Neural Correlates of Prospective Memory in Individuals With Schizotypal Personality Features

Ya Wang and Tian-xiao Yang
Institute of Psychology, Chinese Academy of Sciences

Chao Yan, Yi Wang, and Jia Huang
Institute of Psychology, Chinese Academy of Sciences

Zhen Jin and Ya-wei Zeng
Beijing 306 Hospital, Beijing, China

Ruben C. Gur
University of Pennsylvania, and the Philadelphia Veterans Administration Medical Center, Philadelphia, Pennsylvania

Li Su
University of Cambridge

Ming-xia Fan and Da-zi Yin
East China Normal University

David H. K. Shum
Griffith University

Raymond C. K. Chan
Institute of Psychology, Chinese Academy of Sciences

Objective: Prospective memory (PM) refers to the ability to remember to perform actions in the future. Schizophrenia spectrum disorders show impairments in PM but neural correlates of these impairments remain unclear. The present study aimed to examine brain activation during PM to identify impairments in individuals with schizotypal personality features.

Method: Nineteen participants with schizotypal features and 22 healthy controls participated in a functional MRI experiment while performing a PM task.

Results: Results showed that the prefrontal cortex (including Brodmann Area [BA] 10), middle temporal gyrus, and precuneus were activated when performing the PM task compared with baseline. The schizotypal and control groups did not differ in behavioral PM performance. However, participants with schizotypal features showed decreased activations in the inferior and medial frontal lobes (BA 45, and 8).

Conclusions: These results confirmed that the PM network involves prefrontal cortex, including BA 10. The lower activation in prefrontal cortex of individuals with schizotypal features when performing a PM task indicates brain activation abnormality. Notably, this abnormality may occur in the absence of any behavioral manifestation. Our findings support the hypothesis of frontal lobe involvement in PM deficits observed in individuals with schizotypal features.

Keywords: prospective memory, schizotypal personality feature, functional imaging
Prospective memory (PM) refers to the ability to remember to perform actions at a particular moment in the future (Ellis, 1996). PM is critical for many daily activities such as remembering to pay utility bills on time or switching off the gas after cooking. Categorized by the cues that trigger the actions, PM can be divided into three types: event-, time-, and activity-based (Kvavilashvili & Ellis, 1996). Event-based PM refers to executing an intended action when an overt cue appears. Time-based PM refers to executing an intended action at a particular time. Activity-based PM refers to executing an intended action at the completion of an activity. Among its roles in daily life, PM is important in medication adherence (Zogg, Woods, Sauceda, Wiebe, & Simoni, 2012).

**Prospective Memory in Schizophrenia Spectrum**

Schizophrenia is a serious, worldwide disorder that affects about 1% of the general population and causes much social and economic burden (Shasby, 2002). It is no longer considered a single entity but a spectrum of disorders including high-risk individuals prone for psychosis such as schizotypal personality disorders (Cadenhead, Perry, Shafer, & Braff, 1999). Schizophrenia spectrum disorders are characterized by social dysfunction and cognitive impairment (Heinrichs & Zakzanis, 1998; McCleery et al., 2012; Raine, 2006). Schizophrenia spectrum disorders also have genetic causes reflected by different degrees of proneness in patients' first-degree relatives (Gottesman & Shields, 1973; Greenwood et al., 2007).

PM deficits have been found in patients with schizophrenia at different stages of the illness, including both early and chronic stages (Chan et al., 2008; Elvevåg, Maylor, & Gilbert, 2003; Henry, Rendell, Kliegl, & Altgassen, 2007; Lui et al., 2011; Shum, Ungvari, Tang, & Leung, 2004; Wang, Chan, Hong, et al., 2008; Wang, Chan, Yu et al., 2008; Woods, Twamley, Dawson, Narvaez, & Jeste, 2007). A meta-analysis (Wang et al., 2009) has also shown medium to large degrees of impairments for event-, time-, and activity-based PM in this clinical group. Notably, studies reported similar but attenuated PM deficits in both the genetically at-risk individuals, such as nonpsychotic first-degree relatives of patients (Lui et al., 2011; Wang et al., 2010) and clinically at-risk individuals with schizotypal features (Chan et al., 2008; Wang, Chan, Yu et al., 2008).

The dysfunctions and impairments of schizophrenia spectrum disorders have been related to brain abnormalities. Structural and functional neuroimaging studies have demonstrated that patients with schizophrenia show abnormalities in the frontal and temporal lobes and connections between the frontal lobes and other brain areas (Kindermann, Karimi, Symonds, Brown, & Jeste, 1997; Kubicki et al., 2007; Pearson & Marsh, 1999; Satterthwaite et al., 2010). Participants with clinically diagnosed schizotypal personality disorder showed prefrontal, temporal impairments and fronto-temporal disconnectivity (Nakamura et al., 2005; Raine et al., 2002; Raine, Sheard, Reynolds, & Lencz, 1992). Similar abnormalities in the prefrontal and temporal regions have been found in Individuals with schizotypal features (Aichert, Williams, Möller, Kumari, & Ettinger, 2012; Ettinger et al., 2012; Modinos et al., 2010; Premkumar et al., 2012; Raine et al., 1992).

**Neural Basis of Prospective Memory**

A number of studies have demonstrated the importance of prefrontal cortex for PM, particularly rostral (Brodmann Area 10, BA 10) and dorsolateral regions (DLPFC; Burgess, Gonen-Yaacovi, & Volle, 2011; Burgess, Quayle, & Frith, 2001). Brain lesion studies showed that patients with prefrontal lesions are impaired on PM tasks (Burgess, Veitch, Costello, & Shallice, 2000; Daum & Mayes, 2000; Volle, Gonen-Yaacovi, de Lacy Costello, Gilbert, & Burgess, 2011). Neuroimaging studies with healthy participants supported the important role of BA10 in PM. These studies included stimuli such as letters, words, digits, and pictures (Burgess, Quayle, & Frith, 2001; Burgess, Scott, & Frith, 2003), with both event- and time-based PM tasks (Okuda et al., 2007), and measures of different stages of PM processing such as encoding, storage, cue identification and intention retrieval (Gilbert, 2011; Poppenk, Moscovitch, McIntosh, Ozcelik, & Craik, 2010; Simons, Scholvinck, Gilbert, Frith, & Burgess, 2006). Results suggested that BA 10 was activated in PM across types of stimuli and processing stages. In addition to BA 10, other brain regions such as the temporal lobe and precuneus have been involved in PM in neuroimaging studies with healthy participants (Burgess et al., 2011; Okuda et al., 1998).

**The Present Study**

Despite the extensive literature concerning the neural mechanisms of PM in healthy volunteers, and the evidence on behavioral deficits of PM in schizophrenia spectrum disorders, there is a lack of studies examining the neural mechanism of PM in schizophrenia spectrum disorders. The present study aimed to address this gap by examining neural activation during an event-based PM task to test for impairments in individuals with schizotypal features. Thus, we compared brain activations measures from fMRI between individuals with schizotypal features and matched controls while undertaking a PM task. Given the important role of the frontal lobes (especially BA 10) and its related brain regions, we hypothesized that individuals with schizotypal features would demonstrate abnormal prefrontal activations while performing the PM task compared with the controls.

**Method**

**Participants**

Twenty-two individuals with schizotypal features and 22 controls participated in this study. These two groups were selected from a larger group of 426 university students screened using a Chinese version of the Schizotypal Personality Questionnaire (SPQ; Chen, Hsiao, & Lin, 1997; Raine, 1991) in Shanghai, China. Participants with schizotypal features (i.e., the schizotypal group) were randomly selected from those students who scored the highest 10% (n = 42) on the SPQ, and participants without schizotypal features (i.e., the control group) were randomly selected from those who scored the lowest 50% (n = 213) on the same questionnaire. IQ of the participants were estimated by prorating scores on four subscales (Information, Arithmetic, Similarities, and Digit Span) of the Wechsler Adult Intelligence Scale-Chinese Version (Gong, 1992). Three participants in the schizotypal group were excluded from the analyses because of excessive
head movements during scanning, resulting in a total of 19 participants in the schizotypal group. The two groups did not differ in age, gender ratio, education, and IQ (see Table 1). All participants had normal or corrected to normal vision, no history of psychiatric or neurological disorders, and no drug/alcohol abuse. They were all right-handed as assessed by the Annett Handedness Questionnaire (Annett, 1970). This study was approved by the ethics committee of the Institute of Psychology, Chinese Academy of Sciences. All participants provided their written informed consent before the study.

Materials and Procedure

Design. Because event-based PM is most widely used in neuroimaging studies, we also incorporated this paradigm in the present study. We used a combination of block and event-related design based on the approach of (Simons et al., 2006). The task consisted of four sessions: a baseline session and three PM sessions. In the baseline session, participants were asked to perform an idiom-judgment task that did not have any PM instructions. The baseline session was always conducted first. After the baseline session was finished, PM instructions were given to participants and then they performed three PM blocks including PM trials and ongoing trials. We compared the brain activities evoked by PM trials (trials with PM cues and responses embedded in the judgment task) and baseline trials uncontaminated by PM instructions (judgment tasks that did not have any PM instructions).

Stimuli and task. The stimuli were four-character phrases presented in white color at the center of the screen against a black background. During the baseline session, participants were asked to judge whether each phrase was a Chinese idiom or not, without mentioning the PM task. If the phrase was an idiom, they were instructed to press the left button on the response box, otherwise to press the right button. During the three PM sessions, participants were again asked to judge whether each phrase was an idiom or not (i.e., the ongoing task). In addition, they were also asked to monitor whether or not there was an animal name in the phrase. If they saw an animal name while doing the ongoing task, they were instructed to press both response keys together (i.e., the PM task). There were 32 trials in the baseline session, and 52 trials in each of the three PM sessions. There were 10 PM trials and 42 ongoing trials in the first PM session, and 11 PM trials and 41 ongoing trials in the second and third PM session. There were at least three ongoing trials between two adjacent PM trials in order to keep participants’ attention focused on the ongoing task. For each trial, there was a 500-ms fixation followed by a 1500-ms stimulus, and then a blank screen. The duration of the blank screen was jittered at 2 s, 4 s, or 6 s (see Figure 1). Thus, the average duration of a trial was 6 s. We were mainly interested in the contrast of PM trials with baseline trials.

Image Data Acquisition

Functional and structural MRI data were acquired (SIEMENS 3T-Trio A Tim, Erlangen, Germany) using a 32-channel head coil. Functional images were obtained using a T2-weighted single-shot gradient echo pulse sequence (TR: 2000, TE: 30, 90° flip angle, FOV: 210 mm, matrix: 64 × 64, voxel size: 3 × 3 × 3 mm³). Each volume included 32 axial slices (thickness 4 mm with 0 mm gap), which covered the whole brain, acquired in sequential order. The baseline session contained 106 volumes, and each PM session contained 166 volumes. The first two volumes of each session were discarded to allow for T1 equilibration. In addition, T1-wighted anatomical MR images were acquired using a magnetization-prepared rapid gradient-echo (MP-RAGE) 3D MRI sequence (192 slices, sagittal acquisition, TR: 2300ms, TE: 3.01ms, flip angle: 9°, FOV: 240 × 256, matrix: 256 × 256, voxel size: 1 × 1 × 1 mm³).

Image Data Analyses

Image data were preprocessed and analyzed using the Statistical Parametric Mapping software package (SPM8; Wellcome Department of Imaging Neuroscience, London, U.K.) implemented in MATLAB 2008b (Mathworks Inc., Sherborn, MA). Preprocessing of the EPI volumes of the four fMRI sessions included motion correction (realign), slice timing correction,
Table 2

Behavioral Performance Comparison Between Groups

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 22)</th>
<th>Schizotypal (n = 19)</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Baseline accuracy</td>
<td>0.86</td>
<td>0.07</td>
<td>0.84</td>
<td>0.05</td>
</tr>
<tr>
<td>Baseline RT</td>
<td>950.87</td>
<td>175.06</td>
<td>977.22</td>
<td>385.9</td>
</tr>
<tr>
<td>PM accuracy</td>
<td>0.9</td>
<td>0.07</td>
<td>0.9</td>
<td>0.1</td>
</tr>
<tr>
<td>PM RT</td>
<td>879.95</td>
<td>152.19</td>
<td>872.3</td>
<td>264.43</td>
</tr>
<tr>
<td>Ongoing accuracy</td>
<td>0.84</td>
<td>0.03</td>
<td>0.84</td>
<td>0.05</td>
</tr>
<tr>
<td>Ongoing RT</td>
<td>985.18</td>
<td>206.75</td>
<td>1007.13</td>
<td>350.5</td>
</tr>
</tbody>
</table>

Note. Control = participants without schizotypal personality features; Schizotypal = participants with schizotypal personality features; PM = prospective memory; RT = reaction time.

Table 3

Significant Brain Activations of PM in Control Group

<table>
<thead>
<tr>
<th>Anatomical label</th>
<th>Hemisphere</th>
<th>Brodmann area</th>
<th>Peak MNI coordinates</th>
<th>Cluster size (voxels)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PM &gt; baseline</td>
<td></td>
<td></td>
<td>x</td>
<td>y</td>
</tr>
<tr>
<td>Superior frontal gyrus</td>
<td>L</td>
<td>10</td>
<td>−18</td>
<td>59</td>
</tr>
<tr>
<td>Precuneus</td>
<td>L</td>
<td>31</td>
<td>−15</td>
<td>−58</td>
</tr>
<tr>
<td>Middle temporal gyrus</td>
<td>L</td>
<td>39</td>
<td>−42</td>
<td>−64</td>
</tr>
<tr>
<td>Superior frontal gyrus</td>
<td>R</td>
<td>9/10</td>
<td>18</td>
<td>65</td>
</tr>
<tr>
<td>Postcentral gyrus</td>
<td>R</td>
<td>40</td>
<td>33</td>
<td>−31</td>
</tr>
<tr>
<td>Medial frontal gyrus</td>
<td>R</td>
<td>8</td>
<td>15</td>
<td>41</td>
</tr>
<tr>
<td>Paracentral lobule</td>
<td>R</td>
<td>6</td>
<td>12</td>
<td>−19</td>
</tr>
<tr>
<td>Superior frontal gyrus</td>
<td>R</td>
<td>8</td>
<td>24</td>
<td>38</td>
</tr>
<tr>
<td>Medial frontal gyrus</td>
<td>L</td>
<td>8</td>
<td>−9</td>
<td>53</td>
</tr>
<tr>
<td>Superior frontal gyrus</td>
<td>L</td>
<td>8</td>
<td>−24</td>
<td>32</td>
</tr>
<tr>
<td>Baseline &gt; PM</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postcentral gyrus</td>
<td>L</td>
<td>2</td>
<td>−66</td>
<td>−19</td>
</tr>
<tr>
<td>Inferior parietal lobule</td>
<td>L</td>
<td>40</td>
<td>−48</td>
<td>−34</td>
</tr>
</tbody>
</table>

Note. p < .001 with alphasim correction. For the labeling, the MNI coordinates were transformed to Talairach space and labeled using Talairach Client 2.4.2 (Lancaster et al., 2000).

Results

Behavioral Data

The behavioral performances of the two groups are summarized in Table 2. The schizotypal and the control groups did not show any significant differences in accuracy and reaction time (RT) for baseline, ongoing, and PM tasks.

fMRI Data

Results for the control group. The contrast comparing the PM and the baseline trials revealed activation in several brain regions including the superior frontal gyrus (BA 8, 9, 10), precuneus (BA 31), postcentral gyrus (BA 40), middle temporal gyrus (BA 39), medial frontal gyrus (BA 8), and paracentral lobule (BA 6). The reverse contrast revealed that the postcentral gyrus (BA 2) and inferior parietal lobule (BA 40) showed more activation in the baseline than PM trials (see Table 3 and Figure 2). Parameter estimates for PM and baseline in left BA10, right BA10, and left inferior parietal lobe were presented in Figure 3.

Comparison between schizotypal and control groups. Group comparisons showed that the schizotypal group had significantly less activation in the inferior frontal gyrus (BA 45) and medial frontal gyrus (BA 8) than the control group for the
PM compared with baseline trials. The schizotypal group did not show any significantly higher activation than the control group (see Table 4 and Figure 4). Parameter estimates for PM and baseline in inferior frontal gyrus (BA 45) and medial frontal gyrus (BA 8) are presented in Figure 5.

**Discussion**

To our knowledge, this is the first neuroimaging study of PM in individuals with schizotypal features. The main findings of the study are as follows: (1) participants with schizotypal features did not show behavioral impairments in the PM task; (2) PM was associated with activations in the prefrontal cortex, precuneus, middle temporal gyrus, postcentral gyrus, and paracentral lobe; (3) participants with schizotypal features showed decreased activations in the inferior and medial frontal gyrus compared to controls while performing the PM task.

**Behavioral Results**

The finding that the schizotypal group did not show PM impairments is not consistent with those reported by previous behavioral studies (Chan et al., 2008; Wang, Chan, Yu et al., 2008). This could be because the frequency of PM trials was higher in the current study (about 20%) than in previous studies (about 5%). For example, Czernochowski, Horn, and Bayen (2012) showed that the frequency of PM trials could affect the performance of PM, that is, more frequent PM trials would result in a better PM performance, likely because of increased salience for the PM task and enhanced cognitive control. The absence of group difference in behavioral results might be attributable to a ceiling effect for the PM task (both groups showed a mean accuracy of 0.9). High proportion of PM trials might have reduced the difference in PM task performance between the schizotypal and the control groups in our study. Another reason for the absence of group difference in this study might be the longer time allowed for participants to respond in this study (6 s on average) compared with that in previous studies (3.5 s on average). From the standpoint of functional neuroimaging methodology, the similar performance level for the two groups is an advantage because it removes performance as a potential confound when interpreting group differences in activation (Gur et al., 1997).

**Imaging Results**

Imaging results showed that event-based PM activated several brain regions, including superior frontal gyrus, medial...
frontal gyrus, middle frontal gyrus, precuneus, and middle temporal gyrus, in the control group. These results are consistent with those reported in previous studies (Burgess et al., 2011; Burgess, Quayle, & Frith, 2001; Burgess, Scott, & Frith, 2003; Okuda et al., 1998). The BA 10 has been widely reported to be activated when performing PM tasks, and many components of PM (e.g., dual processing, PM encoding, attentional preparatory process, monitoring, disengagement, attention switching, maintenance of the PM intention in the context of ongoing task, and intention execution) are considered to be related to this brain area (Benoit, Gilbert, Frith, & Burgess, 2012; Hashimoto, Umeda, & Kojima, 2011; Poppenk et al., 2010; Reynolds, West, & Braver, 2009). The precuneus is another brain area activated and involved in PM, particularly in the encoding or maintenance (Burgess, Quayle, & Frith, 2001; Burgess, Gonen-Yaacovi, & Volle, 2011; Okuda et al., 2011). Finding activations in the BA 10 and precuneus supports the validity of our PM paradigm.

Schizotypal participants had hypo-activation in the inferior and medial frontal gyrus (BA 45 and BA 8). In Aron’s (2011) review, he suggested that the right inferior frontal gyrus facilitates the attentional switch by inhibiting the previously attended object or dimension, thereby allowing attention to disengage and relocate. Thus the decreased activation in these brain areas for the schizotypal group may indicate impairment in switching attention from the ongoing to the PM task and inhibiting their ongoing response impulse, although this subtle impairment did not manifest behaviorally.

Rushworth, Walton, Kennerley, and Bannerman (2004) suggested that the medial frontal gyrus (BA 8) is involved in motor sequencing and cognitive control. Passingham, Bengtsson, & Lau (2010) suggested that the medial frontal cortex is crucially involved in self-generated action and self-reflection. Thus the decreased activation in BA 8 found in the schizotypal group may indicate impairments in inhibiting ongoing task response sequence and in making a PM response when the PM cue was detected. For both BA 45 and BA 8, the schizotypal group showed more activation in the baseline condition and less activation in the PM condition compared to controls, suggesting that schizotypal individuals process the PM task differently, that is, they need more resources to perform the idiom decision task, and have less additional resources to accomplish the PM task. Such a potential difference in processing pattern in schizotypal participants merits further study.

The present results are generally consistent with findings in patients with schizophrenia in showing decreased activation in the frontal cortex (Hill et al., 2004; Whalley et al., 2008).

Table 4
Comparison Between Schizotypal and Control Group for PM-Baseline Comparison

<table>
<thead>
<tr>
<th>Anatomical label</th>
<th>Hemisphere</th>
<th>Brodmann area</th>
<th>Peak MNI coordinates</th>
<th>t</th>
<th>Cluster size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control &gt; schizotypal</td>
<td>R</td>
<td>45</td>
<td>51 23 7</td>
<td>4.64</td>
<td>26</td>
</tr>
<tr>
<td>Inferior frontal gyrus</td>
<td>R</td>
<td>8</td>
<td>15 41 34</td>
<td>3.98</td>
<td>29</td>
</tr>
<tr>
<td>Medial frontal gyrus</td>
<td>R</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>none</td>
</tr>
<tr>
<td>Schizotypal &gt; control</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>none</td>
<td>none</td>
</tr>
</tbody>
</table>

Note.  p < .001 with alphasm correction. For the labeling, the MNI coordinates were transformed to Talairach space and labeled using Talairach Client 2.4.2 (Lancaster et al., 2000).

Figure 4. Comparison of brain activations between schizotypal and control group for PM and baseline contrast. NS = control group; S = schizotypal group; Med FG = medial frontal gyrus; IFG = inferior frontal gyrus.
Furthermore, individuals at high risk for schizophrenia also showed decreased activations in the frontal lobes. For example, Broome et al. (2009) found that high-risk individuals showed decreased activation compared with healthy controls in the inferior frontal and dorsolateral prefrontal cortex during a semantic working memory task (letter n-back task). In another study, they found high-risk individuals showed less activation in the medial and superior frontal gyrus when performing a visual-spatial working memory task (Broome et al., 2010). Allen et al. (2011) found that high-risk participants showed decreased activations in the medial frontal gyrus and middle frontal gyrus (BA 8) while performing a verbal episodic memory task. Choi et al. (BA) 2012) found that compared with controls, increased activations in the medial frontal gyrus and middle frontal gyrus (BA 8) while performing a verbal episodic memory task (letter n-back task). In another study, they found high-risk individuals showed less activation in the medial and superior frontal gyrus when performing a visual-spatial working memory task (Broome et al., 2010). Allen et al. (2011) found that high-risk participants showed decreased activations in the medial frontal gyrus and middle frontal gyrus (BA 8) while performing a verbal episodic memory task. Choi et al. (BA) 2012) found that compared with controls, increased activations in the medial frontal gyrus and middle frontal gyrus (BA 8) while performing a verbal episodic memory task. Furthermore, individuals at high risk for schizophrenia also showed decreased activations in the frontal lobes. For example, Broome et al. (2009) found that high-risk individuals showed decreased activation compared with healthy controls in the inferior frontal and dorsolateral prefrontal cortex during a semantic working memory task (letter n-back task). In another study, they found high-risk individuals showed less activation in the medial and superior frontal gyrus when performing a visual-spatial working memory task (Broome et al., 2010). Allen et al. (2011) found that high-risk participants showed decreased activations in the medial frontal gyrus and middle frontal gyrus (BA 8) while performing a verbal episodic memory task. Choi et al. (BA) 2012) found that compared with controls, increased activations in the medial frontal gyrus and middle frontal gyrus (BA 8) while performing a verbal episodic memory task. 

Conclusions

The current study showed that individuals with schizotypal features have reduced brain activations in the prefrontal cortex, suggesting a subtle impairment in switching attention from ongoing task to PM task and inhibiting ongoing response impulse to make a PM response. Notably, brain abnormality as assessed by fMRI activations occurred without behavioral manifestations in these individuals.

References


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