# A functional MRI study of face recognition in patients with prosopagnosia

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An fMRI investigation was conducted to determine whether patients with impaired face recognition, a deficit known as prosopagnosia, would show functional activation in the fusiform gyrus, the neural substrate for face processing, when viewing faces. While the patients did show activation in the fusiform gyrus, with significantly more voxels in posterior areas than their control subjects, this activation was not sufficient for face processing. In one of the patients, the posterior activation was particularly evident in the left hemisphere, which is thought to be involved in feature-based strategies of face perception. We conclude that an increased reliance on feature-based processing in prosopagnosia leads to a recruitment of neurons in posterior regions of the fusiform gyrus, regions that are not ideally suited for processing faces. *NeuroReport* 12:1581–1587 © 2001 Lippincott Williams & Wilkins.

**Key words**: Face recognition; fMRI; Neuropsychology; Prosopagnosia

## INTRODUCTION

In humans, considerable evidence for a neural substrate mediating face recognition has been obtained from studies using fMRI and from studies of individuals with acquired deficits in face processing, an impairment known as prosopagnosia. These two approaches, however, have rarely been used in combination and yet, understanding what neural mechanisms are affected in patients with prosopagnosia can significantly improve our understanding of how face recognition is normally carried out and, specifically, what brain regions contribute necessarily (and not just sufficiently) to the recognition of faces.

The processing of faces is thought to be subserved by an extensive neural network that encompasses many of the ventro-medial regions of the right hemisphere, from the occipital pole to the temporal pole, throughout the inferotemporal cortex and superior temporal sulcus. In macaque monkeys, many of the cells in these regions have been found to respond best to complex visual stimuli, such as faces and objects [1]. Within ventral temporal cortex, a number of neuroimaging studies of face perception have identified a discrete region in the middle fusiform gyrus, the fusiform face area (FFA), that responds preferentially to faces as compared to assorted common objects [2–6]. These studies have demonstrated that this region is selectively involved in the perception of faces and responds more to passive viewing of intact than scrambled two-tone faces, full front-view face photos than front-view photos of houses, and three-quarters view face photos than photos of human hands. While the consensus from these studies is that the FFA is optimally tuned to the broad category of faces, exactly what func-

tion is served by the FFA is the matter of an ongoing, rather heated controversy [7,8]. Among the issues being debated is whether the FFA is solely and exclusively dedicated to the processing of faces, whether this system is innately prespecified and whether the FFA is optimized for the processing of stimuli in a configural and holistic fashion.

One approach to addressing these issues is to examine the behavior and underlying neural mechanisms of face recognition in individuals who have sustained damage to the FFA. Bilateral damage to the inferior aspect of the temporal cortex, in the region of the fusiform gyrus is often associated with prosopagnosia [6,9], although unilateral damage to the same region in the right hemisphere is sufficient to produce the deficit [10]. Prosopagnosic patients are typically impaired at identifying familiar or known faces (assigning a name to the face), with some patients also failing to discriminate between faces (deciding whether they are the same or different); they do not confuse faces with other objects. One explanation for this pattern of results is that damage to face-specific mechanisms results in an impairment in representing shape holistically [11]. Face recognition is normally thought to depend on a holistic, face-specific system, which processes faces as undifferentiated wholes with relatively little or no part-decomposition [12,13], but can be achieved through a time-consuming integrative analysis of individual features. Damage to the holistic, face-specific processor may force prosopagnosic patients to become increasingly reliant on feature- or part-based mechanisms to process faces. Such a reliance could affect the pattern of activation seen in their fusiform gyri when viewing faces.

Support for the idea that the increased dependence on part-based processing could influence activation patterns comes from the finding that functional activation of the right fusiform gyrus depends on whether faces are processed holistically or not. When intact subjects match whole faces, the right middle fusiform region is activated whereas the opposite pattern is observed in the left homologous region when subjects match face parts [14]. These lateralized differences appear to be specific to faces since common objects processed either as wholes or parts did not induce any change of activity within these regions. Although previous studies observed either bilateral face-specific activity in regions of the middle fusiform or differences between faces and objects in the right hemisphere only, Rossion et al. proposed that face-selective activity can be even greater in the left FFA than in the right FFA if subjects focus their attention on particular features of the face [14]. In other words, the right fusiform gyrus is involved in the holistic processing of faces, while the left fusiform gyrus tends to process a feature-based representation of the face. If the face recognition ability that has been lost in prosopagnosia is the representation of faces as wholes, then a reliance on parts-based processing may be reflected in the activation pattern of prosopagnosic patients when viewing faces by an increase in activation in the left fusiform gyrus.

To date, there has been no functional imaging study of patients with acquired prosopagnosia. There are, however, neuroimaging reports of patients with developmental prosopagnosia, including those that have acquired prosopagnosia at an early age. For example, structural and functional imaging data was obtained from prosopagnosic patient RP, who was 49 years old at the time of testing but who suffered a closed head injury at age seven [15]. No damage was visible on structural MRIs at the time of testing (perhaps not surprising given that RP suffered a closed head injury at an early age). More striking was the finding that there was not a single voxel in the entire ventral pathway of RP's brain that produced a significantly stronger MR signal during face than object viewing. de Gelder and Kanwisher [15] took this null finding as support that the FFA may be necessary for face recognition but admit that prosopagnosia is a heterogeneous syndrome and that the FFA is difficult to detect even in some normal subjects. Since the damage in patient RP occurred at an early age, however, it is possible that plasticity changes may have affected the activation pattern and that generalization to the normal system might not be possible. A similar finding with a congenital prosopagnosic was obtained using event-related brain potentials [16]. Patient YT, age 36, admitted to having severe problems in face recognition from childhood and, on a structural MRI scan, was shown to have a smaller than normal right temporal lobe. In contrast to normal subjects who show an early brain potential (N170) that is specifically elicited by faces, YT showed no specificity. No activation in the entire ventral stream is puzzling, however, since individuals with prosopagnosia know when they are looking at a face. Could other neurons, which are not ideally suited for face recognition, be recruited for the purpose of face recognition by individuals with prosopagnosia?

In summary, while several fMRI studies have high-

lighted the role of the fusiform gyrus in the processing of faces in intact subjects, the pattern of activation associated with face processing in patients with prosopagnosia is still unclear. The current study examined the functional activation pattern in the fusiform gyrus of prosopagnosic patients and their control subjects while they examined faces in a passive viewing task.

## MATERIALS AND METHODS

*Subjects:* Two right-handed male individuals with prosopagnosia, SM and CR, and eight intact control subjects (six males and two females; age range 19–30 years old; mean age 24 years old) voluntarily consented to participate in the study, which was approved by the University of Pittsburgh Institutional Review Board. SM was 24 years old at the time of testing. He sustained a closed head injury and loss of consciousness in a motor vehicle accident in 1992. CT scans indicated a contusion in the right anterior and posterior temporal regions accompanied by deep shearing injury in the corpus callosum and left basal ganglia. CR was 19 years old at the time of testing. He suffered from a right temporal lobe abscess with a complicated medical course including a history of Group A toxic shock syndrome, pneumonia, cardiac arrest, candida bacteremia and metabolic encephalopathy in 1996. MR scans on CR revealed a right temporal lobe lesion consistent with acute micro-abscesses of the right temporal lobe and medial occipital lobe (see Fig. 1).

Both SM and CR perform within the normal range on all tests of low-level visual processing (judging size, length and orientation of stimuli) as well as on tests that require matching of objects from different viewpoints or along a foreshortened axis. Both patients perform poorly on tests
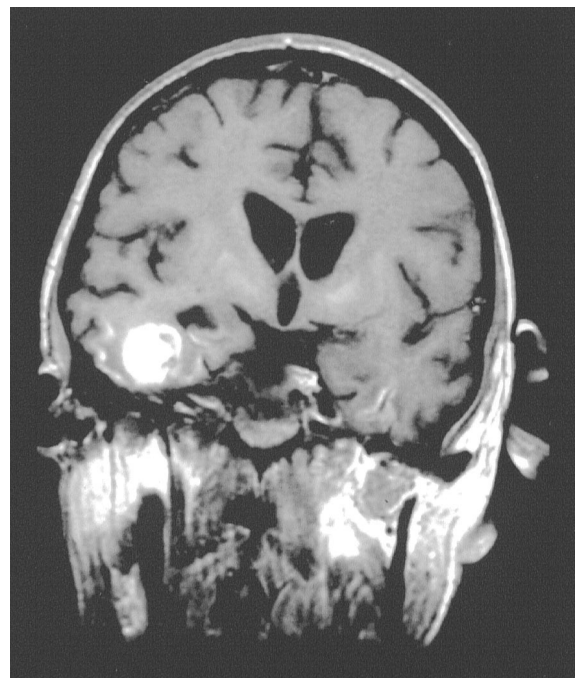


**Fig. 1.** Coronal section of CR's brain revealing a right temporal lobe lesion and damage to the right fusiform gyrus. MR scan is presented in radiological format (the right hemisphere is on the left side of the image).

of face recognition, with performance in the severely impaired range on the Benton Facial recognition test (with scores of 36/54 for SM, and scores of 36/54 and 37/54 for CR on two separate administrations of the test) and both are unable to recognize pictures of any famous people (such as former president Bill Clinton).

*Stimuli:* The visual stimuli consisted of grayscale images of faces, common objects, jumbled images (see Fig. 2) and a fixation cross. The stimuli were projected onto a rear projection screen that the subject viewed from an angled mirror fixed to the head coil. The face stimuli were taken from a database that was provided by the Max-Planck Institute for Biological Cybernetics in Tuebingen, Germany, and consisted of images of real faces scanned using a 3D laser and cropped to remove cues from the hairline. The jumbled images were created by taking images of faces, common objects and a class of novel objects called Greebles, segmenting them into nine equal panels, and then randomly combining them. Greebles are a homogenous class of computer-generated complex 3D objects organized along three categorical dimensions: race, gender and family. They were originally designed as a control set for faces. Like faces, Greebles are visually similar in that they are all made up of the same number of parts in the same configuration.

*Procedure:* The visual stimuli were presented in separate 30 s epochs (20 stimuli/epoch); each epoch was repeated five times. One control subject did not receive the jumbled condition and that subject, along with two others, was presented with 30 stimuli/epoch. The subjects were instructed to look at the stimuli while keeping their head still and to press a button on a button box when a circle appeared around one of the pictures. Circles were drawn around 10% of the stimuli in order to maintain subjects' interest level (the first three control subjects were not given this task). The subjects were positioned within a head coil and head motion was minimized with firm cushions.

*Data acquisition:* Functional imaging was performed on 3.0 T and 1.5 T Signa whole body scanners (General Electric Medical Systems, Milwaukee, WI) with resonant gradient echo planar capabilities. Fourteen 3 mm adjacent axial planes (voxel size $3 \times 3 \times 3$ mm) were imaged while subjects passively viewed the stimuli (TR = 3.0 s, TE = 25 ms, single shot, matrix size = $128 \times 64$; for CR and the three control subjects on the 1.5 T magnet TE = 50 ms; for the last two control subjects the matrix size = $64 \times 64$).

*Statistical analysis:* We compared patient and control data after mapping each subject's anatomical and functional data into Talairach coordinates. To localize FFA, we first identified voxels that had a statistically significant ($p < 0.01$) increase in signal for faces *vs* objects under a two-sample *t*-test. We then selected from among these voxels according to the following criteria: (1) there were two or more contiguous voxels like this in the fusiform gyrus; (2) the percent signal change (%SC) for faces versus fixation was greater than for objects versus fixation; (3) a voxel's %SC for faces versus fixation was greater than half the %SC for the maximum voxel in the region of interest (ROI). Criteria like these are commonly used in the literature to localize FFA [1,4,7,17].

To compare the activation patterns of the controls and patients, we used a method that controls the false discovery rate (FDR) [18,19] to select a threshold for the voxel-wise t-statistics that accounts for multiple statistical testing. FDR is the expected proportion of rejected tests that are false discoveries. Methods that control this rate guarantee that the FDR will be below a target level q on average. We used q = 0.01 along with an adjustment to the method that makes it applicable to arbitrary dependent tests. FDR-based methods have been shown to be more powerful than other available approaches to multiple statistical testing (see references for a full discussion).

In order to investigate the overall pattern of activation between the controls and the patients, a region of interest (ROI) was defined for subsequent tests that covered the entire fusiform gyrus in both hemispheres. We examined the distribution of activated voxels along the entire length of the fusiform gyrus and then divided the ROI into six
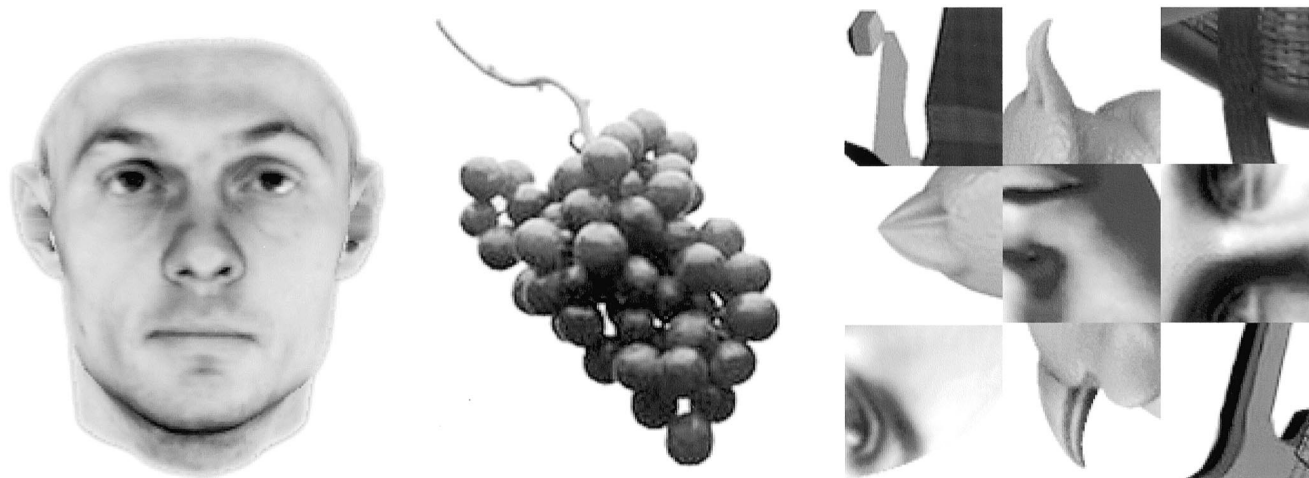


**Fig. 2.** Examples of the visual stimuli, which consist of grayscale images of faces, common objects and jumbled images.

regions of interest along the anterior–posterior plane in each hemisphere and calculated the 95% confidence intervals for the number of activated voxels produced by the control subjects. We then plotted the degree of activation of the patients against that of the control subjects and examined the similarities and differences.

## RESULTS

Activated voxels meeting the criteria for FFA were found for both the prosopagnosic patients and control subjects (see Fig. 3). The location of this activation, however, appears to differ between the patients and the control subjects.

The three-dimensional plots presented in Fig. 4a,b illustrate the significantly activated voxels ($p < 0.003$, based on the FDR method for multiple testing under dependent tests) for the controls and patients in the fusiform gyrus for a faces–objects subtraction and a jumbles–fixation subtraction, respectively. It appears that differing patterns of activation emerge when the controls and patients view faces, with the patients showing more activation in posterior regions of the fusiform gyrus compared with the controls (see Fig. 4a). When viewing jumbles, however, their activation patterns appear more similar (see Fig. 4b).

By binning the activated voxels into 15 mm segments along the length of the fusiform gyrus, the differences in functional activation patterns between the prosopagnosic patients and the control subjects are made even clearer. The results of a faces–objects subtraction indicate that, when viewing faces, SM and CR exhibited significantly more activation in the posterior edges of the right and left fusiform gyri than the control subjects ($p < 0.05$; see Fig. 5a,b). In CR, this was particularly true in the left posterior fusiform ($p < 0.05$). These differences appear to be specific to faces, since a jumbles–fixation subtraction revealed that SM and CR do not show differing patterns of activation from the control subjects when viewing jumbled images (Fig. 6a,b).

## DISCUSSION

The goal of this study was to explore the differences in functional brain activation for a pair of patients with prosopagnosia, an acquired impairment in face recognition, and a group of normal control subjects. The critical question was whether patients with prosopagnosia would show functional activation in their fusiform gyrus when viewing faces and if so, whether the pattern of activation would differ from that obtained in the intact brain. When the
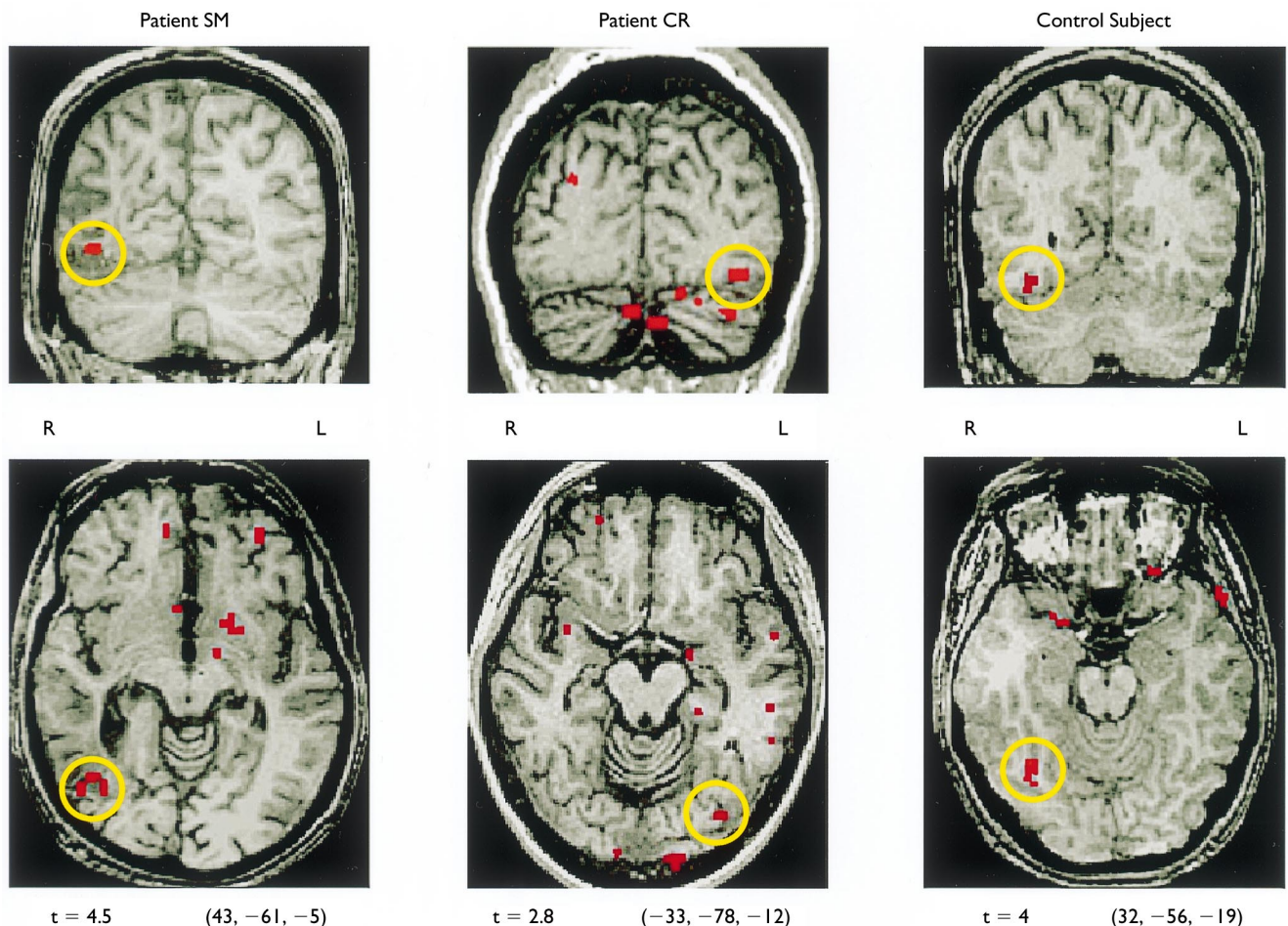


**Fig. 3.** Functional activation patterns for a faces–objects subtraction in patients SM and CR and one control subject. Thresholds and Tailarach coordinates of activated voxels meeting the criteria for the fusiform face area (circled) are provided.
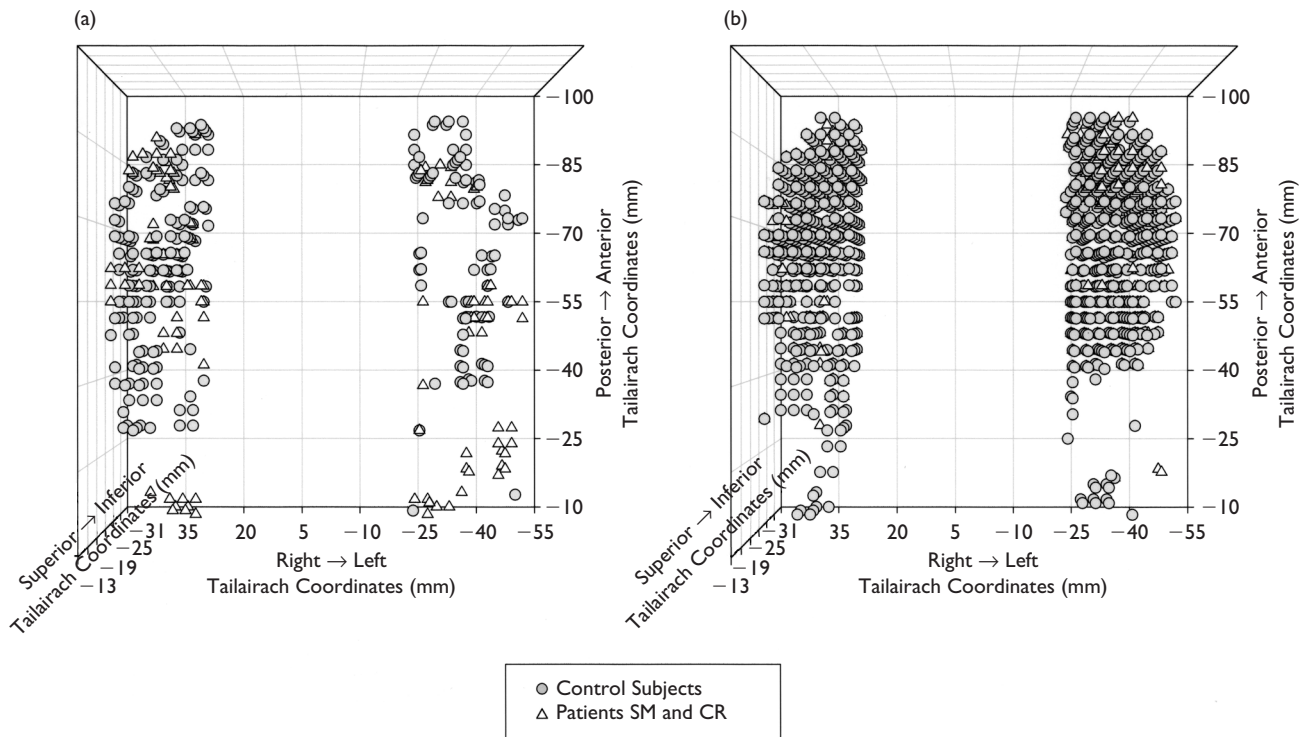
**Fig. 4.** Three-dimensional plot of significantly activated voxels for (**a**) faces–objects subtraction and (**b**) jumbles–fixation subtraction (open triangle Patients SM and CR, closed circle Control subjects).
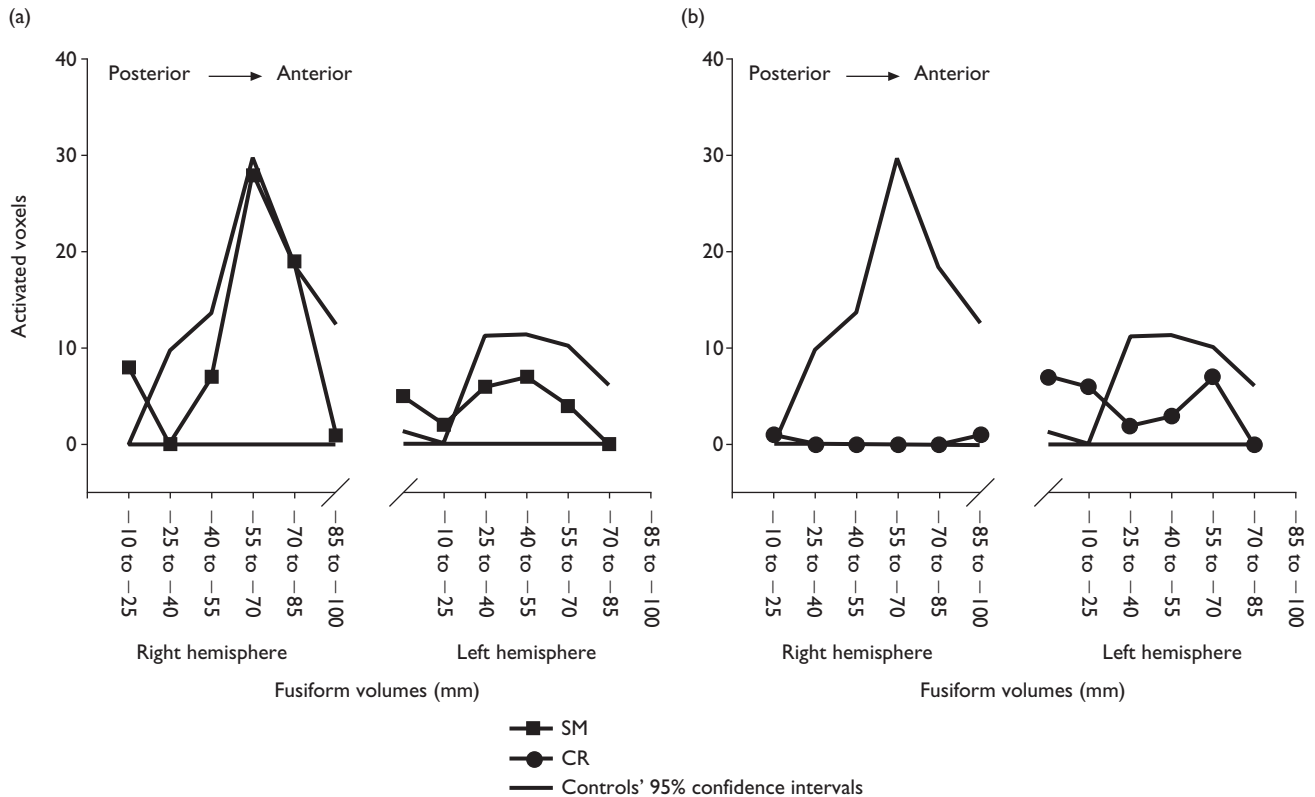


**Fig. 5.** Activated voxels for a faces–objects subtraction as a function of volumes along the posterior–anterior plane of the fusiform gyrus for (**a**) Patient SM and (**b**) Patient CR (closed square Patient SM, closed circle Patient CR, line Controls' 95% confidence intervals).
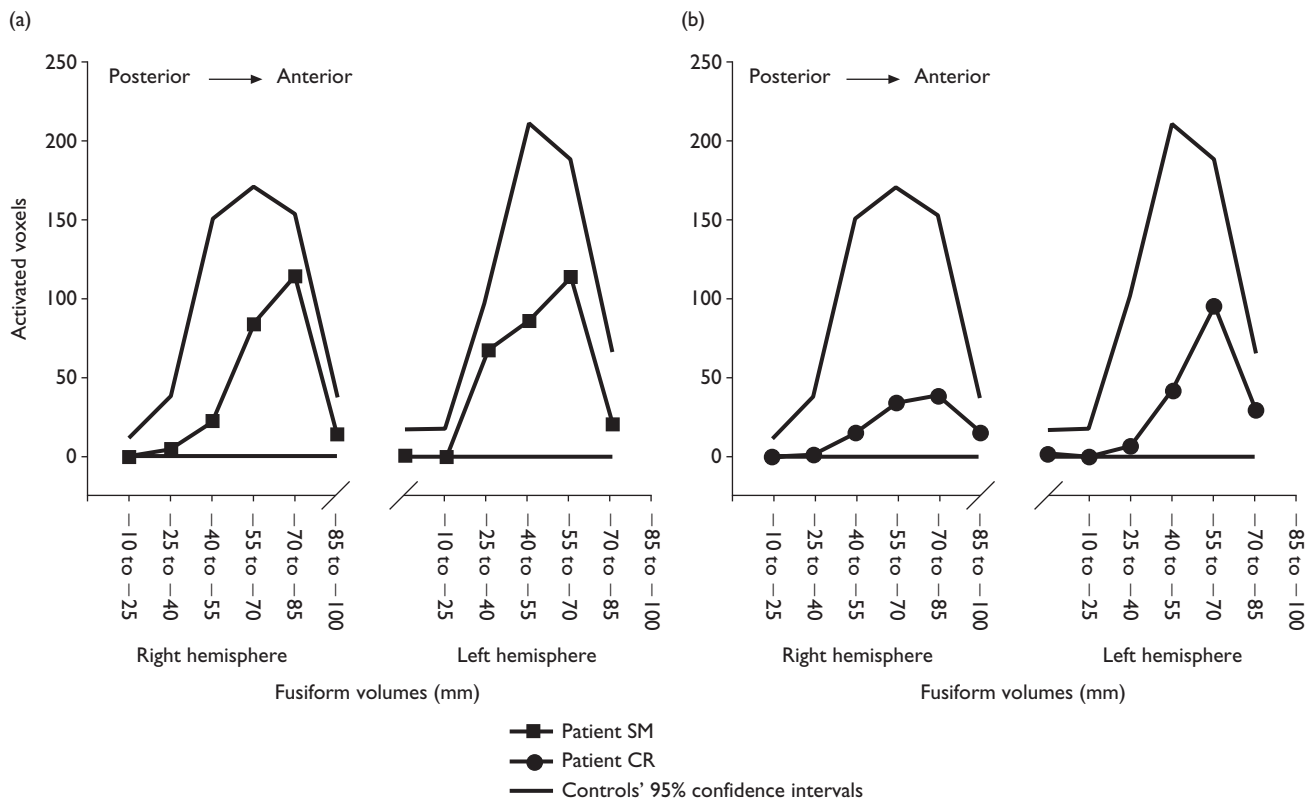
**Fig. 6.** Activated voxels for a jumbles–fixation subtraction as a function of volumes along the posterior–anterior plane of the fusiform gyrus for (**a**) Patient SM and (**b**) Patient CR (closed square Patient SM, closed circle Patient CR, line Controls' 95% confidence intervals).

patients were presented with faces, activation was apparent in voxels meeting the criteria for the fusiform face area. However, the prosopagnosic patients also showed significantly more activated voxels in more posterior regions of the fusiform gyrus than their control subjects. In patient CR, this activation was particularly evident in the left hemisphere, which is believed to be involved in feature-based strategies of face perception [14]. This increased posterior activation occurred only when prosopagnosic patients viewed faces, not when they viewed images that were composites of features taken from faces as well as from other objects. Recent work in our laboratory further supports the idea that an increased reliance on feature-based processing occurs in prosopagnosia, particularly when it comes to patient CR [20,21]. This study has shown that while CR shows a clear local advantage in a global/local task, SM, like control subjects, showed a global advantage.

While previous PET studies have reported bilateral middle and posterior fusiform activation for face processing [2,22], the recruitment of the left posterior fusiform region for face processing is observed far less frequently [23]. In fact, several studies have shown that when faces are compared to complex objects there is no evidence of left posterior fusiform activation in intact subjects [4,5,17], except in two recent fMRI studies [3,24]. In contrast, activation in the right posterior fusiform is commonly observed when faces are compared to objects. The recruit-

ment of the left hemisphere is also not evident in patients with prosopagnosia in whom the deficit is either congenital or acquired early in life. In those cases of developmental prosopagnosia where the neural substrate has been examined, no selectivity (activation for faces but not other objects) is apparent in either hemisphere [16,25].

In light of these previous findings, the activation we have observed in the posterior fusiform gyrus of prosopagnosic patients is all the more surprising, particularly the left posterior fusiform activation evident in CR. The interpretation of this unusual pattern of activation in patients needs to be undertaken with caution. One potential problem with activation studies in patients is that one does not know to what extent the existing lesions affect the physiology of the BOLD response. The results of such imaging studies in patients are likely to reflect a complex interaction between activity related to the specific cognitive process being studied, the overall effects of lesions on brain physiology, and the compensation strategies the patient employs in trying to perform the task. Bearing this in mind, we suggest that the observed posterior activation reflects the compensatory process that occurs in prosopagnosia, following damage to more anterior regions of the fusiform gyrus. This compensatory process, which is less than optimal for the purpose of face recognition, likely entails the increased reliance on feature-based processing and the concurrent recruitment of neurons in more posterior regions of the fusiform gyrus.

## CONCLUSION

While the patients with prosopagnosia do reveal cortical activation in voxels meeting the criteria for the FFA, this activation was not sufficient for face processing. Our results indicate that the overall pattern of activation in the fusiform gyrus represents a more feature-based than holistic process. It would behove researchers, then, to keep in mind overall pattern differences in the fusiform gyrus when viewing faces rather than just focusing on whether or not the FFA is activated.

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**Erratum**

J.J. Marotta, the corresponding author of 'A functional MRI study of face recognition in patients with prosopagnosia', *NeuroReport* Volume 12 Number 8, pages 1581–1587, wishes us to publish the following Erratum:

An inadvertent reflection of the posterior/anterior axis occurred in Figures 4, 5 and 6. The posterior -> anterior label should be reversed. The patients, therefore, showed significantly more activated voxels in anterior (rather than posterior) areas of fusiform gyrus than their control subjects; although SM does show an increased area of activation as well ($-70$ to $-85$ mm).

The main points of the article still hold:

1) The prosopagnosic patients showed functional activation in the fusiform gyrus but this activtion was not sufficient for face processing.
2) In one of the patients, the increased activation was particularly evident in the left hemisphere, which is thought to be involved in feature-based strategies of face perception.
3) An increased reliance on feature-based processing in prosopagnosia leads to a recruitment of neurons in regions adjacent to FFA in the fusiform gyrus, regions that are not ideally suited for processing faces.