Published in final edited form as:

Am J Psychiatry. 2006 March ; 163(3): 455–462. doi:10.1176/appi.ajp.163.3.455.

Functional and Structural Deficits in Brain Regions Subservicing Face Perception in Schizophrenia

Toshiaki Onitsuka, M.D., Ph.D., Margaret A. Niznikiewicz, Ph.D., Kevin M. Spencer, Ph.D., Melissa Frumin, M.D., Noriomi Kuroki, M.D., Lisa C. Lucia, B.S., Martha E. Shenton, Ph.D., and Robert W. McCarley, M.D.

From the Clinical Neuroscience Division, Laboratory of Neuroscience, Department of Psychiatry, VA Boston Healthcare System, Brockton Division, and Harvard Medical School; the Department of Neuropsychiatry, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan; and the Surgical Planning Laboratory, MRI Division, Brigham and Women's Hospital, Department of Radiology, Harvard Medical School, Boston

Abstract

Objective—Schizophrenia impairs many cognitive functions, including face perception. Veridical face perception is critical for social interaction, including distinguishing friend from foe and familiar from unfamiliar faces. The main aim of this study was to determine whether patients with schizophrenia show less activation in neural networks related to face processing, compared with healthy subjects, and to investigate the relationships between this functional abnormality and anatomical abnormalities in the fusiform gyrus shown with magnetic resonance imaging (MRI).

Method—Twenty male chronic schizophrenia patients and 16 healthy comparison subjects matched with the patients for age, gender, handedness, and parental socioeconomic status underwent high-spatial-resolution MRI. Event-related potentials elicited by images of faces, cars, and hands were recorded in a separate session.

Results—Compared to the healthy subjects, the patients with schizophrenia showed bilateral N170 amplitude reduction in response to images of faces but not to images of other objects. The patients also had smaller bilateral anterior and posterior fusiform gyrus gray matter volumes, compared to the healthy subjects. In addition, right posterior fusiform gyrus volume was significantly correlated with N170 amplitude measured at the right posterior temporal electrode site in response to images of faces in the schizophrenia patients but not in the healthy comparison subjects.

Conclusions—The results provide evidence for deficits in the early stages of face perception in schizophrenia. The association of these deficits with smaller fusiform gyrus volume in patients with schizophrenia, relative to healthy subjects, suggests that the fusiform gyrus is the site of a defective anatomical substrate for face processing in schizophrenia.

Schizophrenia has long been associated with the limited ability to interact effectively in social environments. Effective social communication depends largely on the capacity to extract social and affective cues from faces. Accumulating evidence has suggested that schizophrenia patients may have deficits in both facial recognition and recognition of facial expressions (1–3).

Address correspondence and reprint requests to Dr. McCarley, Department of Psychiatry (116A), VA Boston Healthcare System, Brockton Division, Harvard Medical School, 940 Belmont St., Brockton, MA 02301; robert_mccarley@hms.harvard.edu.

Supplementary tables are available with the online version of this article.

The fusiform gyrus, located on the ventromedial surface of the temporal and occipital lobes, has been demonstrated to be a key brain region for face perception (4–6). The findings of both neurophysiological and functional magnetic resonance imaging (fMRI) studies have suggested that faces are perceived, at least in part, by a processing stream separate from that used in processing other objects (7). Data from studies of event-related potentials have demonstrated that the negative potential recorded at occipitotemporal leads, the N170 potential, is larger in response to faces than to objects in healthy subjects (8,9). On the basis of converging evidence from electroencephalography (6) and magnetoencephalography (9), the fusiform gyrus has been considered to be one of the main neural sources of the N170 potential in response to human faces. The N170 potential is considered to be an index of aspects of face analysis (8). Liu et al. (10) have suggested that the N170 potential recorded with magnetoencephalography is associated with extraction of the identity of individual faces. However, there is no uniform agreement that the fusiform gyrus is the main neural source of the N170 potential; for example, the superior temporal sulcus region has been also reported to be the site of N170 generation (11). One of the goals of the present study was to determine whether anatomical abnormalities of the fusiform gyrus revealed by MRI are associated with N170 abnormality. Data confirming this association would strengthen the evidence for a link between the fusiform gyrus and the N170 potential.

Despite extensive research on face recognition in healthy subjects and the potential relevance of face processing in social interactions, few functional and anatomical studies have examined face processing in schizophrenia. Existing studies have focused primarily on facial affect recognition (12,13). However, very few studies have examined the functional integrity of early processes related to face sensory features. There is also a paucity of data on the relationship between functional indices of face processing and structural correlates. Previously we reported an association between structural abnormalities of the fusiform gyrus and behavioral measures of memory function for faces in schizophrenia (14). These results provided the impetus for the present study, which focuses on linking electrophysiological and structural correlates of face processing in schizophrenia.

The present study was designed to test the hypotheses that patients with schizophrenia, compared with healthy subjects, show less activation in early visual processing for faces, as measured by the N170 potential in response to faces, and that this functional abnormality is associated with smaller fusiform gyrus volume in schizophrenia patients, compared with healthy subjects. Confirmation of these hypotheses would further clarify the contributions of the fusiform gyrus to the N170 potential.

Method

Subjects

Twenty male patients with chronic schizophrenia and 16 male healthy comparison subjects with normal/corrected vision, age 20–55 years, all right-handed, participated in this study. After a complete description of the study, all participants signed an informed consent form, in accordance with Harvard Medical School and VA Boston Healthcare System guidelines. Demographic data for all subjects are presented in Data Supplement 1, which is available with the online version of this article at <http://ajp.psychiatryonline.org>. The exclusion criteria were 1) a history of neurological illness or major head trauma that would result in an abnormal EEG, 2) a history of ECT, 3) a history of alcohol or drug dependence, 4) alcohol or drug abuse within the past 5 years, and 5) verbal IQ below 75. Healthy comparison subjects were recruited through newspaper advertisement and were screened with the Structured Clinical Interview for DSM-III-R—Non-Patient Edition (SCID-NP). No comparison subjects had an axis I psychiatric disorder, nor did their first-degree relatives.

The patients were recruited from the VA Boston Healthcare System, Brockton Division, and had a diagnosis of schizophrenia on the basis of their medical records and assessment with the patient edition of the SCID for DSM-IV. All patients were receiving neuroleptic medication, with a mean dose equivalent to 383.8 mg/day of chlorpromazine (SD=266). Five of the 20 patients were receiving typical neuroleptics, 14 were receiving atypical neuroleptics, and one patient was receiving both types of neuroleptics. No significant correlations existed between chlorpromazine-equivalent doses and N170 amplitudes at any electrode site in response to any stimuli ($-0.20 \leq r \leq 0.24$, $0.31 \leq p \leq 0.91$). The Positive and Negative Syndrome Scale (PANSS) (15) was administered to patients. Mean scores on the PANSS positive symptom scale, negative symptom scale, and the general psychopathological scale were 19.0 (SD=7.7), 21.2 (SD=5.8), and 37.2 (SD=10.0), respectively. Handedness was assessed with the Edinburgh Inventory (16), and the socioeconomic status of subjects and their parents was measured by using the Hollingshead two-factor index.

Electrophysiological Recording and Processing

The EEG was recorded (0.01–100 Hz, 500 Hz digitization) by using 64 silver-silver chloride sintered electrodes in preconfigured caps (ElectroCap International, Eaton, Ohio). The electrode sites were Fp1/Fp2, F7/F8, F5/F6, F3/F4, F1/Fz/F2, FT9/FT10, FT7/FT8, FC5/FC6, FC3/FC4, FC1/FC2, T9/T10, T7/T8, C5/C6, C3/C4, C1/Cz/C2, TP7/TP8, CP5/CP6, CP3/CP4, CP1/CP2, P9/P10, P7/P8, P5/P6, P3/P4, P1/Pz/P2, PO9/PO10, PO7/PO8, PO1/PO2, and O1/Oz/O2 referenced to the right earlobe, with the ground electrode placed on the forehead. The vertical electro-oculogram (EOG) was recorded from two electrodes located medially to the right eye, one above and one below the eye. The horizontal EOG was recorded at the outer canthi. Electrode impedances were $<5 \text{ k}\Omega$. In the off-line analyses, the event-related potential responses were convolved with a zero phase shift digital low-pass filter at 32 Hz (24 db/octave). Epochs were 800 msec in duration, including a 100-msec prestimulus interval. Epochs at each electrode site were baseline corrected by subtraction of the average prestimulus voltage and mathematically corrected for eye movement artifacts (17). Subsequently, epochs exceeding $\pm 100 \mu\text{V}$ at any electrode site were rejected, resulting in average of 28.9 trials per stimulus in the patient group and 29.3 trials per stimulus in the comparison group; no group differences were found for any stimulus type ($-0.53 \leq t \leq 1.0$, $df=34$, $0.31 \leq p \leq 0.83$).

Final event-related potential responses were recalculated with an average reference montage, consistent with recent event-related potential studies of faces (18,19). The N170 amplitude peak was defined as the most negative datapoint between 120 and 270 msec poststimulus.

Stimuli and Experimental Procedures

The stimuli were 32 colored pictures of emotionally neutral faces (16 male and 16 female faces; one-half of all faces were Asian, and one-half were Caucasian) (20), 32 pictures of hands, 32 pictures of cars, and 32 pictures of butterflies, all edited to measure $24 \times 24 \text{ cm}$ and all viewed by subjects seated 1 m distant from the computer screen. The pseudo-randomly ordered images appeared in the center of the screen for 500 msec, each preceded by a 200-msec interval in which a fixation point appeared in the middle of the screen and then a 200-msec interval in which the screen was blank. The interstimulus interval was 1900 msec. Subjects were instructed to click a mouse button (left and right hands counterbalanced between subjects) as soon as they saw the target picture (butterflies). A no-response was scored if the response time exceeded 1500 msec.

MRI Procedures and Definition of the Fusiform Gyrus

Magnetic resonance images were acquired in 16 of the 20 patients (one patient refused MRI, one had metallic braces, and two were too large for the scanner) and in 13 of 16 healthy comparison subjects (two subjects refused, and one was too large for the scanner).

Demographic data for all subjects for whom MRI data were available are presented in Data Supplement 1, which is available with the online version of this article at <http://ajp.psychiatryonline.org>. The acquisition was done with a 1.5-T General Electric scanner (GE Medical Systems, Milwaukee) at the Brigham and Women's Hospital in Boston. The mean intervals between EEG and MRI were 10.1 months ($SD=9.2$, range=0–24) for the healthy comparison subjects and 7.9 months ($SD=7.8$, range=-3 to 21) for the patients, with no group difference ($t=0.71$, $df=27$, $p=0.49$). The protocol and neuroanatomical boundaries were similar to those used in our previous work (14). Briefly, the anterior landmark was reliably defined by one slice posterior to the mammillary body. The posterior landmark was determined by the anterior tip of the parietal-occipital sulcus in the midsagittal plane. The last slice, including the crux of the fornix, provided the boundary for division of the fusiform gyrus into anterior and posterior subregions. The collateral sulcus was used as the medial border. The occipito-temporal sulcus was used to determine the lateral border. Figure 1 shows the fusiform gyrus in a coronal slice as well as a three-dimensional reconstruction.

Manual drawings of regions of interest were performed on the realigned and resampled coronal slices. The fusiform gyrus of four of the 29 subjects had been delineated in a previous MRI study (14) by the same rater (T.O.). In the remaining 25 subjects, the region was newly delineated for this study. Interrater reliability was computed for the regions of interest by three independent raters who were blind to the subjects' group membership but not to hemisphere. The intraclass correlations were 0.94 for the left anterior, 0.94 for the right anterior, 0.95 for the left posterior, and 0.95 for the right posterior fusiform gyrus.

Statistical Analyses

Group differences in accuracy in detecting the target pictures and in median reaction times were assessed with t tests. The N170 component was used to assess electrophysiological response to images of faces relative to other stimuli. The event-related potential elicited by the butterfly stimulus, which required a motor response (to ensure that subjects were attending to the stimuli), was not analyzed because we wished to focus on the purely sensory responses. On the basis of previous findings (18,19), N170 amplitude was measured at P7/P8 and at the more ventral electrode sites P9/P10 and PO9/PO10 (the same level as theinion). The N170 peak amplitude was submitted to repeated-measures analysis of variance (ANOVA) with group as the between-subjects factor and stimulus type (three types), hemisphere (left or right), and electrode site (three sites) as within-subjects factors. The degrees of freedom were adjusted with the Huynh-Feldt epsilon for factors with more than two levels. Two-tailed tests were used, with an alpha of ≤ 0.05 required for statistical significance.

To determine if some MRI regions of interest were more affected than others, region-of-interest volumes were converted to z scores by using the mean and standard deviation for the comparison group to calculate the z scores, as follows: $z_i = (V_i - V_n) / SD_n$, where V_i is the individual fusiform gyrus volume and V_n and SD_n are the mean fusiform gyrus volume and standard deviation, respectively, in the comparison group. For the region-of-interest analysis, the standardized scores were submitted to a mixed-model repeated-measures analysis of covariance (ANCOVA) with the total intracranial contents as a covariate, group (schizophrenia patients or comparison subjects) as a between-subjects factor, and hemisphere (left or right) and subregion (anterior or posterior) as within-subjects factors.

As in our previous study (21), Pearson product-moment correlation was used to examine the association between absolute fusiform gyrus gray matter volume and N170 amplitude measured at P7/P8, P9/P10, and PO9/PO10. We hypothesized that smaller fusiform gyrus volumes would be correlated with smaller N170 amplitudes (less negativity) in schizophrenia. Thus, we assessed negative correlations of N170 amplitude at these electrodes with fusiform

gyrus volumes (using a significance level of $p \leq 0.05$) in both the schizophrenia group and the healthy comparison group.

Results

Demographic Characteristics and Behavioral Performance

No significant group differences were found in age, handedness, or parental socioeconomic status. The patients had significantly lower socioeconomic status than the healthy comparison subjects ($t = -3.84$, $df = 34$, $p = 0.001$), consistent with deficits in functioning due to the disorder. No significant group differences were found in total intracranial contents ($t = 1.23$, $df = 27$, $p = 0.23$), accuracy of target responses (patients: 98.7%; comparison subjects: 99.4%) ($t = 1.02$, $df = 34$, $p = 0.32$), or median reaction time (patients: median = 498 msec; comparison subjects: median = 478 msec) ($t = -0.75$, $df = 34$, $p = 0.46$).

N170 Amplitude

For N170 amplitude (illustrated in Figure 2), a repeated-measures ANOVA demonstrated a significant main effect of stimulus ($F = 4.46$, $df = 2, 33$, $p = 0.02$) and electrode site ($F = 16.03$, $df = 2, 33$, $p < 0.001$) but no main effect of hemisphere ($F = 1.33$, $df = 1, 34$, $p = 0.26$) or group ($F = 3.79$, $df = 1, 34$, $p = 0.06$). There was a significant stimulus-by-group interaction ($F = 4.92$, $df = 2, 33$, $p = 0.02$). To further delineate this result, Helmert's contrasts were performed on the stimulus-by-group interaction. The groups differed in average N170 amplitude in response to images of faces, compared to the average amplitude in response to images of hands and cars ($F = 9.79$, $df = 1, 34$, $p = 0.004$), but they did not differ in the average amplitude in response to images of hands, compared to the average amplitude in response to images of cars ($F = 2.45$, $df = 1, 34$, $p = 0.13$). Thus, the group difference in N170 amplitude was specific to faces. In addition, the N170 amplitude for each stimulus was analyzed by using two-factor ANOVAs, with electrode site (three sites) as a within-subjects factor and group as a between-subjects factor. In these follow-up analyses, the schizophrenia patients showed significant N170 amplitude reduction in response to faces, compared to the healthy comparison subjects ($F = 6.94$, $df = 1, 34$, $p = 0.01$), as well as a reduction in response to images of hands ($F = 3.41$, $df = 1, 34$, $p = 0.07$), but not to images of cars ($F = 0.75$, $df = 1, 34$, $p = 0.39$). Finally, to examine the stimulus effect in each group, N170 amplitude was analyzed using two-factor ANOVAs with stimulus (images of faces, cars, or hands) and electrode site (three sites) as within-subjects factors. The healthy comparison subjects showed a significant main effect of stimulus ($F = 6.24$, $df = 2, 14$, $p = 0.01$), with the most negative N170 amplitude recorded in response to images of faces (group mean: $-7.83 \mu V$), relative to images of hands (group mean: $-6.44 \mu V$) and cars (group mean: $-5.66 \mu V$). The schizophrenia patients did not show this effect ($F = 0.16$, $df = 2, 18$, $p = 0.86$), indicating that their N170 amplitude was not moderated in response to the different stimuli. For the patients, the N170 amplitude was $-4.6 \mu V$ in response to images of faces, $-4.5 \mu V$ in response to images of hands, and $-4.7 \mu V$ in response to images of cars.

Fusiform Gyrus Volume

The scattergrams in Figure 3 show the anterior and posterior fusiform gyrus absolute volumes on the left and right side in 16 patients with schizophrenia and 13 healthy comparison subjects. The three-factor ANCOVA of the standardized region-of-interest values (z scores) revealed a significant main effect of group ($F = 6.21$, $df = 1, 27$, $p = 0.02$) but no significant main effects of hemisphere ($F = 2.61$, $df = 1, 27$, $p = 0.12$) or subregion ($F = 0.10$, $df = 1, 27$, $p = 0.76$) and no significant group-by-hemisphere-by-subregion ($F = 0.37$, $df = 1, 48$, $p = 0.55$), group-by-hemisphere ($F = 0.01$, $df = 1, 27$, $p = 0.93$), or group-by-subregion interactions ($F = 0.16$, $df = 1, 27$, $p = 0.70$). These results suggest that patients with schizophrenia have bilaterally reduced anterior and posterior fusiform gyrus gray matter volumes, relative to healthy comparison subjects.

Correlations Between Fusiform Gyrus Volume and N170 Amplitude

For the schizophrenia patients, significant negative correlations were found between right posterior fusiform gyrus volumes and N170 amplitudes in response to images of faces at P8 ($r=-0.69$, $N=16$, $p=0.003$) and PO10 ($r=-0.52$, $N=16$, $p=0.04$) and between left posterior fusiform gyrus volumes and N170 amplitudes in response to images of faces at P8 ($r=-0.53$, $N=16$, $p=0.03$). However, no significant correlations were found between fusiform gyrus volumes and N170 amplitudes in response to images of cars and hands ($-0.48 \leq r \leq -0.01$, $N=16$, $0.05 < p \leq 0.97$). For the healthy comparison subjects, no significant correlations were found between fusiform gyrus volumes and N170 amplitudes in response to any stimuli ($-0.11 \leq r \leq -0.02$, $N=13$, $0.73 \leq p \leq 0.95$). Table 1 shows the results of Pearson product-moment correlations of absolute fusiform gyrus volumes and N170 amplitudes at P7/P8 in response to images of faces for both groups. The scattergrams in Figure 4 show the relationship between right posterior fusiform gyrus volumes and N170 amplitudes at P8 in response to images of faces in both groups. The correlation coefficients for this relationship were significantly different between groups ($z=2.7$, $p=0.006$).

To further explore the specificity of the relationship between N170 amplitudes and fusiform gyrus subregion volumes, we performed multiple linear regression analyses for the correlations that were found to be significant. In each group, the relative volumes of fusiform gyrus subregions were the dependent variables, and the N170 amplitudes in response to images of faces, cars, and hands at each electrode site with a significant correlation of N170 amplitude and fusiform gyrus volume were the independent variables. The results indicated that N170 amplitude at P8 (but not at any other site) in response to images of faces was a significant predictor of right posterior fusiform gyrus volume in the schizophrenia patients ($\beta=-0.18$, $SE=0.07$, $t=-2.69$, $p=0.02$) and that N170 amplitudes in response to images of hands and to images of cars were not significant predictors of right posterior fusiform gyrus volume ($\beta=-0.04$, $SE=0.12$, $t=-0.37$, $p=0.72$ and $\beta=0.09$, $SE=0.09$, $t=0.90$, $p=0.39$, respectively). In addition, N170 amplitudes at P8 in response to any stimuli were not significant predictors of left posterior fusiform gyrus volume in the schizophrenia patients (response to faces: $\beta=-0.04$, $SE=0.05$, $t=-0.77$, $p=0.46$; response to hands: $\beta=0.02$, $SE=0.09$, $t=0.23$, $p=0.82$; response to cars: $\beta=-0.06$, $SE=0.07$, $t=-0.74$, $p=0.48$). We interpreted these results as further evidence supporting the specificity of the relationship between N170 amplitude in response to images of faces, but not other types of stimuli, and volumetric measures of the right posterior fusiform gyrus.

Discussion

In the current study we investigated the N170 visual evoked potential elicited by objects (including faces), fusiform gyrus gray matter volume assessed with high-resolution MRI, and their interrelationship in schizophrenia patients and healthy comparison subjects. We found that 1) schizophrenia patients, relative to healthy comparison subjects, showed bilateral N170 amplitude reduction specifically in response to images of faces (it is important to note that no stimulus effect was observed in the patient group); 2) patients, relative to healthy comparison subjects, had smaller bilateral anterior and posterior fusiform gyrus gray matter volumes; and 3) for patients, but not for healthy comparison subjects, there was a significant negative correlation between right posterior fusiform gyrus volume and N170 amplitude at right posterior temporal electrode sites in response to images of faces but not to images of other objects.

This study's finding of an association between smaller gray matter volume in fusiform gyrus and N170 amplitude reduction in schizophrenia strengthens the evidence linking the fusiform gyrus to the N170 potential, and the results are consistent with a major role of the fusiform gyrus in generation of the N170 potential. This result underlines the utility of linking in vivo

MRI volumetric evaluation and measurement of event-related potentials to find an association between putative anatomical substrates and event-related potentials, as the authors have found in a previous evaluation of the superior temporal gyrus and the P300 potential (21). In the previous study also, only the schizophrenia patients showed a significant correlation between the event-related potential and the MRI findings. We believe that deficits in gray matter volume may contribute to pathological findings for event-related potentials in schizophrenia. In the present study, we cannot exclude contributions to the N170 potential from other anatomical regions, because not all anatomical regions that might be considered as its putative generators were evaluated. Moreover, although the correlational analyses indicated an association between both left and right posterior fusiform gyrus volumes and N170 amplitude at P8, the multiple regression analyses pointed only to an association between right posterior fusiform gyrus volume and N170 amplitude. This discrepancy may be related to a strong correlation between left and right fusiform gyrus volumes, a less tight relationship between the left posterior fusiform gyrus volume and N170 amplitude, or both.

The N170 potential is considered to be an index of the analysis of face information (8). A recent EEG study reported that schizophrenia patients showed less difference in N170 amplitudes in response to images of faces versus images of buildings than did healthy comparison subjects (22). In the present study, the patients with schizophrenia showed significant bilateral N170 amplitude reduction in response to images of faces, compared with the healthy subjects, but not in response to images of cars. These data suggest that schizophrenia may be associated with deficits in face perception that are already evident in the early stages of visual processing and are perhaps related to the extraction of the identity of the individual face. This deficit was clearly specific to the response to faces, versus cars, although the patients also showed an N170 amplitude reduction that approached significance in response to images of another body part, hands. Furthermore, when the specificity of the association between N170 amplitude and subregion volumes in the fusiform gyrus was probed in a multiple linear regression analysis, we found that N170 amplitude in response to images of faces, but not in response to images of hands or cars, was a predictor of right posterior fusiform gyrus volume in schizophrenia patients. These findings further support the specificity of the structure-function association between fusiform gyrus volume reduction and N170 amplitude in response to faces.

It has been suggested that a specific brain processing network that is present early in development underlies face perception (23,24). Evidence from fMRI studies has related face processing to activation in the region defined here as the posterior fusiform gyrus (Figure 1), with Kanwisher et al. (5) reporting that the middle fusiform gyrus responded selectively to faces. They termed this region the “fusiform face area” and suggested that their data supported neither a generic within-category identification role of the fusiform gyrus nor an objects-of-expertise interpretation (25). Our data in patients with schizophrenia, who showed a pathological deficit in fusiform gyrus volume, also support the role of fusiform gyrus in face perception. Significant correlations between fusiform gyrus volumes and N170 amplitudes in the patients were observed only for responses to images of faces and not for responses to other stimuli, indicating a deficit in the anatomical substrate involved in face processing. This anatomical deficit, at the cellular level, may consist of a reduction of the dendritic tree, the strongest source of event-related potentials.

Some fMRI studies have suggested that the right fusiform face area, which is also associated with face perception, can be recruited in the processing of objects that subjects are highly familiar with, as in cases of expert knowledge (26,27). After repeated training, EEG findings similar to those associated with responses to faces have been reported in response to other objects (28,29). Because we did not measure the degree of “expert knowledge” in processing stimuli (19,26), we cannot be certain whether the observed N170 amplitudes and fusiform gyrus deficits reflect a disturbance of an innate system for face processing or a disturbance of

the capability for developing “expert knowledge.” However, to our knowledge, our data provide the first combined functional and anatomical evidence for disturbed face processing in schizophrenia.

The limitations of our study must be considered in interpreting the conclusions. First, we were unable to rule out the contribution of chronic neuroleptic treatment to abnormalities in the N170 potential (although no significant correlations between N170 amplitudes and neuroleptic doses were observed) nor, in the present group of subjects, could we demonstrate the specificity of N170 abnormalities to schizophrenic psychosis as contrasted to affective psychosis. It will thus be important to investigate whether N170 abnormalities are observed in patients with schizophrenia and affective psychosis at first hospitalization, when most patients have a minimal or no medication history. Second, because this study did not include female subjects, we do not know if female patients show the N170 abnormalities observed in this study.

In summary, patients with schizophrenia showed significant bilateral N170 amplitude reduction in response to images of faces, compared to healthy subjects. In addition, right posterior fusiform gyrus volumes were significantly correlated with N170 amplitudes in response to faces at the right posterior temporal electrode sites. These results provide evidence for deficits in the neural substrate for face processing in patients with schizophrenia.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Supported in part by the VA Merit and REAP Awards (M.E.S. and R.W.M.), NIMH grants K02 MH-01110 and R01 MH-50747 (M.E.S.) and R01 MH-40799 (R.W.M.), the Welfide Medicinal Research Foundation, Osaka, Japan (T.O.), and the MIND Foundation, Albuquerque, N.Mex. R.W.M.).

The authors thank Marie Fairbanks for administrative support and Rakibul Mannan, Ph.D., Meredith C. Klump, B.A., and Sarah M. Rabbitt, B.A., for research assistance.

References

1. Gruzelier JH, Wilson L, Liddiard D, Peters E, Pusavat L. Cognitive asymmetry patterns in schizophrenia: active and withdrawn syndromes and sex differences as moderators. *Schizophr Bull* 1999;25:349–362. [PubMed: 10416736]
2. Penn DL, Combs D. Modification of affect perception deficits in schizophrenia. *Schizophr Res* 2000;46:217–229. [PubMed: 11120434]
3. Whittaker JF, Deakin JF, Tomenson B. Face processing in schizophrenia: defining the deficit. *Psychol Med* 2001;31:499–507. [PubMed: 11305858]
4. Damasio A, Damasio H, Van Hoesen GW. Prosopagnosia: anatomic basis and behavioral mechanisms. *Neurology* 1982;32:331–341. [PubMed: 7199655]
5. Kanwisher N, McDermott J, Chun MM. The fusiform face area: a module in human extrastriate cortex specialized for face perception. *J Neurosci* 1997;17:4302–4311. [PubMed: 9151747]
6. Allison T, Puce A, Spencer DD, McCarthy G. Electrophysiological studies of human face perception, I: potentials generated in occipitotemporal cortex by face and non-face stimuli. *Cereb Cortex* 1999;9:415–430. [PubMed: 10450888]
7. Martin A, Chao LL. Semantic memory and the brain: structure and processes. *Curr Opin Neurobiol* 2001;11:194–201. [PubMed: 11301239]
8. Bentin S, Allison T, Puce A, Perez E, McCarthy G. Electrophysiological studies of face perception in humans. *J Cogn Neurosci* 1996;8:551–565.
9. Watanabe S, Kakigi R, Koyama S, Kirino E. Human face perception traced by magneto- and electroencephalography. *Brain Res Cogn Brain Res* 1999;8:125–142. [PubMed: 10407202]

10. Liu J, Harris A, Kanwisher N. Stages of processing in face perception: an MEG study. *Nat Neurosci* 2002;5:910–916. [PubMed: 12195430]
11. Itier RJ, Taylor MJ. Source analysis of the N170 to faces and objects. *Neuroreport* 2004;15:1261–1265. [PubMed: 15167545]
12. Streit M, Ioannides A, Sinnemann T, Wölwer W, Dammers J, Zilles K, Gaebel W. Disturbed facial affect recognition in patients with schizophrenia associated with hypoactivity in distributed brain regions: a magnetoencephalographic study. *Am J Psychiatry* 2001;158:1429–1436. [PubMed: 11532727]
13. Gur RE, McGrath C, Chan RM, Schroeder L, Turner T, Turetsky BI, Kohler C, Alsop D, Maldjian J, Ragland JD, Gur RC. An fMRI study of facial emotion processing in patients with schizophrenia. *Am J Psychiatry* 2002;159:1992–1999. [PubMed: 12450947]
14. Onitsuka T, Shenton ME, Kasai K, Nestor PG, Toner SK, Kikinis R, Jolesz FA, McCarley RW. Fusiform gyrus volume reduction and facial recognition in chronic schizophrenia. *Arch Gen Psychiatry* 2003;60:349–355. [PubMed: 12695311]
15. Kay SR, Fiszbein A, Opler LA. The Positive and Negative Syndrome Scale (PANSS) for schizophrenia. *Schizophr Bull* 1987;13:261–276. [PubMed: 3616518]
16. Oldfield RC. The assessment and analysis of handedness: the Edinburgh Inventory. *Neuropsychologia* 1971;9:97–113. [PubMed: 5146491]
17. Semlitsch HV, Anderer P, Schuster P, Presslich O. A solution for reliable and valid reduction of ocular artifacts, applied to the P300 ERP. *Psychophysiology* 1986;23:695–703. [PubMed: 3823345]
18. Itier RJ, Taylor MJ. Inversion and contrast polarity reversal affect both encoding and recognition processes of unfamiliar faces: a repetition study using ERPs. *Neuroimage* 2002;15:353–372. [PubMed: 11798271]
19. Gauthier I, Skudlarski P, Gore JC, Anderson AW. Expertise for cars and birds recruits brain areas involved in face recognition. *Nat Neurosci* 2003;3:191–197. [PubMed: 10649576]
20. Ekman, P.; Friesen, W. Facial Action Coding System. Palo Alto, Calif: Consulting Psychologists Press; 1978.
21. McCarley RW, Salisbury DF, Hirayasu Y, Yurgelun-Todd D, Tohen M, Zarate C, Kikinis R, Jolesz FA, Shenton ME. Association between smaller left posterior superior temporal gyrus volume on magnetic resonance imaging and smaller left temporal P300 amplitude in first-episode schizophrenia. *Arch Gen Psychiatry* 2002;59:321–331. [PubMed: 11926932]
22. Herrmann MJ, Ellgring H, Fallgatter AJ. Early-stage face processing dysfunction in patients with schizophrenia. *Am J Psychiatry* 2004;161:915–917. [PubMed: 15121660]
23. Morton J, Johnson MH. CONSPEC and CONLERN: a two-process theory of infant face recognition. *Psychol Rev* 1991;98:164–181. [PubMed: 2047512]
24. Tzourio-Mazoyer N, De Schonen S, Crivello F, Reutter B, Aujard Y, Mazoyer B. Neural correlates of women face processing by 2-month-old infants. *Neuroimage* 2002;15:454–461. [PubMed: 11798279]
25. Grill-Spector K, Knouf N, Kanwisher N. The fusiform face area subserves face perception, not generic within-category identification. *Nat Neurosci* 2004;7:555–562. [PubMed: 15077112]
26. Gauthier I, Tarr MJ, Anderson AW, Skudlarski P, Gore JC. Activation of middle fusiform “face area” increases with expertise in recognizing novel objects. *Nat Neurosci* 1999;2:568–573. [PubMed: 10448223]
27. Gauthier I, Nelson CA. The development of face expertise. *Curr Opin Neurobiol* 2001;11:219–224. [PubMed: 11301243]
28. Tanaka JW, Curran T. A neural basis for expert object recognition. *Psychol Sci* 2001;12:43–47. [PubMed: 11294227]
29. Rossion B, Gauthier I, Goffaux V, Tarr MJ, Crommelinck M. Expertise training with novel objects leads to left lateralized face-like electrophysiological responses. *Psychol Sci* 2002;13:250–257. [PubMed: 12009046]

FIGURE 1.
Delineation of the Anterior and Posterior Fusiform Gyrus Regions of Interest

FIGURE 2.

Mean N170 Waveforms in Response to Three Types of Stimuli at the P7/P8 and PO9/PO10 Electrode Sites in Patients With Schizophrenia and Healthy Comparison Subjects^a

^a N170 amplitudes were measured at the typical N170 potential recording sites (P7/P8) and at more ventral sites, which showed the largest effect (PO9/PO10). A significant main effect of stimulus was found in the healthy comparison group ($F=6.24$, $df=2, 14$, $p=0.01$) but not in the patient group ($F=0.16$, $df=2, 18$, $p=0.86$), indicating that the N170 amplitude was not modulated in response to different stimuli in patients with schizophrenia.

FIGURE 3.

Absolute Volumes of the Right and Left Anterior and Posterior Fusiform Gyrus Gray Matter in Patients With Schizophrenia and Healthy Comparison Subjects^a

^a Means are indicated by horizontal lines. Patients with schizophrenia had smaller right and left anterior and posterior fusiform gyrus gray matter volumes, compared with healthy comparison subjects ($F=6.21$, $df=1, 27$, $p=0.02$).

FIGURE 4.

Correlation Between Absolute Volume of the Right Posterior Fusiform Gyrus and N170 Amplitude at the P8 Electrode Site in Response to Images of Faces in Patients With Schizophrenia and Healthy Comparison Subjects^a

^a Correlation coefficients (patients: $r=-0.69$, $p=0.003$; comparison subjects: $r=0.29$, $p=0.33$) were significantly different between groups ($z=2.7$, $p=0.006$).

TABLE 1
Correlation Between Fusiform Gyrus Gray Matter Volumes and N170 Amplitudes at the P7 and P8 Electrode Sites in Response to Images of Faces in Patients With Schizophrenia and Healthy Comparison Subjects

Fusiform Gyrus Region	Correlation					
	Patients With Schizophrenia (N=16)			Healthy Comparison Subjects (N=13)		
	N170 Amplitude at P7			N170 Amplitude at P8		
	r	p		r	p	
Left anterior	-0.42	0.11		-0.33	0.21	
Right anterior	-0.18	0.50		-0.30	0.25	
Left posterior	-0.44	0.09		-0.53	0.03*	
Right posterior	-0.46	0.08		-0.69	0.003**	

* p<0.05.
** p<0.01.