were nonsignificant among groups, $F(2,87) = 2.62, p > .05$.

PM Task

PM was assessed in this study using computerized tasks based on the widely accepted dual-task paradigm developed by Einstein and McDaniel (1990). Specifically, Burgess and colleagues' (2001) Bar Task was adapted for use in this study. The stimuli of the tasks were two arrows between two bars. The bars were either black or white, and the arrows were one black and one white (see Fig. 1a and b). The ongoing task was judging the direction of the black arrow (either left or right) irrespective of the color of the bars. The stimuli appeared in the center of the screen for 1000 ms, followed by a blank screen that lasted for 1000, 1500, 2000, 2500, and 3000 ms randomly. The participants were asked to press "J" on the keyboard if the black arrow points to the right and to press "F" if the black arrow points to the left.

The event-based PM task was to press the spacebar when a down arrow also appears below the stimuli, the down arrow presented on the screen for 1000 ms too (Fig. 1c). Altogether five down arrows would appear in the testing condition. The

Table 1. Demographics of participants

	Healthy younger (<i>n</i> = 30)		Schizophrenia (<i>n</i> = 30)		Healthy older (<i>n</i> = 30)		<i>F</i> -value	<i>p</i> -value
	Mean	<i>SD</i>	Mean	<i>SD</i>	Mean	<i>SD</i>		
Gender (men:women)	13:17		27:3		14:16		16.94	<.001
Handedness (right-handed percentage)	100		97		97		1.02	.600
Age	26.07	8.49	28.90	7.40	72.19	7.37	331.89	<.001
Age range	18–54		18–52		62–85			
Education	14.53	2.84	13.20	2.51	13.10	2.77	2.62	.079
Education range	6–18		9–17		6–18			
MMSE					27.33	1.79		
MMSE range					24–30			
Duration of illness (years)			6.06	8.23				
Medication (chlorpromazine equivalence; mg/day)			290.11	180.46				
PANSS positive			16.27	5.11				
PANSS negative			17.67	4.77				
PANSS general			31.70	6.02				
PANSS total			65.63	11.27				

Notes: MMSE = Mini-Mental State Examination; PANSS = Positive and Negative Symptom Scale. Gender and handedness ratio used χ^2 test.

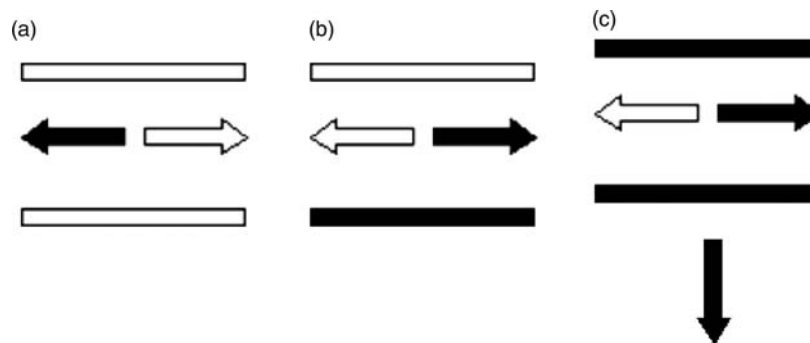


Fig. 1. Stimuli used in the prospective memory task.

time interval between the appearances of the down arrows was approximately 1 min. There were 122 ongoing trials. In total, the testing condition lasted about 5.5 min. After finishing the task, participants were asked to recall the task requirements (see below). The maximum score of this recall was 3, one for arrow judgment, one for PM cue (down arrow), and one for the PM response (press spacebar). PM accuracy and recall of task requirements were recorded. A practice block was given to participants before the formal experiment. There were 20 ongoing trials in the practice block, and following Einstein and McDaniel's (1990) procedure, there was no PM trial in the practice block.

The time-based PM task was basically the same as the event-based one except that the participants were asked to press the spacebar (viz., PM task) once in every minute. No down arrows appeared in this task condition. An external digital clock was placed at the upper right corner of the keyboard for the participants to monitor the passage of time throughout the testing session. There were 120 ongoing trials. This condition took about 5.5 min, and participants were required to press the spacebar at precisely the beginning of each minute (e.g., 12:31:00, when the last two digits are 00). If the responses were made within 5 s around the target time, they were scored as correct. After finishing the condition, participants were also asked to recall the task requirements. The maximum score of this recall was 3, one for arrow judgment, one for PM cue (time), and one for the PM response (press spacebar). PM accuracy and recall of task requirements were recorded. There was a practice block consisted 20 ongoing trials before the formal experiment.

Procedure

This study was approved by the ethics committees of the Institute of Psychology, Chinese Academy of Sciences, and those of the participating hospitals. All participants were given an introduction to the aim of the study and had to sign an informed consent form before the administration of the tasks and interviews. All participants were given oral instructions and practices until they fully understood the tasks before formal testing began. The present study was part of another project on memory and executive function. Thus, some other neurocognitive tests were administered between the practice and actual administration of the event- and time-based PM tasks, the order of event- and time-based PM tasks was counter-balanced in participants. Breaks and rests were allowed when requested. The whole session lasted 1–1.5 h.

Statistical Analysis

PM accuracy and task recall were compared between groups using MANOVA. Correlation analyses was conducted in patients with schizophrenia between PM performance, medication dosage (chlorpromazine equivalence), and clinical symptoms. Correlation analyses between PM performance and age were also calculated in each group and in combined healthy young and healthy older participants.

Results

Table 2 summarizes the PM performance of participants. The results of MANOVA indicated that both event- and time-based PM were significantly different among groups ($p < .001$). Further pairwise comparisons showed that for event-based PM accuracy, healthy older adults performed significantly poorer than patients with schizophrenia ($p < .001$) and healthy younger adults ($p < .001$); patients with schizophrenia and healthy younger adults did not perform significantly different on this measure ($p > .05$). For time-based PM accuracy, healthy older adults did not perform significantly different from patients with schizophrenia ($p > .05$); both healthy older adults and patients with schizophrenia performed significantly poorer than healthy younger adults ($p < .001$). Recall scores of task requirements for event- and time-based PM were not significantly

Table 2. Comparison of PM accuracy among groups

	Healthy younger ($n = 30$)		Schizophrenia ($n = 30$)		Healthy older ($n = 30$)		F-value	p-value	p-value	Cohen's <i>d</i> -value					
	Mean	SD	Mean	SD	Mean	SD				HO vs. HY	Sch vs. HY	HO vs. Sch	HO vs. HY	Sch vs. HY	HO vs. Sch
Event-based PM	0.82	0.24	0.79	0.29	0.34	0.28	27.20	<.001	<.001	.539	<.001	-1.84	-0.11	-1.58	
Time-based PM	0.94	0.11	0.59	0.34	0.50	0.44	13.69	<.001	<.001	.001	.167	-1.37	-1.39	-0.23	
Event PM task recall	3.00	0.00	2.90	0.40	2.97	0.18	1.19	.308	.614	.133	.314	-0.26	-0.35	0.21	
Time PM task recall	3.00	0.00	2.83	0.53	2.97	0.18	2.22	.114	.691	.049	.115	-0.26	-0.44	0.34	

Notes: HO = healthy older; HY = healthy younger; Sch = schizophrenia; PM = prospective memory.

different among groups ($p > .05$); the participants all recall the task requirements well. After controlling for the task recall, the results of PM accuracy remained the same as previous analysis.

Pearson's correlation analyses showed that PM performance did not correlate significantly with clinical symptoms in schizophrenia ($p > .05$), the relationship between event-based PM and medication dosage was significant ($r = -.38, p < .05$). The relationship between PM and age was not significant in healthy older group or healthy younger group ($p > .05$), but relationship between time-based PM and age in patients with schizophrenia was significant ($r = -.41, p < .05$). After combining the healthy younger and healthy older adults as a whole group, age was found to correlate negatively and significantly with event- ($r = -.67, p < .001$) and time-based ($r = -.52, p < .001$) PM.

Discussion

In this study, compared with healthy younger adults, healthy older adults and patients with schizophrenia showed a similar degree of deficits in time-based PM, even after controlling for accuracy of task recall. On the other hand, unlike the healthy older adults, patients with schizophrenia were not found to be impaired in event-based PM when compared with the healthy younger adults. In fact, the patients were found to perform significantly better than the healthy older adults in event-based PM.

The findings that healthy older adults showed event- and time-based PM deficits are consistent with the findings reported in meta-analytic studies (Henry et al., 2004; Uttl, 2008). These studies showed that older participants performed poorer in event- and time-based PM than younger adults in a laboratory setting. For patients with schizophrenia, although deficit on time-based PM found in this study is consistent with findings reported in previous studies (Chan et al., 2008; Wang, Chan, Hong, et al., 2008; Wang, Chan, Yu, et al., 2008; Wang et al., 2009; Woods, Twamley, Dawson, Narvaez, & Jeste, 2007), the failure to find an event-based PM deficit is contrary to findings in previous studies (Chan et al., 2008; Shum et al., 2004; Wang, Chan, Hong, et al., 2008; Wang, Chan, Yu, et al., 2008). One possible reason might be that the event-based PM task in the current study was comparatively easier than those used in previous studies and that the patients with schizophrenia might not be as severe in their brain dysfunctions as the older adults. In this study, the ongoing task was to judge the direction of the black arrow. Because the arrow lasted for a relatively long time on the screen (viz., 1 s), participants might not need much cognitive resources to undertake the ongoing task. Moreover, because the PM cue was a prominent large down arrow that is focal to the ongoing task, detection of this cue might be relatively easy for the participants. In contrast, in previous studies that involved patients with schizophrenia, the PM cues used were non-focal and might be more difficult for patients with schizophrenia (Chan et al., 2008; Wang, Chan, Hong, et al., 2008; Wang, Chan, Yu, et al., 2008).

The time-based PM deficit in healthy older adults and patients with schizophrenia was still significant even after controlling for recall of task requirements, suggesting that the PM deficit found in this study was not likely to be affected by failure to remember the task requirements (Wang, Chan, Hong, et al., 2008; Woods et al., 2007). The PM deficit shown by the patients with schizophrenia and the healthy older adults is most likely to be due to poor self-initiation in monitoring the time or the fact that these two groups had access to less cognitive resources than healthy younger adults.

Taken together, the findings of this study provide only partial support for the accelerated aging hypothesis of schizophrenia (Kirkpatrick et al., 2008). Although results obtained for time-based PM is consistent with this hypothesis, the results obtained for event-based PM is not. The similar degree of impairment in time-based PM in healthy older individuals and patients with schizophrenia is likely to be caused by deficiency in the functions of the prefrontal and cortex (Braver & Barch, 2002; Hedden & Gabrieli, 2004; West, 1996), decline in the function of the dopamine system projection to the prefrontal cortex (Callicott et al., 2000; Goldman-Rakic, 1999; Tanaka, 2006; Volkow et al., 1996, 1998; Weinberger et al., 2001), and similar structural abnormality in the prefrontal regions in both groups (Buchsbaum & Hazlett, 1997; Convit et al., 2001; Waddington, 1988). On the other hand, results obtained for event-based PM do not provide support for this hypothesis. This could be because even though the healthy older adults and patients with schizophrenia are similar in the nature and location of cortical dysfunctions, they might be different in terms of severity. That is, the healthy older adults might have more severe cortical dysfunctions than the patients with schizophrenia. Consequently, the latter group would show a deficit on a PM task that is more difficult and required more initiatives and cognitive resources (viz., time-based) but not on one that is easier and has more obvious PM cue (viz., event-based). Given that our results are preliminary and not entirely consistent with those reported by previous studies, more research and evidence (behavioral and/or functional imaging) are needed to test the accelerated aging hypothesis. For example, one can use a more difficult event-based PM task to see if patients with schizophrenia will show impairment.

There are some limitations in the present study. First, the gender ratio was significantly different between the three groups. Nevertheless, gender difference on PM performance was not found. Second, results of the present study are based on behavioral findings and other evidence is needed to clarify if these impairments have the same or different underlying neural mechanisms. Third, the patients with schizophrenia in the present study were treated with antipsychotic medication. Using medication, naïve cases could provide more conclusive finding without the confounding effects of medication.

Overall, findings of this study suggest that patients with schizophrenia show a similar pattern of performance on one type but not another type of PM and provide only partial support for the accelerated aging hypothesis of schizophrenia. More research is needed to replicate these preliminary findings and to compare the underlying changes in neural mechanisms associated with aging and schizophrenia.

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Conflict of interest

None declared.

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