Neuropsychologia 49 (2011) 2217–2224

Contents lists available at ScienceDirect

Neuropsychologia

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

Prospective memory in patients with first-onset schizophrenia and their non-psychotic siblings

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ARTICLE INFO

Article history:
Received 4 August 2010
Received in revised form 30 March 2011
Accepted 4 April 2011
Available online 9 April 2011

Keywords:
Prospective memory
First-onset schizophrenia
Non-psychotic siblings

ABSTRACT

This behavioral study used a dual-task paradigm to compare PM performance in 35 patients with first-onset schizophrenia, 40 non-psychotic siblings and 35 healthy controls. It aimed specifically to examine the effect of schizophrenia group status on PM, the differential effect of group status on PM type, and correlations between PM and other neurocognitive functions and clinical data in first-onset schizophrenia. It also aimed to test the hypothesis that non-psychotic siblings had poorer PM performance than controls. The cohort of first-onset schizophrenia patients had relatively short illness durations (M = 1.7 years). The three groups of participants were matched in terms of age, gender and years of education. Results of the study confirmed that first-onset schizophrenia status had a primary effect on PM after controlling for other neurocognitive functions. We also found that first-onset schizophrenia status did not differentially affect two different types of PM. In the first-onset schizophrenia cohort, PM was found to correlate significantly with IQ, executive functions and sustained attention. Finally, contrary to the findings of the previous study, this study did not find siblings of schizophrenia patients to have impaired PM. Taking into account the previous findings of PM in chronic schizophrenia, we concluded that schizophrenia has a primary effect on PM regardless of illness duration.

1. Introduction

Prospective memory (PM) is the ability to remember to carry out intended actions in the future and is very important for maintaining independent everyday functioning. PM can be classified, according to the nature of the cues associated with the planned intention, into three subtypes: time-based (remembering to perform an intention at a specific time or after a period of time), event-based (remembering to perform an intention when a cue appears), and activity-based (remembering to perform an intention upon the completion of an activity) PM (Einstein & McDaniel, 1996). The main characteristics of PM are (1) a delay between the encoding and execution stages, (2) engagement in other activities during the delay, (3) absence of an external reminder, and (4) self-initiation (Ellis, 1996). PM is typically assessed by a dual-task (a PM task and an ongoing task) paradigm (Einstein & McDaniel, 1996). In such a paradigm, participants are usually engaged by an ongoing task during the time-lapse between the encoding and execution stages of PM, and they have to retrieve and execute a delayed intention at a specific time (or passage of a certain amount of time) or the appearance of an external event cue. Given its dual-task nature, it is understandable that PM involves not only retrospective memory (RM; for encoding, retaining and retrieving the intention), but also working memory (WM; for maintaining and retaining the intention during the time-lapse), cognitive flexibility (for switching between PM and ongoing task) and sustained attention (for monitoring the passage of time or recognizing the agreed upon event cue; Shum, Ungvari, Tang, & Leung, 2004; Twamley et al., 2008; Ungvari, Xiang, Tang, & Shum, 2008; Wang, Chan, Hong, et al., 2008).

Schizophrenia is associated with a wide-range of cognitive dysfunctions, in particular memory impairment (Heinrichs & Zakzanis, 1998; Pelletier, Achim, Montoya, Lal, & Lepage, 2005) and executive dysfunctions (Walker, Kestler, Bollini, & Hochman, 2004). Patients with schizophrenia have problems in everyday functions such as remembering to attend medical appointments and remembering to take medications (Shum, Leung, Ungvari, & Tang, 2001;

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doi:10.1016/j.neuropsychologia.2011.04.002

Shum et al., 2004; Ungvari et al., 2008). These problems seem to be related to PM deficits, and are common and difficult- to-overcome obstacles in the clinical care and management of these patients.

To date, there is a substantial body of empirical findings which consistently show that schizophrenia is associated with PM deficits (Wang et al., 2009). Table 1 lists 14 previous studies of PM in schizophrenia. Three studies (Kondel, 2002; Ritch, Velligan, Tucker, Dicocco, & Maples, 2003; Twamley et al., 2008) did not include healthy comparison groups. The other eight studies included healthy comparison groups but did not measure or control for IQ (Kumar, Nizamie, & Jahan, 2005, 2008; Shum et al., 2004; Ungvari et al., 2008; Woods, Twamley, Dawson, Narvaez, & Jeste, 2007), executive functions (Altgassen, Kliegel, Rendell, Henry, & Zollig, 2008; Elvevag, Maylor, & Gilbert, 2003; Kumar et al., 2005; Wang, Chan, Yu, et al., 2008; Woods et al., 2007) and other memory functions (Kumar et al., 2005; Shum et al., 2004; Ungvari et al., 2008; Woods et al., 2007). Controlling for these variables is important, and notably three studies (Chan, Wang, Ma, et al., 2008; Henry, Rendell, Kliegel, & Altgassen, 2007; Wang, Chan, Hong, et al., 2008) found a significant schizophrenia group effect on PM after controlling for executive functions, IQ, and other memory functions, and therefore suggested that PM is a primary rather than secondary deficit in patients with schizophrenia. The duration of illness (DOI) in the schizophrenia samples recruited in these three studies were relatively long. The schizophrenia samples in Henry et al.'s (2007), Wang, Chan, Hong, et al., (2008) and Chan, Wang, Ma, et al., (2008) studies had a DOI of 12.7 years, 7.2 years and 8.3 years respectively. For the remaining 11 studies, the samples had a relatively long DOI that ranged from 4.7 to 26.1 years. In a recent meta-analysis, Wang et al. (2009) reported that PM correlated significantly with age, negative symptoms and DOI in a cohort of 485 schizophrenia subjects pooled from 11 previous studies. Thus, the PM deficits found in these 14 previous studies could have been confounded by the long-term medication and hospitalization effect of the samples.

Empirical findings also suggest that PM type (viz., time-based versus event-based) may be differentially affected in schizophrenia patients. However, since different studies used PM paradigms of varied designs and task difficulties, a definitive conclusion has yet to be drawn. For instance, while the Virtual Week used in Henry et al.'s (2007) study is an ecologically-valid paradigm simulating life-like activities, the Memory for Intention Screening Test (MIST) used in Woods et al.'s (2007) study and the computerized PM task used in Shum et al.'s (2004) and Ungvari et al.'s (2008) studies are dual-task paradigms that have little resemblance with everyday life-like activities. The MIST comprises eight PM tasks which require participants to execute verbal or action response (e.g., "when I hand you a poster card, self-address it") and uses a word search puzzle as the ongoing task. The paradigm in Shum et al.'s (2004) and Ungvari et al.'s (2008) studies used a general knowledge task as the ongoing task and had a PM task which required participants to contact a research assistant every 5 min or at the appearance of certain cues. In Wang, Chan, Hong, et al., (2008), Wang, Chan, Yu, et al., (2008) and Chan, Wang, Ma, et al., 2008 studies, a different experimental PM paradigm (see Table 3) was used. Notably, only three previous studies (Chan, Wang, Ma, et al., 2008; Henry et al., 2007; Wang, Chan, Hong, et al., 2008) examined the main and interactive effects between group status and PM type while controlling for IQ and other neurocognitive functions. Nevertheless, the results were inconclusive. Henry et al. (2007) reported that the interaction between schizophrenia status and PM type (time-based versus event-based) was not significant, while Wang, Chan, Hong, et al., (2008) found that the same interaction was significant; compared with controls, schizophrenia patients showed significantly more severe impairment on time-based than event-based PM.

Empirical evidence in the literature also consistently shows that PM correlates significantly with other neurocognitive functions in patients with schizophrenia. A meta-analysis (Wang et al., 2009) found that PM correlated significantly with IQ in a cohort of 175 patients pooled from five studies. Seven previous studies had examined the correlation between PM and executive functions, and found that event-based PM correlated significantly with cognitive flexibility and non-verbal switching (Shum et al., 2004; Ungvari et al., 2008), time-based PM correlated with cognitive flexibility and non-verbal switching (Ritch et al., 2003; Ungvari et al., 2008) as well as planning (Shum et al., 2004; Ungvari et al., 2008); whereas activity-based PM correlated with set-shifting (Kumar et al., 2008). Henry et al. (2007), Twamley et al. (2008) and Wang, Chan, Hong, et al., (2008) reported that PM correlated significantly with initiation. Finally, verbal inhibition and sustained attention were found to correlate significantly with PM in Twamley et al.'s (2008) study but not in Henry et al.'s (2007) study. To date, no study has examined the nature and extent of the relationships between PM and other neurocognitive functions in a first-onset sample. In view of the significant relationships between PM and DOI, the correlations obtained in chronic samples may be different from those obtained in an early-stage sample.

Given that psychosis may be a continuous phenotype (Linscott & van Os, 2010), it is reasonable to extend recruitment of participants who are not diagnosed with schizophrenia but have a high risk of developing the disorder. To date, only two studies have examined PM deficits in participants with schizophrenia-spectrum disorders such as schizotypal disorder (SPD) (Wang, Chan, Yu, et al., 2008) and non-psychotic first-degree relatives of schizophrenia patients (Wang et al., 2010). In the latter study, 26 non-psychotic relatives (mean age: 50 years), compared with 26 healthy controls, were found to have poorer PM performance (after controlling for IQ), more perseverative errors in the Wisconsin Card Sorting Test (WCST) and poorer visuospatial working memory in the 2-back task. The effect size (Cohen's d) of group status on PM was 0.59, and was smaller than the effect size of schizophrenia on PM (weighted mean $d = 1.33$; Wang et al., 2009). However, evidence from this study is inconclusive. First, given that there was a group difference in WCST (uncontrolled), it is possible that the PM deficit in non-psychotic relatives could be secondary to executive dysfunctions. Secondly, the first-degree relatives sample had a wide variation in age because both parents and siblings of patients with schizophrenia were analyzed as a single group.

It would be of theoretical and practical interest to examine whether PM deficits are found in patients with first-onset schizophrenia with a shorter duration of medication treatment and fewer negative symptoms in the early stage of illness. The inconclusive findings of Wang et al.'s (2010) study also call for further clarification using a more robust methodology to address the confounding effect of age and executive dysfunctions. The present study specifically examined PM using a dual-task behavioral paradigm in patients with first-onset schizophrenia and their non-psychotic siblings. Given the ample evidence for significant correlations between PM and other neurocognitive functions (IQ and executive functions), it is necessary to measure and account for the effect of these possible confounders on the group difference of PM (if any), and thus to clarify whether PM is a primary deficit in first-onset schizophrenia. Based on previous empirical findings, we hypothesized that patients with first-onset schizophrenia would perform more poorly on the PM tasks than healthy comparison subjects after controlling for IQ and other neurocognitive functions. We also hypothesized that PM performances in these patients would correlate significantly with IQ and executive functions. Finally, we hypothesized that the non-psychotic siblings group would also perform more poorly in PM than the healthy comparison group.