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The influence of emotional distraction on verbal working memory: An fMRI investigation comparing individuals with schizophrenia and healthy adults

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The ability to maintain information over short periods of time (i.e., working memory) is critically important in a variety of cognitive functions including language, planning, and decision-making. Recent functional Magnetic Resonance Imaging (fMRI) research with healthy adults has shown that brain activations evoked during the delay interval of working memory tasks can be reduced by the presentation of distracting emotional events, suggesting that emotional events may take working-memory processes momentarily offline. Both executive function and emotional processing are disrupted in schizophrenia, and here we sought to elucidate the effect of emotional distraction upon brain activity in schizophrenic and healthy adults performing a verbal working memory task. During the delay period between the memoranda and memory probe items, emotional and neutral distractors differentially influenced brain activity in these groups. In healthy adults, the hemodynamic response from posterior cingulate, orbital frontal cortex, and the parietal lobe strongly differentiated emotional from neutral distractors. In striking contrast, schizophrenic adults showed no significant differences in brain activation when processing emotional and neutral distractors. Moreover, the influence of emotional distractors extended into the memory probe period in healthy, but not schizophrenic, adults. The results suggest that although emotional items are highly salient for healthy adults, emotional items are no more distracting than neutral ones to individuals with schizophrenia.

1. Introduction

Schizophrenia is a disorder characterized by disruptions in perception. Individuals with schizophrenia may perceive stimuli that are not present (e.g., auditory or visual hallucinations) or may respond to stimuli in an uncharacteristic manner (e.g., lack of affective response to emotional stimuli). In addition, schizophrenia can profoundly impair cognitive functioning. Some have suggested that a primary deficit in working memory may underlie many of the cognitive deficits seen in schizophrenia (Goldman-Rakic, 1994). For example, verbal dysfluencies (Conklin et al., 2000; Heinrichs and Zakzanis, 1998) may persist due to an inability to maintain an ordered progression of thoughts or words. A focus on external stimuli may indicate a lack of ability to maintain an internal list of thoughts or goals (Goldman-Rakic, 1994).

Working memory, the ability to maintain and manipulate information over brief periods of time, is vital to many cognitive processes including language, planning, and decision-making. Verbal working memory, working memory in sentences, words, and letters, relies heavily on prefrontal cortices (Cohen et al., 1994, 1997; McCarthy et al., 1994; Petrides et al., 1993). Middle frontal gyrus has been shown to be engaged by several working memory tasks including spatial working memory (McCarthy et al., 1994), number generation and number memory (Petrides et al., 1993), and letter memory (Sweet et al., 2008). Activation in inferior frontal gyrus (IFG) has been observed during a variety of linguistic tasks such as memory for letters (Cohen et al., 1997), semantic categorization (Kapur et al., 1994; Roskies et al., 2001), semantic association (Noppenney et al., 2004), semantic priming (Copland et al., 2007; Demb et al., 1995; Gold et al., 2006), rhyme judgments

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(Paulesu et al., 1993; Roskies et al., 2001), pseudo-homophone naming (Owen et al., 2004), and phoneme monitoring (Demonet et al., 1992; Zatorre et al., 1996).

The neural infrastructure of working memory is of considerable relevance to clinical disorders in which executive function is impaired, such as schizophrenia. Several studies suggest that individuals with schizophrenia elicit less brain activation compared to healthy adults during working memory tasks. Using a two-back task with Korean alphabetical letters, individuals with schizophrenia elicited decreased activation in inferior frontal, middle frontal, and superior temporal gyri compared to healthy controls (Pae et al., 2008). Similarly, during an *N*-back task using English letters patients elicited less activation in right dorsolateral prefrontal cortex (DLPFC) than healthy adults (Perlstein et al., 2003). Decreased activation in DLPFC for patients compared to healthy controls has also been observed during continuous performance tasks (Barch et al., 2001; Perlstein et al., 2003). Children of schizophrenic individuals (high risk offspring) have also been found to elicit less activation in DLPFC and inferior parietal cortex compared to healthy controls during a spatial working memory task (Keshavan et al., 2002).

In addition to differences in levels of activation, the extent of activation may be influenced by task difficulty. At lower difficulty levels (e.g., 0-back, 1-back) activation was similar among patients and controls, but at more difficult loads, activation continued to increase linearly for healthy adults, but declined in patients (Perlstein et al., 2001). Moreover, they found that load-dependent increases in prefrontal activation were negatively correlated with the severity of disorganized symptoms in the patients. In a separate study, although load-dependent increases in activation were found for all participants, the magnitudes of the increases were significantly smaller in patients compared with healthy controls (Perlstein et al., 2003).

Beyond DLPFC, others have reported reduced activation for adults with schizophrenia. During a spatial working memory task, although there were no differences in fMRI activation in DLPFC, patients elicited less activation in left anterior cingulate and bilateral parietal cortex compared to healthy controls (Kindermann et al., 2004). Similarly, Schneider and colleagues found that patients elicited decreased activation in the precuneus during an *N*-back task compared to healthy controls, although they also reported increased activation in ventrolateral prefrontal cortex (Schneider et al., 2007).

However, others have reported no significant differences in brain activation comparing individuals with schizophrenia and control participants. Honey and colleagues (Honey et al., 2002) found that both patients and healthy controls strongly activated the frontal–parietal network during a verbal *N*-back task, with no significant differences between groups. Interestingly, activation in posterior parietal cortex was positively correlated with reaction time in healthy adults, but not in patients.

There have been several reports of differences in brain activation between patients and controls that indicate increases in activation in dorsolateral prefrontal cortex (DLPFC) for patients (Manoach et al., 2000, 1999; Potkin et al., 2009). In a recent study, both groups showed significant activation in DLPFC during a Sternberg Item Recognition Paradigm (SIRP), however, patients elicited significantly greater activation than healthy controls (Potkin et al., 2009). Moreover, the pattern of increased activation remained when performance was matched across a subset of participants from the two groups. The authors characterized these changes as inefficiencies in processing because the increased activation did not correspond to performance improvements. Van Raalten and colleagues examined the role of familiarity in working memory processes by comparing activation during the SIRP with practiced and novel stimuli. With novel stimuli, patients elicited larger patterns of activation in left prefrontal regions than healthy controls. Although both groups showed decreases in activation with practiced stimuli, only in healthy controls did the magnitude of this decrease correspond to improvements in performance (van Raalten et al., 2008). Increased brain activation was also found among first-degree relatives of individuals with schizophrenia during a verbal auditory continuous performance task (Thermenos et al., 2004). Relatives elicited greater task-related activation in prefrontal regions, as well as in thalamus and anterior cingulate compared to healthy adults. These findings suggest that neurocognitive dysfunction associated with schizophrenia extends across a variety of cognitive tasks and may extend to close relatives. Additionally, the behavioral (Honey et al., 2002) and functional differences in individuals with first-episode schizophrenia (Barch et al., 2001; Perlstein et al., 2001; Schneider et al., 2007), and in relatives (Keshavan et al., 2002; Thermenos et al., 2004) suggest that neurocognitive changes may be at least partially independent of symptom duration. While these studies have examined executive function in patient and control participants, they have not examined the interaction of emotional processing and executive function in individuals with schizophrenia.

Previous research has suggested that different networks are involved in executive function and emotional processing. Several lines of research have proposed a dorsal–ventral distinction such that a dorsal network including middle frontal gyrus, parietal cortex, and posterior cingulate is involved in executive tasks, while ventral brain regions such as inferior frontal gyrus, orbital frontal cortex, and the amygdala are involved in emotional processing (Anticevic et al., 2010; Fichtenholtz et al., 2004; Phan et al., 2002; Phan et al., 2004; Phelps and Ledoux, 2005; Wang et al., 2006; Wang et al., 2005; Yamaskai et al., 2002). Others have suggested that the insula, in particular anterior insular cortex, is involved in interoceptive and emotional sensation, and that the insula along with anterior cingulate cortex may underlie consciousness (Craig, 2002, 2009).

More recently, research has probed how emotion and distraction interact in working memory among individuals with schizophrenia. Dichter and colleagues investigated the role of emotional and neutral distractors during a visual oddball task in individuals with schizophrenia and healthy control participants (Dichter et al., 2009). Consistent with previous results, healthy control participants elicited activation in dorsolateral prefrontal regions to target stimuli, while emotional stimuli elicited activation in ventral–frontal brain regions. However, individuals with schizophrenia elicited less activation to target stimuli in dorsolateral prefrontal regions and less activation to emotional distractors in ventral–frontal brain regions. In addition, the schizophrenic patients also showed less deactivation within these brain regions when compared to healthy adults. These results suggest that brain regions involved in both emotional processing and executive function may be dysfunctional in schizophrenia.

In the present study, we utilized a verbal working memory task that incorporated emotional and neutral distractors. Participants were instructed to remember a series of eight words that were followed by a delay period that contained either emotional or neutral distracting photographs (International Affective Picture System: IAPS). Following the delay period, participants were shown eight pairs of words and asked to decide which word in each pair was presented in the initial memoranda. Of greatest interest is the comparison between emotional and neutral trials in patients and controls. We hypothesized that healthy adults, would show greater activation to emotional distractors compared to neutral distractors in ventral brain regions, such as amygdala, and orbital frontal cortex. Moreover, we predicted that patients would not differentiate emotional and neutral distractors as strongly as healthy adults.