Lesions of the fusiform face area impair perception of facial configuration in prosopagnosia

Jason J.S. Barton, MD, PhD, FRCPC; Daniel Z. Press, MD; Julian P. Keenan, PhD; and Margaret O’Connor, PhD

Abstract—Background: Prosopagnosia, the inability to recognize faces, is associated with medial occipitotemporal lesions, especially on the right. Functional imaging has revealed a focal region in the right fusiform gyrus activated specifically during face perception. Objective: The study attempted to determine whether lesions of this region were associated with defects in face perception in patients with prosopagnosia. Methods: Five patients with acquired prosopagnosia were tested. They were asked to discriminate faces in which the spatial configuration of features had been altered. This was contrasted with their discrimination of changes in feature color, an alteration that does not affect spatial relations. Results: All four patients whose lesions included the right fusiform face area were severely impaired in discriminating changes in the spatial position of features. The one patient with anterior bilateral lesions was normal in this perceptual ability. For three of the five patients, accuracy was normal for changes in eye color. When subjects knew that only changes in mouth position would be shown, performance improved markedly in two of the four patients who were impaired in the initial test. Conclusion: Perception of facial configuration is impaired in patients with prosopagnosia whose lesions involve the right fusiform gyrus. This deficit is especially manifest when attention must be distributed across numerous facial elements. It does not occur with more anterior bilateral temporal lesions. Loss of this ability may contribute to the recognition defect in some forms of prosopagnosia.

Prosopagnosia is the inability to recognize familiar faces. Most cases are caused by lesions of the medial occipitotemporal cortex, either right-sided1-3 or bilateral.4,5 Functional imaging has confirmed the existence of a fusiform face area6-8 located in the midsection of the fusiform gyrus, a region involved in the lesions of some but not all patients with prosopagnosia.

Although this fusiform region is activated by faces in preference to other visual objects,6-8 the role of this region in face perception is uncertain. Indeed, the type of processing required for face recognition in general is an area of ongoing research. There are considerable data from normal subjects that face perception involves a “holistic” encoding of facial structure, in which the spatial relationships between facial features play a critical role.9,10 Faces are examples of classes of stimuli that share a basic configuration, differing from each other only in subtle variations of this spatial structure. The ability to discern the relevant differences between individual members of such classes is a highly developed skill that requires considerable experience with such stimuli.11 Furthermore, this perceptual ability is specific for the usual orientation in which such stimuli are encountered: hence the inversion effect, in which recognition is impaired when faces are turned upside down.12,13 We have shown that face inversion has little effect on perception of facial features (eye or mouth color) but significantly degrades the discrimination of their spatial relationships, particularly in the less salient regions of the face, such as the mouth.14 Others have also found an impairment in processing spatial relations in inverted faces15-17 and confirmed that this occurs at a stage of perceptual encoding rather than memory retrieval.18

If perception of such subtle changes in the spatial configuration of faces is critical to recognition of identity, it is possible that the loss of this perceptual ability contributes to the deficit in some forms of prosopagnosia. We tested this hypothesis in a series of five patients with prosopagnosia, using a series of faces in which either feature color or spatial position was altered with computer-aided graphics, as employed in our prior study of normal subjects.14 One patient (Patient 1) had bilateral anterior temporal lesions, sparing the fusiform face area; the other four had mainly or solely right-sided lesions that involved this region.

From the Departments of Neurology (Drs. Barton, Press, Keenan, and O’Connor) and Ophthalmology (Dr. Barton), Beth Israel Deaconess Medical Center and Harvard Medical School; and Department of Biomedical Engineering, Boston University (Dr. Barton), MA.

J.B. was supported by a grant from the National Institute of Neurological Disorders and Stroke.

Presented in part at the annual meeting of the American Academy of Neurology; Toronto, Ontario, Canada; April 19, 1999.

Received June 21, 2001. Accepted in final form September 18, 2001.

Address correspondence and reprint requests to Dr. Jason J.S. Barton, Department of Neurology, KS 452, Beth Israel Deaconess Medical Center, 330 Brookline Avenue, Boston, MA 02215; e-mail: jbarton@caregroup.harvard.edu

Copyright © 2002 by AAN Enterprises, Inc. 71
Methods. Subjects. All patients and normal subjects gave informed consent in a protocol approved by the hospital’s institutional review board. All subjects had assessments of near acuity, with corrected Snellen acuities of better than 20/40 for participation, visual fields by confrontation, and handedness, using the Edinburgh handedness battery. Control subjects were 10 men and four women ranging in age from 16 to 43 years: 12 were right handed. Patients, all right handed, had more extensive testing, with neuro-ophthalmologic assessment of vision and eye movements, including Goldmann perimetry. Neuropsychological assessment included the Wechsler Adult Intelligence Scale–Revised, WMS-III, Warrington Recognition Test, Benton Line Orientation Test, Benton Face Recognition Test (BFRT), and the Warrington Visual Spatial and Object Perception Battery. Prosopagnosia was confirmed by the Famous Faces Test (administered by author MOC), as well as by a test of overt familiarity that used a series of famous and unknown faces, reported elsewhere. This asked patients to indicate which of a series of 20 famous and 20 anonymous faces were familiar. (Because this method yields both false-positive and false-negative results, discriminative power can be assessed independent of criterion bias with signal detection methodology.)

Case histories. Patient 1 is a 33-year-old woman who had had a severe closed head injury and right temporal lobe resection 10 years previously and subsequently could not recognize familiar faces. She also complains that the world looks flat and that she cannot appreciate shadows, though colors appear normal. She has no symptoms of topographagnosia (the inability to find one’s way around a familiar environment). She has an old left strabismic amblyopia. Snellen acuity was 20/15 in her right eye and 20/400 in her left eye. She saw 11/14 Ishihara pseudoisochromatic plates with her right eye. She had full visual fields by Goldmann perimetry. She had a small exotropia but otherwise normal eye movements. Her IQ was estimated in the 91% percentile. Her copying of the Rey–Osterreith figure was mildly impaired. Memory for verbal and nonverbal material was impaired. Her score on the BFRT was 25/54, and on the Famous Faces Test 0/68. MRI showed bilateral anterior temporal lobar lesions, sparing the lingual and fusiform gyri bilaterally (figure 1).

Patient 2 is a 38-year-old man who was shot in the occiput at age 20 and treated with craniotomy and evacuation of an intracranial hematoma. He has difficulty with face recognition, topographagnosia, and partial impairment of color perception. Visual acuity was 20/20 in both eyes. He saw 10/14 Ishihara pseudoisochromatic plates with either eye. Eye movements were normal. Goldmann perimetry showed complete loss of superior visual fields bilaterally, which extended slightly into the inferior right field. Neuropsychological testing showed full-scale IQ of
Patient 3 is a 37-year-old woman who had a viral encephalitis at age 17. She initially presented with aphasia, memory deficits, and confusion. Subsequently she has difficulty recognizing people and topographagnosia but denies problems with color perception. Visual acuity was 20/20 in both eyes. She saw 12/14 Ishihara pseudoisochromatic plates with either eye. Pursuit and saccadic eye movements were normal. Goldmann perimetry findings were normal, but she had impaired hue discrimination in the left upper quadrant, indicating a partial hemichromatopsia. Neropsychological testing showed an IQ of 82. She had a memory impairment, greater for nonverbal material. She had trouble on recall of the Rey–Osterreith figure and was impaired in recognizing objects seen in noncanonical views. Her score on the BFRT was 39/54 and on the famous faces 6/73. Her MRI showed extensive right-sided lesions, involving the medial occipitotemporal cortex, inferior parietal lobule, and ventromedial frontal lobe; and lesser left-sided lesions of the insula, parahippocampal gyrus, and ventromedial frontal lobe (see figure 1).

Patient 4 is a 59-year-old man seen 10 months after a right medial occipitotemporal stroke. Subsequently he has difficulty recognizing faces, more so for people met since or in the years just before his stroke, but not for long familiar friends. He complains of decreased brightness but not loss of color perception. He has topographagnosia. Snellen acuity was 20/25 in the right eye and 20/20 in the left eye. He had a complete left homonymous hemianopia on Goldmann perimetry. He saw 12/14 Ishihara plates with either eye, missing mainly left-sided digits. His eye movements were normal. Neropsychological testing revealed a verbal IQ of 150. He copied the Rey–Osterreith figure normally. He had memory difficulties, worse for nonverbal items. His score on the BFRT was 35/54 and on the famous faces 33/68. His MRI showed a large right medial occipitotemporal infarct (see figure 1).

Patient 5 is a 52-year-old man seen 7 months after a right occipital hemorrhage from an oligodendroglioma. This was resected and he was treated with irradiation and chemotherapy with vincristine, lomustine, and procarbazine. He complains of blurry vision and difficulty reading. He has topographagnosia. Snellen acuity was 20/25 in either eye, and he had a complete left homonymous hemianopia on Goldmann perimetry. He saw 12/14 Ishihara plates with either eye, missing mainly left-sided digits. His eye movements were normal. Neropsychological testing showed no neglect and mild impairment of visual memory relative to verbal memory. His score on the BFRT score 32/54 and on the Famous Faces 23/68. MRI showed an extensive right medial occipital resection involving the lingual and fusiform gyri (see figure 1).

Apparatus and stimuli. Subjects sat 57 cm away from an Apple Multiscan 1705 monitor (Apple Corp., Cupertino, CA) in standard dim room lighting. The experiments were run with either a PowerMac 9600/233 or a PowerMac 7300/200.

The aim was to create face stimuli that differed in a step-wise quantitative fashion along three dimensions (figure 2). Two of these were second-order spatial relations: the vertical mouth position and the interocular distance. (First-order refers to the categorical feature arrangement universal to all faces, such as eyes above nose, nose above mouth, and so on. The quantitative variations of feature position within these constraints, i.e., how far is the mouth below the nose, are the second-order relations. These were chosen because of prior work showing that humans are highly sensitive to such displacements. The third, a feature change, was eye color, selected because color changes do not alter spatial relationships between features, whereas changes in feature shape invariably have subtle secondary effects on second-order relations. Brightness rather than hue was manipulated because patients with prosopagnosia may have associated dyschromatopsia, which usually impairs perception of hue and saturation but not brightness.

We used full-color digitized frontal images of the faces of one male and one female. Each facial image occupied a square of 250 × 250 pixels, which in the test sequences spanned 8.8° × 8.8° of visual angle at the viewing distance of 57 cm. The interocular distances of the two base images were similar, being 2.1° for the female face and 2.3° for the male face.

Spatial manipulations of the images were done with Paintshop Pro 3.0 (Shareware). We first created base faces with the eyes displaced laterally 4 pixels each and the mouth displaced downward 4 pixels also. This gave us a greater range of possible unidirectional displacements in target faces, before reaching the limits of plausibility or grotesqueness. To generate target faces with altered eye displacement, both eyes were moved simultaneously normally; to generate targets with altered mouth position, the mouth was moved up.

Pilot work was conducted on the authors to determine the range of increments in the three manipulations that would generate accuracy rates ranging from near-chance to near-perfect discrimination. Five different target faces were constructed for each dimension. For eye displacement, interocular distance of the target faces was reduced by 4, 8, 12, or 16 pixels from the base face. For shorter durations, an additional target with a 10-pixel reduction was used; for longer durations, there was an additional target with a 2-pixel reduction. For mouth displacement, target faces had the mouth elevated by 2, 4, 6, 8, or 10 pixels. Each pixel corresponds to 2.1 minutes of visual angle. For eye color, brightness was increased by 3, 6, 9, 12, or 15%, using Adobe Photoshop 5.0 (Adobe, San Jose, CA). Each target face differed from the base face in only one of the three dimensions (see figure 2).

A trial stimulus consisted of three faces, two of which were the base face and one a target face. Because we wished to test perception rather than memory or recognition, we presented all faces simultaneously. The faces were placed in a triangular arrangement so that each face was equidistant from the other two. The lower two faces were also slightly offset vertically to avoid a possible advantage to comparisons between horizontally aligned stimuli. The target face occurred with equal probability at any
of the three face positions. The subject’s task was to indicate which face was the different one, with chance performance being 33% correct.

We constructed testing blocks using the Superlab 1.71 (Cedrus, Phoenix, AZ) program. Each trial stimulus was presented nine times. Because there were two test faces, there were 18 stimuli for each gradation of change within a dimension. With five levels of change and three dimensions, there were a total of 270 trials in a block.

We presented several blocks of trials with different viewing durations. Our report on normal subjects used durations of 1, 2, and 4 seconds, as well as unlimited duration: the latter was used to obtain reaction times as well as accuracy rates. The patients performed a more limited version of testing. In addition to unlimited duration, Patients 3 and 4 did trials with 2- and 4-second durations, whereas Patient 1, who was more accurate, did trials with 1- and 2-second durations. Patients 2 and 5 did trials with 2-second durations. Also, because of fatigue, Patients 2 and 5 were tested only with the three largest (easiest) levels of stimulus manipulation, reducing the number of trials per block to 162. The order of blocks was randomized for each subject and interspersed with other visual tests over several days.

Analysis. For any given viewing duration, we wished to determine whether patients performed in the normal range for each of the three stimulus dimensions of eye color, eye position, and mouth position. In all individuals we measured the mean accuracy for the three easiest levels of difficulty, which corresponded to the data at or above perceptual threshold in normal subjects. The mean and variance of the data from normal subjects were then used to construct 95% prediction intervals.

Results. Only Patients 2 and 5 were consistently impaired on discrimination of eye color (figure 3). With unlimited viewing time, Patient 1 had a mild deficit for eye color.

Patients 2, 3, 4, and 5 were severely and consistently impaired on discrimination of both eye position and mouth position at all viewing durations, the only exceptions being low-normal scores for mouth position in Patients 2 and 4 with unlimited viewing duration (see figure 3). This does not necessarily indicate normal ability, however, as these scores in Patients 2 and 4 were obtained with extremely long reaction times, about 10 times that of normal subjects (figure 4).

In contrast, Patient 1 had normal discrimination of eye position at all viewing durations. She was in the low-normal range for discrimination of mouth position, except for one low score at viewing duration of 2 seconds (see figure 3). Her reaction times were also normal. This good performance held even in trials with viewing durations of only 1 second.

Normal subjects improve their discrimination of mouth position if they are given trials in which they know that this is the only change that will occur. Also, the inversion effect for mouth position is eliminated by this manipulation of expectancy. When told to focus their attention on mouth position, Patients 3 and 4 were able to dramatically improve their performance to the low-normal range, but Patients 2 and 5 could not (figure 5).
The reaction time data for trials with unlimited viewing duration largely mirrored the accuracy results (see figure 4). Patients 2, 3, and 4 had exceedingly prolonged reaction times, whereas those of Patient 1 fell at the upper limit of normal. Patient 5, whose accuracy scores were similar to those of Patients 2, 3, and 4, did not show the markedly increased reaction times they did.

Despite the severe deficits displayed by some of our subjects on these tests, these were not due to a generalized failure of attention or vision. In other perceptual tests reported elsewhere, all subjects performed normally on spatial resolution, and all but Patient 5 on curvature perception, for example.32

**Discussion.** We found that most of our patients with prosopagnosia had good discrimination of the facial feature of eye color. Perception of eye color was most impaired in Patients 2 and 5, who had the most extensive peristriate occipital damage. In contrast, Patients 2, 3, 4, and 5, in whom extensive damage to the right occipitotemporal lobe included the fusiform face area,6 were severely impaired in discriminating shifts in eye or mouth position. This was true both for limited and unlimited viewing durations, and in the latter, Patients 2, 3, and 4 had dramatically elevated reaction times. Conversely, Patient 1, who had bilateral damage to more anterior regions in the temporal lobes, had normal accuracy and reaction times in spatial discrimination.

**Comparison with the inversion effect in normal subjects.** The dual-mode hypothesis proposes that there are (at least) two processing modes that can be applied to a complex stimulus such as a face.33 The
various formulations of such a dichotomy have been summarized, including serial/parallel, local/global, first-order/second-order, relations/attributes, component/configuration, and analytic/holistic. It is argued that inverted faces cannot engage the more efficient parallel/global/holistic alternative that operates on upright faces. Similarly, it is argued that some patients with prosopagnosia may have lost the parallel/global/holistic processing route, which has often been assigned a right hemispheric locus. If so, then the defect in prosopagnosia should resemble the performance of normal subjects viewing inverted faces.

We have studied the effect of stimulus inversion on normal subjects viewing the stimuli used in this report. We found that the impairment on spatial relation perception from stimulus inversion was evident mainly at short viewing durations and restricted to less salient regions of the face, such as the mouth. In contrast, Patients 2, 3, 4, and 5 were impaired in spatial discriminations at both the highly salient eye region and the less salient mouth region. With few exceptions they also did not improve with increased viewing time, even in the unlimited trials. Thus their deficit is more profound, being modulated by neither salience nor viewing time.

Effects of attentional allocation. Like normal subjects, some of our patients did better when they could concentrate on a single face alteration. Just as Figure 4. Reaction times from blocks with unlimited viewing duration. As in figure 3, data are averaged from the trials with the three easiest levels of difficulty for each change. Gray lines indicate means of the 14 normal control subjects with upward error bars showing 1 SD. Patient symbols as in figure 3. Patients 1 and 5 responded near the upper limit of normal, whereas Patients 2, 3, and 4 took much longer to respond in all categories.

Figure 5. Accuracy for mouth position in mouth-only trials. The left graph shows data for discriminating mouth position changes from the first experiment, in which subjects had to watch for one of three possible changes in any given trial. The right graph shows data from the next block of trials, in which subjects had to watch for only one possible change, in mouth position, and knew this in advance. Percent correct is plotted against the degree of change in mouth position, with larger shifts being easier to detect. Gray lines indicate 95% prediction intervals for the normal sample. Patient symbols as in figure 3. Patients 3 and 4 did markedly better in their discrimination of mouth position in these trials.
the inversion effect at the mouth disappears when normal subjects focus their attention in this region. Patients 3 and 4 could discriminate mouth position in upright faces normally under similar conditions. Thus, Patients 3 and 4 retain the ability to make accurate spatial judgments, even within faces, but are not able to implement these when they must divide their attention among multiple facial dimensions. This suggests that their perceptual deficit may include a “top-down” problem with attentional allocation. This attentional aspect complements other recent demonstrations of problems with attentional allocation after lesions of the ventral form-processing stream. Lesions of V4 and TEO in monkeys impair the ability to attend to targets in the presence of distractors of greater contrast. Similarly, one patient with prosopagnosia with bilateral occipitotemporal lesions could not discriminate the “lesser” members of texture or pattern items, as reported in monkeys with V4 lesions. It is likely that the efficiency of complex form processing will be compromised by an inability to direct attention to relevant stimulus aspects and away from items with prominent low-level visual properties.

This proposed defect of attentional allocation could be overcome in Patients 3 and 4 by instructing them to focus on a specific spatial relation, but not by allowing more time, despite the fact that the latter permitted them to search faces in a more leisurely serial manner, as evidenced by their very long reaction times with unlimited duration blocks. Thus their ability to selectively attend to a single facial spatial processing task is preserved, whereas their ability to process spatial relations in a task that requires distributed attention is impaired. This is consistent with a reduction in the capacity of their processing of the spatial properties of faces. Patients 2 and 5, conversely, did not improve when told to focus on the mouth. Whether this implies a basic defect in perceiving spatial relation, or an additional inability to selectively attend to a single facial region, cannot be determined specifically from the current data. However, the fact that Patients 2 and 5 had the greatest peristriate damage and were also impaired on discrimination of eye color suggests that they may have perceptual dysfunction at a more elementary level.

A contribution to apperceptive prosopagnosia? The contribution of impaired face perception to prosopagnosia is controversial. It has been proposed that there are subtypes of prosopagnosia, the most fundamental distinction being between an associative form, in which perception is intact but access to facial memories is impaired, and an apperceptive form, in which poor recognition is due to the failure to generate an adequately specific facial percept. Others have proposed that bilateral anterior temporal lesions may be the substrate for associative prosopagnosia, whereas unilateral right lesions of the fusiform and lingual gyri may cause the apperceptive type. Our findings are consistent with this proposal, in that Patient 1, with bilateral anterior temporal lesions, performed normally on our tests of facial configuration perception, whereas the other four subjects with lesions of the right fusiform area in common were impaired.

However, several cautions are in order. First, we cannot determine from this evidence whether the face perceptual deficits in Patients 2, 3, 4, and 5 are at least partly responsible for their prosopagnosia or merely associated but irrelevant defects. Given the evidence that perceiving such spatial relations is important in normal face recognition, however, it seems implausible that the profound defects of Patients 2, 3, 4, and 5 would not contribute to their prosopagnosia. Even if other nonprosopagnosic patients with right occipitotemporal lesions had similar face perceptual defects, this would not mean that such deficits are irrelevant in prosopagnosia. Rather, such a finding would show only that these perceptual deficits are not sufficient to cause prosopagnosia on their own, though they may be necessary in combination with other deficits for this apperceptive prosopagnosic subtype.

Second, the normal performance of Patient 1 on these tests does not exclude the possibility that she has other (untested) face perception deficits. Although others have argued that the BFRT cannot be regarded as a good test of the perceptual abilities involved in face recognition, her performance on this test is impaired and may indicate a face perceptual defect other than those that we have probed. Because the BFRT contains distractor faces from different individuals, it cannot control for the manner in which face stimuli differ from each other, which will include both spatial relations and features. Nevertheless, the posterior lesions of Patients 2, 3, 4, and 5 are at least associated with a more profound face perceptual disturbance than the anterior lesions of Patient 1: a similar poor correlation between BFRT performance and other measures of face perception has been noted by others. Our findings indicate that, regardless of the BFRT score, lesions of the fusiform face area in patients with prosopagnosia are associated with deficient perception of the spatial arrangement of features, an impairment that may have a causal role in their socially disabling recognition defect.

Acknowledgment
The authors thank Dr. A. Pascual-Leone for referring Patient 1 and Drs. B. Dworetzky and A. diBernardo for referring Patient 2. The authors also thank T. Bass and M. Cherkasova for assistance with data collection.

References
2. de Renzi E. Prosopagnosia in two patients with CT scan evidence of damage confined to the right hemisphere. Neuropsychologia 1986;24:385–389.


