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Neural correlates of emotional recognition memory in schizophrenia: Effects of valence and arousal

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ABSTRACT

Schizophrenia patients are often impaired in their memory for emotional events compared with healthy subjects. Investigations of the neural correlates of emotional memory in schizophrenia patients are scarce in the literature. The present study aimed to compare cerebral activations in schizophrenia patients and healthy controls during memory retrieval of emotional images that varied in both valence and arousal. In a study with functional magnetic resonance imaging, 37 schizophrenia patients were compared with 37 healthy participants while performing a yes/no recognition paradigm with positive, negative (differing in arousal intensity) and neutral images. Schizophrenia patients performed worse than healthy controls in all experimental conditions. They showed less cerebral activation in limbic and prefrontal regions than controls during retrieval of negatively valenced stimuli, but had a similar pattern of brain activation compared with controls during retrieval of positively valenced stimuli (particularly in the high arousal condition) in the cerebellum, temporal lobe and prefrontal cortex. Both groups demonstrated increased brain activations in the high relative to low arousing conditions. Our results suggest atypical brain function during retrieval of negative pictures, but intact functional circuitry of positive affect during episodic memory retrieval in schizophrenia patients. The arousal data revealed that schizophrenia patients closely resemble the control group at both the behavioral and neurofunctional level.

1. Introduction

Deficits in cognition and emotional processing have become a hallmark of schizophrenia (Heinrichs and Zakzanis, 1998; Rund and Borg, 1999; Kohler et al., 2000; Kohler and Martin, 2006). Investigating the effect of emotion on subsequent memory in individuals with schizophrenia provides a unique opportunity to examine the potential interaction between the two processes, particularly in light of evidence that in the general population emotionally charged stimuli are often better retained in memory than neutral stimuli (Hamann, 2001; LaBar and Cabeza, 2006). Furthermore, emotional memory paradigms appear more ecologically valid than encoding and/or retrieval of non-emotional material because in everyday life much of our experience holds emotional significance.

Investigations of emotional memory in individuals with schizophrenia are limited and show mixed results. While some studies have found impairment in emotional memory in individuals with schizophrenia compared with that in healthy subjects (Danion et al., 2003; Hall et al., 2007; Herbener et al., 2007; Neumann et al., 2007), others have found comparable levels of performance between the two groups (Koh et al., 1976; Horan et al., 2006). With regard to the effect emotional valence has on memory performance in patients, some studies have demonstrated an enhancement of memory for emotional (both positive and negative) in contrast to neutral stimuli in schizophrenia patients (Hall et al., 2007; Mathews and Barch, 2004), whereas others have reported the opposite (i.e. neutral better remembered than emotional stimuli) (Koh et al., 1976) or no effect of emotional stimuli on memory (Koh et al., 1981; Neumann et al., 2007). The majority of the published studies have focused on the effect of emotional valence of presented stimuli (i.e. stimuli that vary from positive to negative), while the effect of arousal (i.e. stimuli that vary from calm to exciting) on memory performance has rarely been examined despite indications that it contributes significantly to memory in healthy individuals. Specifically, it has been found that highly arousing stimuli are better recalled than low arousing stimuli (Eysenck, 1976; Bradley et al., 1992). Studies investigating the effect of arousal on memory in patients with schizophrenia have found a better memory performance for stimuli of high emotional intensity relative to low intensity (Mathews and Barch, 2004; Horan et al., 2006; Herbener et al., 2007), but others have reported a detrimental effect of arousal on subsequent memory (Hall et al., 2007).

Functional neuroimaging studies of emotional memory in healthy volunteers have reported activity in limbic regions including the

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amygdala, insula and cingulate cortex, as well as a range of areas in the temporal and prefrontal cortex, during recognition of items that were encoded in emotional relative to neutral contexts (e.g. Maratos et al., 2001; Smith et al., 2004). In patients with schizophrenia, studies of episodic memory (of neutral events) have demarcated a consistent and robust pattern of decreased cerebral activations in the prefrontal cortex, cerebellum and temporal lobe regions (for a meta-analysis see Achim and Lepage, 2005b). Increased cerebral activations have also been observed including hyperactivity of the hippocampus during both successful and unsuccessful mnemonic encoding (Zierhut et al., 2010) as well as a relative increase in activity in the cerebellum, visual cortex, and parietal cortex (Crespo-Facorro et al., 2001) during recognition memory in patients compared to healthy participants. Evidence of the neural correlates of emotional episodic memory in schizophrenia is limited in the literature. Whalley et al. (2009) reported robust medial temporal lobe activations in patients with bipolar disorder, patients with schizophrenia and healthy controls during memory encoding that correlated significantly with subsequent recognition memory performance. Nonetheless, there was no direct comparison between the schizophrenia and control group. Another functional magnetic resonance imaging (fMRI) study implemented an emotional memory paradigm with faces and reported emotion-specific differences in cerebral activations (e.g. hippocampus, parahippocampal gyrus, and superior frontal gyrus) associated with memory response bias in patients with schizophrenia and healthy subjects (Sergerie et al., 2010).

The aim of the present study was to investigate the neural correlates associated with memory retrieval of stimuli that varied in both valence and arousal, in schizophrenia patients compared to healthy controls.

In line with some behavioral studies of emotional memory (Danion et al., 2003; Mathews and Barch, 2004; Neumann et al., 2007) and the majority of neuroimaging studies of emotion processing in schizophrenia, which found less sensitivity to emotional stimuli in patients relative to controls (Schneider et al., 1998; Gur et al., 2002; Takahashi et al., 2004), we expected to observe a decreased recognition accuracy of emotional stimuli in schizophrenia patients relative to healthy subjects and decreased cerebral activations in all experimental conditions (positive, negative, high and low arousal) in medial temporal cortex, as well as prefrontal regions previously implicated in emotion processing and memory (medial, middle frontal and orbitofrontal cortex) (LeDoux, 1993; Dolcos et al., 2004a, 2004b). In terms of the influence arousal has on memory for emotional stimuli, it has been found that relative to healthy controls, patients are more likely to misidentify low arousal emotional stimuli as neutral (Kohler et al., 2000), but recognize high intensity emotions without difficulty (Hooker and Park, 2002). Thus, we expected to observe increased brain activations in the high relative to low arousal contrasts of the presented positive and negative stimuli in healthy controls. In comparison, in schizophrenia patients, we did not expect to observe differences in brain activations elicited by memory of neutral and low arousing stimuli but did expect increased activity only in the high arousal conditions. Previous studies investigating the neural correlates of emotional arousal have observed activations in the anterior temporal pole, visual cortex, prefrontal cortex and regions of the medial temporal lobe in high relative to low arousing conditions (Lane et al., 1999; Bradley et al., 2003) (all regions that have previously been implicated in functional neuroimaging studies of emotional memory as well). In this regard, we postulated that a similar pattern of regions would be activated in the high relative to low arousal contrasts in our emotional memory paradigm in both groups. With regard to valence the literature has reported mixed results, with some studies revealing different neural deficits underlying processing of positive and negative affect (Schneider et al., 1998; Gur et al., 2007; Reske et al., 2009), and others showing comparable brain activations during exposure to positive and negative stimuli in schizophrenia (Dowd and Barch, 2010). Behavioral studies of emotional memory have also yielded inconsistent results (Herbener, 2008). Consequently, no predictions were made with regards to the effect of positive vs. negative emotion on subsequent memory in patients or controls.

2. Methods

2.1. Subjects

Thirty-seven schizophrenia patients (19 men, 18 women) meeting the DSM-IV criteria for schizophrenia (APA, 1994), in a stable phase of their illness (defined as no relapse within the last 2 months and no change in their antipsychotic treatment within the last month) and 37 healthy controls (19 men, 18 women) participated in the study. The groups were matched for age, sex, handedness (Edinburgh Inventory) (Oldfield, 1971) and parental socio-economic status (National Occupational Classification; NOC) (Census, 2001) (Table 1).

All patients were re-evaluated by experienced psychiatrists before being assigned to the research group (DSM-IV, criteria A-E); affective, schizoaffective and schizophreniform psychoses were excluded. Control participants were screened with the non-patients edition of the Clinical Interview for DSM-IV (SCID) (Spitzer et al., 1992).

Symptom severity was rated according to the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987). Illness onset was defined as the date of the first psychiatric consultation. All the patients received at least one atypical antipsychotic (27 patients received one, nine received two, one received three. Clozapine: $n=19$, mean dosage=452.63 mg$\pm$77.23 mg; olanzapine: $n=12$, mean dosage=14.58 mg$\pm$5.4 mg; risperidone: $n=11$,mean dosage=3.73$\pm$1.67 mg; quetiapine: $n=7$, mean dosage=585.71 mg$\pm$238.85 mg).

General exclusion criteria included age below 18 or above 45 years, past or present neurological or Axis-I psychiatric disorder, alcoholism or drug abuse, non-compliance with testing procedures, abnormal uncorrected vision or any contra-indication for MRI such as

Table 1
Demographic and clinical data of participants.

	Schizophrenia patients		Healthy controls		*P* (independent sample, two-tailed)
	Mean	S.D.	Mean	S.D.	
Age	32.46	7.66	31.81	6.91	0.70
Parental SES	2.36	1.09	2.68	0.88	0.18
Sex (% male)	51	–	51	–	–
Handedness (% right)	89	–	91	–	–
Medication (chlorpromazine equivalence)	613.92	361.02	–	–	–
PANSS positive	18.84	6.93	–	–	–
PANSS negative	12.59	10.95	–	–	–
PANSS general	24.05	22.59	–	–	–

SES = socioeconomic status; S.D. = standard deviation.