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Prospective memory deficits in subjects with schizophrenia spectrum disorders: A comparison study with schizophrenic subjects, psychometrically defined schizotypal subjects, and healthy controls

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Abstract

Memory impairment is one of the core deficits in schizophrenia. This study explored the memory profiles of schizophrenic and psychometrically defined schizotypal subjects. The study participants included 15 patients with schizophrenia, 41 schizotypal subjects, and 20 healthy controls. All of the participants completed verbal and visual memory, working memory, and prospective memory tasks. The results showed that patients with schizophrenia were impaired in all aspects of memory function, whereas the schizotypal subjects tended to show moderate to large impairment effect sizes in prospective memory. It is suggested that prospective memory be considered a potential endophenotype of schizophrenia.

Keywords: Memory; Prospective memory; Schizophrenia; Schizotypal; Endophenotype

1. Introduction

Schizophrenia is a heritable disorder (Kendler and Diehl, 1993), but traditional linkage and association studies produce inconsistent findings regarding the susceptibility loci (Tsuang and Owen, 2002). Thus, in recent years researchers have adopted the endophenotype approach to study the gene basis of schizophrenia (Gottesman and Gould, 2003; Gould and Gottesman, 2006). Endophenotypes are more proximal functions of gene action than the diagnosis of schizophrenia itself, and hence it should be simpler to localize the genetic loci of endophenotypes than to localize those for schizophrenia (Gottesman and Gould, 2003; see Gur et al., 2007 for a review). There are different kinds of endophenotypes, and cognitive endophenotypes have been extensively studied.

Cognitive dysfunction has been identified as one of the central abnormalities that is found in schizophrenic patients (Roitman et al., 2000), and memory impairment is one of the core deficits in schizophrenia (Loughland et al., 2007;

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Saykin et al., 1994; Weiss and Heckers, 2001). Patients with schizophrenia have been found to be impaired in verbal memory (Cirillo and Seidman, 2003; Joyce, 2005; Wittorf et al., 2004), verbal working memory (Conklin et al., 2000, 2005), visuospatial working memory (Lencz et al., 2003; Goldberg et al., 2003) and prospective memory (Elvevag et al., 2003; Shum et al., 2004; Kumar et al., 2005; Woods et al., 2007). Most studies have found that cognitive dysfunction is correlated with negative symptoms (e.g., O'Leary et al., 2000; Chan et al., 2006a,b).

In addition to patients with schizophrenia, the schizophrenia spectrum population includes clinically defined schizotypal personality disorder (SPD) subjects, relatives of schizophrenic patients, psychosis-prone subjects (those who score high on psychometric tests for schizotypy) and schizoaffective disorder (Cadenhead et al., 1999). These populations may demonstrate cognitive impairment and are more likely to develop schizophrenia in comparison to the general population.

In particular, researchers have found impairments in the verbal memory and working memory of clinically identified SPD subjects (Cadenhead et al., 1999; Mitropoulou et al., 2002, 2005; Roitman et al., 2000; Voglmaier et al., 1997, 2000; Siever et al., 2002; Smith et al., 2006) and unaffected biological relatives of schizophrenic patients (Cannon et al., 1994; Conklin et al., 2000, 2005; Lyons et al., 1995; Toomey et al., 1998; Keri et al., 2001; Whyte et al., 2005; Wittorf et al., 2004). Psychometric schizotypes have also been found to have impaired spatial working memory (Gooding and Tallent, 2003; Park et al., 1995; Park and McTigue, 1997; Tallent and Gooding, 1999).

Gur et al. (2007) reviewed the literature in schizophrenia on verbal memory and working memory, and found they fulfilled the criteria of endophenotype (i.e., association with illness; state independent; heritable; found in unaffected relatives at a higher rate than in the general population, in addition to at least partially known neurobiological substrate) and suggested that verbal memory and working memory are endophenotypes for schizophrenia.

However, previous studies have mainly focused on retrospective memory, and the prospective function of memory has not yet been fully studied. Prospective memory (PM) refers to remembering to perform an intended action in the future. This kind of memory is important in daily living, for example, remembering to turn up for a doctor's appointment, or remembering to make a telephone call at the right time are examples of activities that require the good working of prospective memory. Also, failure in prospective memory (forgetting to take medication on time, forgetting to turn off an electrical appliance) may lead to undesirable consequences (Shum et al., 2001). PM is classified as event based (remembering to perform an action when a particular event occurs in the environment), time based (remembering to perform an action at a certain time or after a period of time), or activity-based (remembering to do something after finishing a certain activity) (Einstein and McDaniel, 1990; Kvavilashvili and Ellis, 1996).

Research indicates that prospective memory is related to frontal lobe function, and includes studies of frontal lesion patients (Burgess et al., 2000; Daum and Mayes, 2000) and neuroimaging studies (Okuda et al., 1998, 2006; Burgess et al., 2001, 2003; den Ouden et al., 2005; Simons et al., 2006). Neuroimaging studies have found that the lateral prefrontal cortex and rostral frontal cortex (BA 10) especially are activated when subjects perform PM tasks, and that the activations cannot be attributed to task difficulty. Schizophrenic patients have showed impairment of frontal lobe functioning, especially in the dorsal lateral prefrontal cortex (DLPFC), whether they were chronic or first episodic (Callicott et al., 2000; Goldman-Rakic, 1999; Ritter et al., 2004; Curtis et al., 1998; Fu et al., 2005).

There are few studies of PM in schizophrenic patients. In a study by Elvevag et al. (2003) that assessed habitual PM in patients with schizophrenia, participants were asked to play a game and do a PM task once per trial. Participants had to repeat the game 10 times. The results showed that patients made more omission errors (did not do the PM task) than did the healthy controls. Shum et al. (2004) found chronic schizophrenic patients performed worse in all event, time-, and activity-based PM tasks, and did especially worse in time-based tasks; patients also showed time monitoring deficits and performed worse in all frontal lobe tasks (Design Fluency Test (DFT), Tower of London test, and Wisconsin card sorting test). Kumar et al. (2005) found that even drug-free or drug-naïve schizophrenic patients showed impairment in event-based PM. The impairment could not be attributed to motivation or memory of instructions, and their PM performance did not correlate with any clinical symptoms. Woods et al. (2007) also found schizophrenic patients showed impairments in both event and time-based PM, and mainly the cue detection and self-initiated retrieval components of PM were impaired.

Taken together, these studies indicate a PM deficit can be found in schizophrenic patients and that this deficit is relatively stable. We explore the PM deficits in schizophrenia by using semantic and perceptual materials as ongoing tasks and suggest that PM is a general