Brief report

Preserved function of the fusiform face area in schizophrenia as revealed by fMRI

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Abstract

Many lines of evidence suggest that individuals with schizophrenia suffer from face processing deficits. However, the specificity of these deficits and the neural dysfunction underlying them remain unclear. To address these questions, we evaluated the functional status of a critical region for face processing, the fusiform face area (FFA), in subjects with schizophrenia. Fourteen schizophrenia patients and 10 healthy control subjects participated in an fMRI experiment to determine the functional status of the FFA by viewing a series of faces and exemplars of other object categories, while completing a low-level task designed to verify their engagement with the stimuli. Behavioral performance and activation of the FFA were equivalent between groups. Thirteen of 14 patients and all control subjects displayed FFA activation. Furthermore, the degree of FFA activation, as measured by FFA volume and magnitude of activity, was similar between groups. The FFA, a critical region in the neural system subserving the perceptual processing of faces, appears to be intact in schizophrenia. These results call into question the presence of a specific face processing deficit in schizophrenia.

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1. Introduction

Schizophrenia is a complex, severe illness, affecting many cognitive and affective processes. The social and affective deficits associated with schizophrenia (Mueser et al., 1996; Gur et al., 2002; Quintana et al., 2003) are a particularly important source of disability (Penn et al., 1996; Kee et al., 2003), and appear to be refractory to traditional treatment modalities (Arango et al., 2004; Herbener et al., 2005). Investigators have proposed that aberrant processing of faces may contribute to at least some of these deficits. Consequently, the investigation of the neural basis of face processing deficits has become an important area of research.

A number of studies have documented abnormal performance on tasks utilizing faces in individuals with schizophrenia (Addington and Addington, 1998; Whitaker et al., 2001; Pinkham et al., 2005). However, the specificity of the face processing deficits and the neural basis of these deficits remain unclear. The presence of

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higher-order cognitive deficits, presumably of the prefrontal cortex in schizophrenia (Weinberger et al., 1986; Callicott et al., 2000; Perlstein et al., 2001), presents a plausible alternative hypothesis for poor performance on face processing tasks. Consistent with this alternative account, some investigators were unable to identify face processing deficits independent of disturbances in attention or executive function (Addington and Addington, 1998; Whittaker et al., 2001).

The presence of a specialized neural system for face perception and processing (for review, see Kanwisher, 2000; Haxby et al., 2002) presents an opportunity to address the question of the primacy and specificity of face processing deficits in schizophrenia. Monkey electrophysiological studies have demonstrated the presence of face-specific neurons in the temporal cortex (Perrett et al., 1982; Hasselmo et al., 1989). In humans, distinct functional regions in the occipital–temporal cortex support the processing of ecologically important categories of visual stimuli including faces (Haxby et al., 1996; Kanwisher et al., 1997; McCarthy et al., 1997), scenes (Epstein and Kanwisher, 1998) and everyday objects (Malach et al., 1995). The so-called “fusiform face area” (FFA), located mostly in the middle and posterior aspects of the fusiform gyrus, appears to be specialized for the visual processing of faces (Haxby et al., 1996; Kanwisher et al., 1997; Grill-Spector et al., 2004). fMRI studies have documented the critical involvement of the FFA in face processing by demonstrating its selective engagement by faces compared to other stimuli (Kanwisher et al., 1997), enhanced activation during the detection of faces (Grill-Spector et al., 2004) and preferential activity for upright compared to inverted faces (Kanwisher et al., 1998). Cases of acquired prosopagnosia resulting from injury of the fusiform gyrus in adulthood, in which individuals cannot discriminate between faces even though they retain the ability to discriminate between non-face objects, provide strong evidence for the necessity of the FFA in face recognition (Barton et al., 2002).

Several neuroimaging studies have examined the fusiform gyrus, part of the ventral visual stream subserving visual object and face processing in schizophrenia; these have shown structural (Kuperberg et al., 2003; Onitsuka et al., 2003, 2005) and functional (Gur et al., 2002; Quintana et al., 2003; Herrmann et al., 2004) abnormalities. The fMRI studies have suggested abnormal functioning of the fusiform gyrus based on the absence of activity in this region during face processing (Gur et al., 2002; Quintana et al., 2003). In an ERP study (Herrmann et al., 2004), subjects with schizophrenia showed the characteristic N170 component elicited by faces, but the magnitude of the N170 was diminished. Contradicting the hypothesis of dysfunction in the neural system subserving face processing, a series of studies conducted by Butler et al. (2001) and Foxe et al. (2005) suggests that the ventral visual system is preserved, while the dorsal system is perturbed.

The goal of our experiment was to test the hypothesis that subjects with schizophrenia exhibit a specific deficit in the perceptual processing of faces. Given the presence of a specialized neural system for the perceptual processing of faces and the importance of the FFA in this system, the examination of the FFA in schizophrenia may produce important evidence regarding this hypothesis. Abnormalities in FFA function would provide a compelling argument for the presence of a specific perceptual deficit in face processing, whereas normal FFA function would be consistent with the preservation of this system in schizophrenia. We evaluated the FFA by employing a reliable fMRI paradigm designed to identify and engage the FFA (Kanwisher et al., 1997; Epstein et al., 2003; Ranganath et al., 2004), in a group of subjects with schizophrenia and healthy control subjects. To our knowledge, while there have been other fMRI studies examining fusiform activity in response to faces (Gur et al., 2002; Quintana et al., 2003), this is the first published schizophrenia report on the functional status of the FFA, a more specialized module within the fusiform gyrus.

2. Methods

2.1. Subjects

Fourteen individuals with schizophrenia and 10 healthy control subjects participated in this experiment. A summary of the demographic data of our subjects is displayed in Table 1. All controls were recruited via community advertisement. All subjects with schizophrenia were stable and chronically ill outpatients at time of testing, and were recruited through a variety of methods, including referrals from psychiatric colleagues and advertisement in local mental health advocacy groups. Control subjects and patients underwent diagnostic assessment with a Structured Clinical Interview for DSM-IV to either confirm the diagnosis of schizophrenia or schizoaffective disorder in the latter, or to exclude any individuals with a lifetime history of an Axis I disorder or a family history of psychotic disorders in the former. The symptom status of patients was obtained by administering the Brief Psychiatric Rating Scale (24-item version), Scale for the Assessment of Negative Symptoms (SANS) and Scale for the Assessment of Positive Symptoms (SAPS). For the
Table 1
Demographic data

<table>
<thead>
<tr>
<th></th>
<th>Schizophrenia patients (n=14)</th>
<th>Healthy controls (n=10)</th>
<th>Difference (P&lt;0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>36.1 (11.8)</td>
<td>30.3 (7.9)</td>
<td>NS</td>
</tr>
<tr>
<td>Gender (% male)</td>
<td>79%</td>
<td>50%</td>
<td>NS</td>
</tr>
<tr>
<td>Parental education (years)</td>
<td>13.3 (2.5)</td>
<td>16.0 (3.5)</td>
<td>0.01</td>
</tr>
<tr>
<td>Subject education (years)</td>
<td>12.5 (1.8)</td>
<td>16.6 (2.9)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Handedness (% right)</td>
<td>93%</td>
<td>100%</td>
<td>NS</td>
</tr>
<tr>
<td>BPRS</td>
<td>51.2 (14)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>SANS</td>
<td>8.6 (4.2)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>SAPS</td>
<td>7.6 (3.7)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>GAS</td>
<td>55.4 (4.9)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Neuroleptics</td>
<td>Subjects on typical=2, subjects on atypical=12</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Summary of demographic information for SZ and C subjects expressed as means and standard deviations (in parenthesis). Abbreviations: BPRS—Brief Psychiatric Rating Scale (24-item version); SANS—Scale for the Assessment of Negative Symptoms; SAPS—Scale for the Assessment of Positive Symptoms; GAS—Global Assessment Scale. Results of t-tests are also displayed; NS=non-significant, NA=non-applicable.

BPRS, the total score was obtained by summing all the item scores, whereas for the SANS and the SAPS, summary scores were generated by summing the global subscale scores (Table 1). Exclusion criteria for both groups were: (1) age older than 50 or younger than 18 years of age, (2) mental retardation, (3) meeting DSM-IV criteria for substance dependence within the past 6 months or substance abuse within the past month, (4) lifetime history of significant neurologic disorder or head trauma, or current medical condition that may affect brain function or structure. All SZ subjects were taking neuroleptics at time of study. As indicated in Table 1, the two subject groups were well matched except in the number of years of education of the parents (SZ $M=13.3$, S.D. = 2.5; C $M=16.0$, S.D. = 3.5; $P=0.01$) and of the subjects (SZ $M=12.5$, S.D. = 1.8; C $M=16.6$, S.D. = 2.9; $P<0.01$). Lower number of years of education was expected in the SZ group given the age of onset and the debilitating nature of this illness. As for parental education, we believed that a small difference in this demographic factor would not significantly affect our ability to assess the neural basis of face processing in schizophrenia. Additionally, we conducted post-hoc analysis that supports this assertion. These results are reported in the results section. This study was approved by the IRB at the University of California Davis. All experiments were conducted at the Imaging Research Center at the University of California Davis.

2.2. Activation paradigm

Stimuli were presented and responses recorded with E-Prime (Psychology Software Tools, Inc., Pittsburgh, PA; http://www.pstnet.com). The localizer experiment, Fig. 1, was projected onto a screen, viewed by participants through a mirror mounted on the head radiofrequency (RF) coil while the subject was lying prone in a scanner. In one run of the localizer experiment, there are four series of stimuli, with each series consisting of four visual category blocks. The series were interleaved with a baseline period consisting of a cross hair displayed on a blank background for 24 s. Within each series, the four category blocks (faces, scenes, everyday objects, e.g. toaster, ladder, umbrella, etc., and scrambled images of everyday objects) were displayed. Within a category block, 20 exemplar images (courtesy of Nancy Kanwisher, MIT) of the category were presented, with each stimulus being shown for 600 ms. A fixation cross was displayed for 600 ms between images. Thus, each block lasted 24 s. The order of presentation of a category block within a series was counter-balanced over the entire run. For example, faces were the 3rd, 4th, 1st and 2nd blocks presented in series 1, 2, 3 and 4, respectively. In order to increase power in detecting activations, each subject underwent two runs of the localizer experiment. A critical aspect of conducting between-group studies is to obtain on-line verification that the subjects are attending to the stimuli during scanning. Consequently, during the viewing of the visual stimuli described above, subjects were required to press both thumbs on the response pad when the current image was the same as the image immediately preceding it (two to three responses were required for each block of images). While this 1-back task involves working memory, numerous studies have consistently demonstrated that SZ subjects perform this type of task very well and at a level comparable to that of controls (Perlstein et al., 2001, 2003; Kim et al., 2004). Consequently, any differences in FFA activity between groups would likely not reflect deficits in working memory.

2.3. Behavioral data analysis

Performance on the behavioral task was calculated for each individual by dividing the number of responses made during the presentation of a consecutively repeated stimulus (i.e. 1-back match) by the total
number of 1-back matches to calculate the “hit rate”. Average reaction time (RT) was calculated for hits. Subject groups were compared on hit rate and RT by t-tests on SPSS. We also calculated rates for “false alarms” and misses; no statistically significant difference between groups was revealed in these measures.

2.4. MRI data acquisition and pre-processing

Functional images were acquired with a Signa Advantage 1.5 Tesla whole-body MRI system (General Electric, Waukesha, Wisconsin). Images were acquired using a single-shot T2*-weighted echo planar imaging (EPI) sensitive to blood oxygenation level dependent (BOLD) contrast in the AC-PC aligned axial plane with a repetition time (TR) of 2.0 s, an echo time (TE) of 32 ms and a flip angle of 90°. Twenty-seven interleaved slices to obtain whole-brain coverage were collected with a 22-cm field of view (FOV), 64 × 64 matrix, slice thickness of 4.0 mm, an inter-slice gap of 0.5 mm and in-plane resolution of 3.5 × 3.5 mm. Coplanar, high-resolution structural T1-weighted scans were also acquired prior to the acquisition of functional images. fMRI data processing was conducted using SPM2 and included sinc interpolation in time to correct for between-slice timing differences in image acquisition and motion-correction using a six-parameter, rigid-body, least-squares alignment procedure. We did not spatially smooth our functional images because one the dependent measures was to be the spatial extent of activity.

2.5. MRI data analysis

GLM was conducted in Voxbo (www.voxbo.org). The convolution matrix included time-domain representation of the 1/f power structure (Zarahn et al., 1997; Aguirre et al., 1998) low pass filter to remove frequencies above 0.4525 Hz and nuisance covariates to model an intercept and global signal orthogonal to the covariates of interest. The BOLD signal was estimated using a four-covariate model in which each covariate modeled the response to each of the four stimulus types as a boxcar function convolved with a canonical hemodynamic response function. Parameter estimates (i.e. β values) served as one of the main dependent measures of FFA activity between groups (see below). We performed linear contrasts of faces minus scenes to identify face-specific voxels (candidate FFA voxels) in the occipital–temporal region.

2.6. Fusiform face area (FFA) analysis

We conducted image data analysis in native space (individual brains were not spatially transformed to
match a common (template brain) to maximize sensitivity to detect spatially variable activations in the visual association cortex. The identification of an FFA for each subject followed a two-step procedure: (1) manual drawing of anatomical masks as defined by the union of parahippocampal, lingual and fusiform gyri (Ranganath et al., 2004; Yoon et al., 2006); (2) identification of the FFA by applying the anatomic mask onto whole brain activation maps resulting from a linear contrast of face minus scenes, thresholded at a t-value corresponding to \( P < 0.05 \), corrected for multiple comparisons. The boundaries of the parahippocampal, lingual and fusiform gyri were defined according to the descriptions given in atlases by Duvernoy (1988) and Duvernoy and Bourgouin (1999). The anatomical masks were drawn on coplanar axial images for each subject. Their creation was facilitated by cross referencing sulcal and gyral landmarks on axial images with those on the cortical surface as visualized by co-registered high-resolution 3D images. The medial and lateral boundaries of the fusiform gyrus were defined by the collateral and lateral occipitotemporal sulcus respectively, whereas the rostral and caudal margins were defined by the anterior and posterior transverse collateral sulci. The parahippocampal and inferior lingual gyri were drawn together as unit. The anterior boundary was defined by a line connecting the lateral most aspect of the uncal sulcus to the rostral most portion of collateral sulcus in a given axial plane. The caudal boundary was delineated by the lingual sulcus. The medial border was defined by the medial cortical surface. We conducted test–retest reliability analysis in which the same rater manually drew the anatomic masks on 10 randomly selected subjects 1 week apart. The Spearman Brown coefficient was 0.90.

The main fMRI group comparison dependent measures were (1) percentage of subjects with FFA activation, (2) FFA volume, i.e. number of above threshold voxels with FFA activation and (3) the magnitude of face-specific activity, as indexed by the difference in parameter estimates between face and scene blocks in the FFA. The latter two values were first determined on an individual subject basis and then these values were group averaged for comparison with a t-test. Note that, when a subject did not show active voxels in the FFA, we did not include this sample in the calculation of mean voxel count or magnitude of activity.

Time series plots were generated by averaging the BOLD signal across all voxels within the FFA within each subject. Percent signal change was calculated by normalizing each value in the time series by the mean fMRI signal across the entire scanning session. We then averaged these time series across all subjects in a group.

2.7. Middle frontal gyrus analysis

To examine activity in the middle frontal gyrus (MFG), an anatomical mask for the left middle frontal gyrus was drawn based on sulcal landmarks (Duvernoy, 1988). Within this anatomic mask, contrasts of faces vs. baseline and scenes vs. baseline, with a threshold corresponding to \( P < 0.05 \) corrected for multiple comparisons, identified task related voxels. The parameter estimates averaged across above threshold voxels were computed for each subject, which were then group averaged and compared across groups with a t-test.

2.8. Group level maps in MNI space

To facilitate comparisons of results between studies, we supplemented our main set of fMRI results with an analysis conducted in MNI template space. This was accomplished by normalizing each subject’s maps onto an MNI template with SPM2. Group level random effects analysis was conducted using a threshold corresponding to \( P < 0.01 \) with an 8-voxel cluster threshold. The 3D coordinates of within group maxima are given in MNI coordinates.

3. Results

3.1. Behavioral task

The results of the 1-back task are displayed in Fig. 2. In summary, both groups performed highly accurately and at equivalent levels of performance in detecting a consecutive repetition of a face. The SZ group displayed 87% accuracy (S.D. = 18) and mean RT of 592 ms (S.D. = 102). The C group showed 92% accuracy (S.D. = 14) and mean RT of 520 ms (S.D. = 110). There was no statistically significant difference between groups in accuracy \((t = 0.80, df = 22, p = 0.43)\) or RT \((t = 1.63, df = 22, P = 0.12)\). We conclude from these results that both groups attended to the stimuli and performed the tasks in an equivalent manner.

3.2. Neuroimaging results

In Fig. 3, we have displayed the activation maps of all subjects showing above threshold activity in the visual association cortex. The maps are derived from the contrast of face vs. scene blocks, thresholded at a t-value corresponding to \( P < 0.05 \), corrected for multiple
comparisons. Consequently, the active areas represent regions highly specific for the processing of faces. The FFA was identified in 13 out of 14 SZ subjects and 10 out 10 C subjects. The percentage of subjects showing FFA activity was not statistically significant difference between groups, \( P = 1.0 \), Fisher’s exact test, two-sided. On a qualitative basis, the location of the FFA and its morphology appear quite similar between groups and are very consistent with published results (Kanwisher et al., 1997; Grill-Spector et al., 2004).

We compared the activity of the FFA between groups by quantifying its volume and magnitude of activity (Fig. 4). In Fig. 4A, we show the FFA volume obtained by calculating the average number of active voxels in the FFA. In the SZ group, there are 24.0 (S.D. = 26.9) voxels bilaterally, with 15.5 (S.D. = 17.3) voxels in the right and 9.8 (S.D. = 10.4) voxels in the left FFA. In the C group, there are 27.0 (S.D. = 20.5) voxels bilaterally, with 17.0 (S.D. = 13.2) voxels in the right and 11.0 (S.D. = 7.9) voxels in the left FFA. None of the comparisons between groups reached statistical significance (for bilateral and right FFA, \( df = 21 \); left FFA, \( df = 19 \); for all comparisons \( t < 0.3 \) and \( P > 0.7 \)). In Fig. 4B and C, we show the beta values (parameter estimates, a measure of the strength of activity) during the viewing of faces. In Fig. 4B, the betas are expressed as the mean of all active voxels’ activity within the FFA. In the SZ group, the average beta values are 0.024 (S.D. = 0.009) bilaterally, with 0.029 (S.D. = 0.019) on the right and 0.023 (S.D. = 0.008) on the left FFA. In the C group, the mean beta values are 0.022 (S.D. = 0.009) bilaterally, with 0.023 (S.D. = 0.009) on the right and 0.018 (S.D. = 0.012) on the left FFA. We have also indexed FFA activity as the beta value of the maximally active voxel within the FFA, Fig. 4C. In neither measure of activity magnitude was there any significant difference between groups in the magnitude of activity in the FFA (for all bilateral and right FFA comparisons \( t < 0.90, df = 21, P > 0.35 \); for left FFA comparisons \( t < 1.00, df = 19, P > 0.30 \)). To investigate the potential impact of parental education on our FFA results, we conducted correlations between our FFA measures and years of parental education. There was no indication that parental education has significant impact on FFA activity, with all correlations showing Pearson’s \( r < 0.25 \) and \( P > 0.28 \).

To further assess the functional characteristics of the FFA in schizophrenia, we obtained the BOLD time series from the FFA for each subject and averaged them for each group. In Fig. 5, the average percent signal change is plotted. Note that the two runs of the localizer scans have been concatenated for display purposes. Two aspects of the FFA time series are pertinent: (1) the rank order of activity between face and non-face stimuli is the same between groups, with faces > non-face objects > baseline; and (2) the magnitude of activity throughout the scan is virtually identical between groups.

We identified FFA activity in group maps in MNI space for both schizophrenia and control patients. At a threshold of \( P < 0.01 \) and a cluster threshold of 8 voxels, the following coordinates for maxima were obtained: schizophrenia group (20, −66, −14) and (−30, −52 m −10); control group (−28, −48, −18) and (30, −48, −18).

To investigate the possibility that our results are due to type II error, we conducted the following analysis. First, a power analysis revealed that the detection of a statistically significant difference between groups at a significance level of 0.05 and power of 0.80 would have required sample sizes of 162, 1005 and 333 for the measures of the proportion of subjects with FFA activity, FFA volume and FFA magnitude of activity, respectively.
Fig. 3. Individual subject FFA maps. For every subject showing above threshold ($P<0.05$, corrected) activity resulting from the linear contrast between faces and scenes, two slices from the occipital temporal region showing FFA activity are displayed. A total of 13 out of 14 SZ subjects showed above threshold activity, while all 10 C subjects showed FFA activity. The dark orange-yellow color gradient indicates the $t$-values of the active voxels. SZ=schizophrenia subjects; C=healthy control subjects.
Fig. 4. FFA volume and magnitude of activity. (A) The volume of the FFA in SZ and C groups are displayed as the mean number of above threshold voxels. Quantification of FFA activity is shown as (B) mean magnitude of activity across all active voxels of the FFA and (C) maximal magnitude of activity of a voxel within the FFA. Error bars indicate S.E.M.
Second, we examined group differences in middle frontal gyrus activity to serve as a positive control region. We found a group difference that approached significance in the level of engagement of the left middle frontal gyrus during face and scene blocks \( P=0.06 \) with patients and controls showing mean betas of 0.097 and 0.017, respectively. This result may reflect greater patient effort and is consistent with other fMRI studies that utilized blocked \( n \)-back task in which patient performance matches that of controls (Callicott et al., 2000; Theremens et al., 2005). The Cohen’s \( d' \) effect size is 0.67. Taken together, these results indicate that the absence of group differences in FFA activity is not likely the result of lack of power.

4. Discussion

In this study, we found that the SZ group exhibited FFA activity that was as prevalent and as strong as in controls. We identified an FFA in all but one subject out of 14 with schizophrenia. The volume and magnitude of activity of the FFA were indistinguishable from that of control subjects. The patients also performed very well on the face recognition task and at an equivalent level compared to controls. These behavioral results provide verification that the subjects remained on task and attended to the stimuli, which in turn strengthens the validity of our neuroimaging findings and conclusions. While there are several studies pointing to intact functioning of lower level visual systems (Katsanis et al., 1996; Braus et al., 2002; Barch et al., 2003; Ford et al., 2005), including the ventral visual stream (Butler et al., 2001; Foxe et al., 2005) in schizophrenia, our study is the first to support the conclusion of intact function of the FFA, a central module in the face processing system.

Our results, which suggest the preservation of the specialized neural system for the perceptual processing of faces, are divergent from other fMRI studies (Gur et al., 2002; Quintana et al., 2003) that have demonstrated abnormalities in the neural correlates of face processing in schizophrenia. These reports found no activations in the fusiform region in subjects with schizophrenia while viewing faces. The following methodological factors or differences may account for our divergent data: (1) Our analysis was conducted in native space to maximize sensitivity in detecting activations at the group level by accounting for inter-subject variability in functional anatomy. In analysis utilizing spatial normalization, a group level map could show an absence of activity even though individual subjects exhibit activations in the general region if there is significant between subject heterogeneity in the specific location of activations.
et (Brett et al., 2002). Native space analysis also avoids possible registration errors that may be introduced by normalization procedures. The fusiform region is particularly prone to this problem. (2) The methods utilized to identify face related activity are different between the studies. In our analysis, we employed a contrast between faces and scenes, which should identify highly face-specific areas. In the other studies, the face blocks were contrasted with baseline, a procedure that could identify voxels responsive to all categories of objects. (3) Our behavioral paradigm was relatively easy, which resulted in equivalent, high-level performance between groups. In the studies that have failed to find significant fusiform activity, the tasks were fairly complicated, requiring the simultaneous evaluation and monitoring of three stimuli (Quintana et al., 2003), or very difficult, resulting in very low performance in the schizophrenia group (Gur et al., 2002). These factors, in the context of studies demonstrating the presence of deficits in the PFC in schizophrenia (Weinberger et al., 1986; Perlstein et al., 2001) and the capacity of the PFC to exert top down modulation of sensory cortical activity (Chao and Knight, 1998; Tomita et al., 1999), leave open the possibility that the under-activations may be the result of dysfunction in the PFC rather than the visual system. Two behavioral studies that have examined the presence of a specific face processing deficit in schizophrenia (Addington and Addington, 1998; Whittaker et al., 2001) concluded that dysfunction in attention or executive function could explain the abnormal performance in face processing tasks. An ERP study (Hermann et al., 2004) found decreased N170 component of the visually evoked signal when viewing faces in schizophrenia. However, this study did not report any behavioral data confirming that subjects with schizophrenia were adequately attending to the stimuli. This point is crucial in evaluating fMRI and ERP studies that compare activity across groups because attention has been shown to modulate the magnitude of FFA activity and N170 amplitude (Gazzaley et al., 2005).

Given the evidence of top down modulation of activity in sensory systems (Chao and Knight, 1998; Tomita et al., 1999; Gazzaley et al., 2005), a key goal of our method was to evaluate face processing in a manner that minimized the effects of dysfunction in higher-order cognition. However, this aim had to be balanced with the need for verification that schizophrenic subjects were attending to the stimuli because inattention to the stimuli could present an even greater confound. This was accomplished by having subjects complete a 1-back while viewing the faces, a task requiring a modest amount of working memory. We believe the imposition of this task did not significantly affect our results or inferences. Firstly, our behavioral results indicate that the SZ group performed the task very well and at an equivalent level of performance compared to controls. Our results are consistent with numerous studies that have consistently demonstrated a high level of performance by SZ patients on the standard version of the 1-back, indistinguishable from that of healthy subjects (Perlstein et al., 2001, 2003; Kim et al., 2004). Thus, we feel reasonably assured that the assessment of face processing was not biased by deficits in higher order cognitive processes. The utilization of eye tracking would have provided useful confirmatory data about perceptual engagement with the stimuli. However, eye-tracking information by itself would still leave open the possibility of insufficient allocation of attention to the stimuli.

We would like to emphasize some of the limitations of our study. An inferential limitation stems from the fact that the demonstration of normal FFA function is not sufficient evidence to claim that the entire face processing neural system or all aspects of face processing are intact in schizophrenia. While the FFA is a critical region in this network, engaged in the detection of (Grill-Spector et al., 2004) and necessary for the discrimination between faces (Barton et al., 2002), it is just one of many regions that constitute the face processing system. The input from additional regions contributes to different aspects of face processing (Perrett et al., 1982; Hasselmo et al., 1989; Hoffman and Haxby, 2000; Haxby et al., 2002). For example, some studies suggest that the FFA is critical in the processing of static facial information (Hasselmo et al., 1989; Barton et al., 2002), e.g. identity, whereas the superior temporal region is required for the processing of dynamic aspects of facial information (Hasselmo et al., 1989), e.g. facial emotion expression. Consequently, future studies must be conducted to evaluate other components of the network prior to making definitive or more general claims about the status of the wider face processing network.

Another potential limitation is related to the complexities required in proving the null hypothesis, i.e. the absence of a difference between the control and schizophrenia groups in FFA function. The power analysis and middle frontal gyrus activity analysis suggest that lack of power was not a critical issue. Nonetheless, we may have been unable to detect differences between groups due to lack of sensitivity in our measures or paradigm. For example, the completion of our task required a minimal working memory load and the possibility exists that FFA function may not be intact.
at other memory loads. Future studies should be conducted to address this possibility.

Comparisons of our demographic data revealed a statistically significant difference between groups in the amount of parental education. However, we believe this difference is unlikely to account for our fMRI findings. We found no evidence in our sample of a correlation between years of parental education and FFA activity. Additionally, it is difficult to imagine a plausible mechanism by which small differences in parental education could directly or indirectly lead to altered FFA development or function in the direction of improved function in the patient group. Differences in the gender composition of the groups should also be kept in mind as a potential confound. However, in our limited sample, we did not find any evidence of a gender effect.

A fundamental step in understanding the neurophysiological basis of schizophrenia is the identification of regions of dysfunction associated with this condition. A corollary of this aim is to identify areas of preserved function. This would help to constrain our interpretation of studies that tap into multiple cognitive processes and brain regions. Despite the limitations noted above, we believe our data provides compelling evidence against gross dysfunction of the FFA in schizophrenia. Additionally, our results, in the context of other studies showing intact function of the ventral visual pathway (Butler et al., 2001; Foxe et al., 2005), are consistent with the proposition that a key component in the neural system supporting the perceptual processing of faces is intact in schizophrenia. The demonstration of normal FFA activity has potential implications for our understanding of the neural basis of deficits in other cognitive processes requiring the decoding of facial information. For example, intact FFA function would imply that the social or emotional processing deficits in schizophrenia are not the direct downstream effects of dysfunction in the FFA, but rather the result of deficits in other regions, such as those more specifically associated with social or emotional processes. We believe our results provide a foundation upon which future functional studies can more precisely identify the dysfunctional neural systems that underlie the affective and social deficits in schizophrenia.

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References