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Encoding deficit during face processing within the right fusiform face area in schizophrenia

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ABSTRACT

Face processing is crucial to social interaction, but is impaired in schizophrenia patients, who experience delays in face recognition, difficulties identifying others, and misperceptions of affective content. The right fusiform face area plays an important role in the early stages of human face processing and thus may be affected in schizophrenia. The aim of the study was therefore to investigate whether face processing deficits are related to dysfunctions of the right fusiform face area in schizophrenia patients compared with controls. In a rapid, event-related functional magnetic resonance imaging (fMRI) design, we investigated the encoding of new faces, as well as the recognition of newly learned, famous, and unfamiliar faces, in 13 schizophrenia patients and 21 healthy controls. We applied region of interest analysis to each individual's right fusiform face area and tested for group differences. Controls displayed higher blood oxygenation level dependent (BOLD) activation during the memorization of faces that were later successfully recognized. In schizophrenia patients, this effect was not observed. During the recognition task, schizophrenia patients exhibited lower BOLD responses, less accuracy, and longer reaction times to famous and unfamiliar faces. Our results support the hypothesis that impaired face processing in schizophrenia is related to early-stage deficits during the encoding and recognition of faces.

1. Introduction

Recognizing and interpreting faces correctly is crucial to social interaction because faces contain a great deal of information about the identity, emotions, intentions, and physical state of the person with whom one is communicating. However, face processing has been shown to be impaired in schizophrenia patients (Archer et al., 1992; Phillips and David 1995; Addington and Addington 1998; Streit et al., 2001; Whittaker et al., 2001; Gur et al., 2002; Hall et al., 2004; Sachs et al., 2004; Surguladze et al., 2006; Chen et al., 2008; Gur et al., 2007). A specific region in the fusiform gyrus, the fusiform face area (FFA), is thought to be critical for face processing in humans (Kanwisher et al., 1997; Nakamura et al., 2000; Tzourio-Mazoyer et al., 2002; Schwarzlose et al., 2005). The fusiform face area represents the connection between the core and the extended system for human face processing (Haxby et al., 2002; Fairhall and Ishai, 2007).

In schizophrenia, the encoding of visual stimuli appears to be generally impaired, with affected patients showing maximal impairments when fine-feature processing is needed (Tek et al., 2002). In fact, studies of event-related potentials in patients who were shown either faces (Herrmann et al., 2004; Herrmann et al., 2006; Onitsuka et al., 2006) or fragmented objects (Doniger et al., 2001) have revealed that visual processing in schizophrenia patients differs from that in healthy controls. Furthermore, impaired working memory in facial image processing has been associated with reduced activity in various brain areas, including the left fusiform gyrus (Yoo et al., 2005). Studies on the recognition of one's "own" face have reported equivocal findings in schizophrenia depending on the task (Irani et al., 2006; Lee et al., 2007).

Right fusiform gyrus volume is reduced in patients with schizophrenia compared with controls (Lee et al., 2002; Onitsuka et al., 2003). This structural deficit has been associated with lower amplitudes of the face-specific N170 potential (Onitsuka et al., 2006), leading to the conclusion that impaired face recognition among schizophrenia patients is possibly related to structural deficits in the right fusiform gyrus. By contrary, a postmortem study reported no differences in right fusiform gyrus volumes between schizophrenia patients and controls (McDonald et al., 2000).

Only one functional neuroimaging study to date has focused on the fusiform face area (FFA) in schizophrenia. The experiment involved a low-level one-back working memory task of faces and objects, which failed to elicit a difference in performance or FFA activation between schizophrenia patients and controls (Yoon et al., 2006). These findings

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called into question the notion of there being a specific face processing deficit in schizophrenia. However, it is important to consider that, while the experiment tested only basic visual face perception, face processing appears to consist of multiple tasks such as encoding, visual–spatial perception, recognition memory, and executive functions (Leveroni et al., 2000; Whittaker et al., 2001; Lehmann et al., 2004). Indeed, the FFA had been shown to be activated during the encoding and recognition of face images (Haxby et al., 1996; Leveroni et al., 2000; Lehmann et al., 2004). Therefore, we wanted to elucidate the FFA activation in schizophrenia during the encoding of face images compared with healthy controls. After identifying the FFA in each individual study participant, we compared the two groups with regard to the encoding of newly learned faces, as well as the recognition of previously learned faces, famous faces, and unfamiliar faces. We used the encoding task developed by Lehmann et al. (2004), but designed a recognition task adapted both from Lehmann et al. (2004) and Leveroni et al. (2000). We hypothesized a reduced BOLD activation within the right FFA during encoding and recognition in schizophrenia patients.

2. Methods

2.1. Subjects

In total, 13 patients suffering from schizophrenia according to ICD-10 and DSM-IV criteria (10 paranoid, 1 catatonic, 1 disorganized, 1 brief psychotic episode), as well as 21 healthy controls, were included in the study. Controls and patients had been matched for age and sex, and all of them were right-handed according to the Edinburgh Handedness Scale (Oldfield, 1971) (Table 1). Because of compliance problems related to the MRI scanner and testing procedures, in particular among the schizophrenia patients, we were only able to include the MRI scans for 13 of the original 20 patients in the final analysis. All participating schizophrenia patients were inpatients at the University Hospital of Psychiatry in Bern, Switzerland. Diagnoses were given by experienced, board-certified psychiatrists (H.H., W.S., and T.J.M.) after extensive exploration and review of the case history. Study participants were free of medical disorders (i.e. other than schizophrenia in the study patients), as determined by an examination and review of their medical history. The average duration of illness (since first diagnosis) was 3.5 (S.D. = 4.1) years. Nine patients were being treated with atypical antipsychotic drugs (6 of them with risperidone), one patient received both typical and atypical antipsychotics, whereas three patients remained drug free until after the experiment (chlorpromazine equivalents are given in Table 1). None of the patients was on patients were being treated with clozapine. Chlorpromazine equivalents were calculated according to the literature (Rey et al., 1989; Woods, 2003). The Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987) was used to assess overall psychopathology. One investigator (H.H.) conducted all the PANSS ratings. He had previously received specialized PANSS rater training. The investigation was conducted in accordance with the Declaration of Helsinki and approved by the local ethics committee. Before entering the study, both patients and healthy controls provided written informed consent.

Table 1
Descriptives.

	Schizophrenia patients		Healthy controls				
N	13		21				
	Men	Women	Men	Women	Test	*df*	*P*-values
Sex	10	3	12	9	$X^2 = 1.376$	1	0.241
Age (pooled) mean ± S.D.	25.82 ± 5.50		26.10 ± 4.17		$t = 0.169$	1	0.867
Duration of illness [years]	2.3 ± 1.6	2.2 ± 1.8					
CPZ	575.69	620.62					
PANSS positive	13.31	4.70					
PANSS negative	16.46	5.59					
PANSS total	56.15	14.32					
TLC	4.92	5.48					

CPZ: Chlorpromazine equivalents.
PANSS positive: Positive symptoms subscale of the PANSS.
PANSS negative: Negative symptoms subscale of the PANSS.
PANSS total: PANSS total score.
TLC: Thought, Language, and Communication Scale.

2.2. Experimental design

The experiment consisted of two parts and had been tested in a pilot study without functional magnetic resonance imaging (fMRI) scanning (Eichenberger, 2004). Procedures and tasks were explained to the participants before they entered the scanner room. Patients were asked to ascertain whether they had been entirely understood. Also, between experiments, instructions were repeated verbally as well as displayed on the computer screen.

1) Encoding task: Study participants were presented with images of neutral faces and were asked to memorize them so that they would be able to recognize them later. During this task, 30 unfamiliar faces and 30 "null events" (Dale and Buckner, 1997) (i.e. blank screens) were presented in random order. Each image and null event was presented for 2 s.
2) Recognition task: Study participants had to recognize the faces they had learned previously. In this task, 30 images of faces and 30 null events were presented in random order. Of the 30 faces shown, 10 had been presented during the encoding task, 10 were of familiar celebrities (e.g. Marilyn Monroe), and 10 were unfamiliar. The category of familiar celebrities was included to enhance the difficulty of the task. Unknown faces were shown as a control variable to check for false-positive recognition.

All of the faces were shown as black and white photographs obtained from the same source as that used in a previous study (Lehmann et al., 2004) (see example of stimulus material in Fig. 1). Each image and null event was presented for 2 s using an MR-compatible goggle system (VisuaStim XGA, Resonance Technology, Inc., USA; field of view = 30°, refresh rate = 60 Hz, resolution = 1024 × 768). Response times and omission rates were recorded with an MR-compatible optical key-press device, which was connected to a personal computer running the experimental task and located outside the scanner room. For the recognition task, study participants were asked to indicate whether the image displayed was familiar or unfamiliar by pressing the MR-compatible optical key-press device as quickly as possible. Beforehand they were instructed to decide whether they had seen the displayed face before (previously learned or familiar celebrity — left mouse button) or whether the face was unfamiliar to them (right mouse button). Stimulus material was tested for recognition outside the scanner by presenting a random choice of seven faces of each category out of our stimulus set to the controls. The mean percentage of famous celebrities who were correctly labeled as being famous was 98.1% (S.D. = 7.4%). Of the presented famous face images, an average of 89.5% (S.D. = 13.7%) were named correctly. A pilot study that tested the stimulation paradigm revealed significant differences in accuracy between controls and schizophrenia patients (72.5% vs. 50.5%; Eichenberger, 2004).

In order to find the brain region with the maximum response to face stimuli for each subject (i.e. the right fusiform face area), we conducted a block-design experiment at the end of the scanning session. The localizer run consisted of blocks of faces, chairs, and fixation crosses. Each image was presented for 2 s over a 30-s period, which was followed by a 20-s