

Emotional attention in acquired prosopagnosia

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The present study investigated whether emotionally expressive faces guide attention and modulate fMRI activity in fusiform gyrus in acquired prosopagnosia. Patient PS, a pure case of acquired prosopagnosia with intact right middle fusiform gyrus, performed two behavioral experiments and a functional imaging experiment to address these questions. In a visual search task involving face stimuli, PS was faster to select the target face when it was expressing fear or happiness as compared to when it was emotionally neutral. In a change detection task, PS detected significantly more changes when the changed face was fearful as compared to when it was neutral. Finally, an fMRI experiment showed enhanced activation to emotionally expressive faces and bodies in right fusiform gyrus. In addition, PS showed normal body-selective activation in right fusiform gyrus, partially overlapping the fusiform face area. Together these behavioral and neuroimaging results show that attention was preferentially allocated to emotional faces in patient PS, as observed in healthy subjects. We conclude that systems involved in the emotional guidance of attention by facial expression can function normally in acquired prosopagnosia, and can thus be dissociated from systems involved in face identification.

Keywords: prosopagnosia; emotion; face processing; FFA; FBA; attentional capture

INTRODUCTION

Prosopagnosia is the inability to recognize the identity of faces. Pure cases of prosopagnosia, where other forms of object recognition remain intact, are rare but several cases have been documented over the last few decades (Grusser and Landis, 1991; Farah, 2004). A distinction can be made between acquired prosopagnosia and developmental prosopagnosia. In the former, prosopagnosia results from lesions to the brain, such as stroke or traumatic head injury. In contrast, individuals with developmental prosopagnosia have no clear signs of neurological damage, but can have similar deficits in face processing (Duchaine and Nakayama, 2006). The occurrence of face-selective processing deficits is of great theoretical interest, as it provides evidence for the existence of face-selective mechanisms in the human brain. Uncovering which particular aspects of face processing are impaired in prosopagnosia can inform us on the functional role of these neural mechanisms, and, more generally, on how faces and objects are recognized.

In the present study, we investigated whether emotional faces are preferentially attended and modulate fMRI activity in visual cortex in patient PS, a pure case of acquired prosopagnosia (Rossion *et al.*, 2003). Patient PS has been studied extensively, and shown to be severely impaired in recognizing face identities (Rossion *et al.*, 2003). As a result of traumatic head injury, PS has lesions in the left mid-ventral and right inferior occipital cortex. Interestingly,

her right fusiform gyrus corresponding to the location of the face-selective area appears anatomically intact, and shows normal face-specific activation in fMRI (Rossion *et al.*, 2003; Schiltz *et al.*, 2006; Sorger *et al.*, 2007), whereas the right occipital face area (OFA) and left fusiform gyrus are lesioned. It has been suggested that PS's lesion in rOFA may have been critical in causing her dense prosopagnosia (Rossion *et al.*, 2003; Sorger *et al.*, 2007), in line with a recent meta-analysis investigating overlap between lesions of several prosopagnosics (Bouvier and Engel, 2006).

In healthy humans, faces expressing emotions (e.g. fear or happiness) have been shown to attract visual attention in a reflexive, bottom-up fashion. For example, in a visual search task, detection times are shorter for emotionally expressive faces compared to emotionally neutral faces, even when expression is not relevant to the task (Eastwood *et al.*, 2001). This effect is not seen when the stimuli are inverted, or when the same features are arranged in a different configuration, indicating that these effects cannot be explained by low-level differences between the stimuli (Eastwood *et al.*, 2001). Other experiments, using a variety of attentional paradigms, have similarly shown that emotional faces are preferentially attended relative to neutral faces (for a review, see Vuilleumier, 2005). Although dissociations between explicit expression and identity recognition have been reported in neuropsychological literature (e.g. Bruyer *et al.*, 1983; Tranel *et al.*, 1988), it is unknown whether emotion interacts normally with attention when identity recognition is impaired. Closely related to this, it is unknown whether emotional faces modulate visual cortical activation in acquired prosopagnosic patients.

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In the first behavioral experiment, a visual search task, PS was required to decide on the gender of a target face presented among an array of distracter faces. This target face could differ from the distracters either by identity alone, by identity and color, or by identity and emotional expression (fearful or happy). If PS's attention is drawn preferentially to emotional faces, as typically observed in healthy adults, we would expect shorter response times in this latter condition (Lucas and Vuilleumier, 2008). A second behavioral experiment used a change detection task (Ro *et al.*, 2001), involving, on each trial, a house and a face stimulus. PS was required to detect possible changes occurring on either or both stimuli. We asked whether change detection performance for the face stimulus would improve when the face was emotional (fearful) as compared to neutral, as typically observed in healthy adults.

A proposed neural basis for the behavioral effects described above is through the modulation of activity within face-selective regions of visual cortex (Vuilleumier, 2005). Recent neuroimaging research on emotional face perception has provided convincing evidence for enhanced activation of face-selective visual areas such as the fusiform face area in response to faces expressing emotions (Vuilleumier *et al.*, 2001; Pessoa *et al.*, 2002; Winston *et al.*, 2003). This enhanced activation is thought to reflect direct modulatory influences from the amygdala, allowing a prioritization of visual processing for emotionally salient events (Vuilleumier *et al.*, 2004; Vuilleumier, 2005). Here we tested whether emotionally expressive faces would similarly modulate face-selective fusiform gyrus in acquired prosopagnosia. We presented short movie clips of emotional and neutral faces to test whether emotional modulation can be observed in ventral visual areas, as typically observed in healthy subjects (Morris *et al.*, 1998; Vuilleumier *et al.*, 2001; Pessoa *et al.*, 2002; Winston *et al.*, 2003).

Finally, in addition to the face conditions, the fMRI experiment also included movie clips of body movements, allowing for an investigation of neutral and emotional body processing in this patient. This is of interest because, in healthy subjects, body-related activity partly overlaps face-related activity (Peelen and Downing, 2005a, 2007), and emotional body expressions also modulate fusiform responses to bodies (Peelen *et al.*, 2007). Moreover, it is unknown whether any response to emotional face expressions in prosopagnosia would dissociate from emotional body processing.

METHODS

Patient history

PS, a right-handed woman born in 1950, became prosopagnosic after a closed head injury in 1992. Her behavioral deficits are restricted to face recognition, and are described in detail in Rossion *et al.* (2003). She is highly impaired in face recognition, as reflected by her failures in matching face identity across views in the Benton Face Recognition Test

Table 1 Summary of visual functions of patient PS

Acuity	0.7
Contrast sensitivity (Nicolet)	OK
Color perception (Ishihara)	12/17 (lower range)
Benton line orientation	57/60 (normal)
Birmingham Object Recognition Battery	
Object copying	OK
Line length	OK
Size	OK
Orientation	OK
Gap position	OK
Overlapping shapes	OK
Minimal feature match	OK
Foreshortened views	OK
Object drawings	OK
Object decision task	OK
Item match (class recognition)	OK
Semantic association	OK
Object naming	OK
Short-term visual memory	OK
Long-term visual memory	OK
Benton face recognition test	27/54 (strongly impaired)
Warrington face recognition battery	18/25 (impaired)
Reading	Slow but accurate
Reaction time (phasic alert)	Slow

Source: Table adapted from Rossion *et al.* (2003).

(total score: 27/54; Benton and Van Allen, 1972), whereas she has no difficulty in recognizing objects, even at a subordinate level (Rossion *et al.*, 2003). See Table 1 for a summary of results from standard clinical and neuropsychological tests. PS can recognize the gender, age and expression of faces, although not as fast and accurately as normal controls (Rossion *et al.*, 2003). Anatomical MRI scans revealed lesions of the left mid-ventral and right inferior occipital cortex. Interestingly, she shows normal face-selective activation in a region of the right mid-fusiform gyrus, at the typical location of the fusiform face area. Her lesions have recently been characterized in relation to a variety of functionally defined visual areas (Sorger *et al.*, 2007), and are centered on left fusiform and right inferior occipital gyri.

Experiment 1: visual search task

Normal control subjects. A group of 12 healthy controls was tested (mean age = 44, range = 29–78 years old, seven females). The performance of PS was compared to the performance of normal controls using modified *t*-tests that take the sample size of the control group into account (Crawford and Howell, 1998).

Stimuli, design and procedure. Sixteen different face identities (eight women and eight men) were selected from the Karolinska Directed Emotional Faces dataset (KDEF; Lundqvist *et al.*, 1998), which could serve as either targets or distracters in different trials. These pictures were carefully normalized in terms of luminance, size and feature-position (eye–mouth; Lundqvist *et al.*, 1998).

Each trial started with a white central fixation cross on black background, shown for 800 ms. Next followed a search array, where eight faces were arranged in an imaginary circle around a central fixation cross. The target always differed from the seven identical neutral-grey distracters by identity. Critically, this target face could differ from the other seven distracter faces by either identity alone (Neutral), identity + emotional expression (Fearful or Happy), or identity + color (Red). Target type and target position were randomly varied across trials. The task was to report the gender of the face singleton as quickly as possible. The next trial started 1500 ms after the response was made. The same simplified visual search task has previously been found to provide a reliable test for assessing attentional biases in both healthy and brain-damaged subjects (Lucas and Vuilleumier, 2008). Both normal subjects and PS performed two runs of 64 trials each. Only correct trials and trials with reaction times within two standard deviations of the conditional means were included in the analysis.

Because attention might also be driven by low-level differences in face pictures, we calculated the inter-stimulus similarity between target and distracter pictures. The amount of low-level pictorial similarity between different faces was computed using pixelwise correlation methods (e.g. Lucas and Vuilleumier, 2008). These correlations provide a quantitative measure of overlap among pictures at the pixel-by-pixel level. The mean pictorial similarity between pictures with different emotions (but same identity) was 0.85, whereas the mean pictorial similarity between pictures with different identity (but same emotion) was 0.56. This indicates that any low-level differences due to emotional facial expression were minor as compared with the variation engendered by identity differences, which were present in all experimental conditions. Furthermore, the mean pixel-wise correlation for two neutral faces with different identity was 0.60 (s.d.=0.15), whereas the mean correlation was 0.55 (s.d.=0.17) between a fearful face and a neutral face with different identity, and 0.55 (s.d.=0.16) between a happy face and a neutral face with different identity. Thus, the mean pictorial similarity was comparable in the different experimental conditions and the distributions of these similarity values mostly overlapped. These results thus confirm that face pictures were well matched and that low-level differences were unlikely to produce any major influences on performance. In other words, if visual search in patient PS was mainly guided by pixelwise differences, we would predict detection speed to be relatively similar in all conditions. This was clearly not the case (see Results section).

Experiment 2: change detection task

Normal control subjects. A group of 15 healthy controls was tested (mean age = 40, range = 25–65 years old, seven females). The performance of PS was compared to the performance of normal controls using modified *t*-tests that

take the sample size of the control group into account (Crawford and Howell, 1998).

Stimuli, design and procedure. We used grey-scale photographs of faces and houses. Face stimuli (10 different identities, four male) were taken from the Ekman set (Ekman and Friesen, 1976). Each of these faces was presented with either a neutral or fearful expression. The house stimuli (10 different houses) consisted of front view photographs of detached houses.

The task was adapted from previous change blindness experiments in healthy subjects (Beck *et al.*, 2001; Pourtois *et al.*, 2006a). Each trial started with a fixation cross for 750 ms, followed by the brief (250 ms) presentation of two images, one to the left and one to the right of the central fixation cross. One of these images was always a house, and the other a fearful or neutral face. After a short gap (250 ms), two images (again a face and a house) were presented for 250 ms at the same locations as the first presentation. The location (left, right) of each category (House, Neutral face, Fearful face) was the same for the first and second presentation, such that if a fearful face was presented to the left of fixation on the first presentation, a fearful face would also be presented to the left of fixation on the second presentation. The identity of these images could change from first to second presentation, and the task was to detect whether the left image (25% of trials), the right image (25%), both (25%), or none (25%) had changed from first to second presentation. The task was self-paced, and accuracy (not speed) was emphasized. Normal subjects performed two runs of the task, while PS performed five runs over two sessions (three runs in session 1, two runs in session 2). Each run consisted of 80 trials. Only trials where one of the two images changed were included in the analysis (PS never correctly detected both changes).

Experiment 3: fMRI responses to emotional faces and bodies

The fMRI experiment was conducted in PS only. No control subjects were included but we refer the reader to previous studies that used identical (Peelen *et al.*, 2007) or similar conditions in healthy participants (Morris *et al.*, 1998; Vuilleumier *et al.*, 2001; Pessoa *et al.*, 2002; Hadjikhani and de Gelder, 2003; Winston *et al.*, 2003). These studies all showed highly reliable emotional modulation of activity in fusiform gyrus in response to either face or body stimuli. *Stimuli, design and procedure.* (i) Emotion experiment: We presented short (3 s) movie clips of faces and bodies (with faces obscured), expressing five basic emotions (anger, disgust, fear, happiness, and sadness) and emotionally neutral movements. For each condition (Anger, Disgust, Fear, Happiness, Neutral, Sadness), six movies performed by four actors (two male, two female) were shown. Face movies were taken from the stimulus set created and validated by Banse and Scherer (1996). Body movies were taken from the set created and validated by Atkinson and colleagues

(Atkinson *et al.*, 2004, 2007). We chose to present dynamic stimuli as these may show greater emotion-related responses than static stimuli (LaBar *et al.*, 2003).

PS performed three runs of the emotion experiment. Each run started and ended with a 10 s fixation period. Within each run, 48 trials of 8.5 s were presented in four blocks of 12 trials. These blocks were separated by 5 s fixation periods. The two blocks differed in the type of stimuli presented (body movies, face movies). The order of the blocks was counterbalanced across runs. Within each block, two different movies (of different actors) of each of the six emotion conditions (Anger, Disgust, Fear, Happiness, Neutral and Sadness) were presented. Trials were presented in random order. Each run lasted approximately 448 s.

Each trial started with a 2 s fixation cross, followed by a 3 s movie clip, a 1 s blank screen, and a 2.5 s response window. The task was to rate the emotion expressed in the movie on a 3-point scale. For example, for Anger, the response was cued by the following text display: “Angry? 1—a little, 2—quite, 3—very much”, where “1”, “2”, “3” referred to 3 response buttons (from left to right) held in the right hand. For a comparable task in the Neutral condition, we asked how “lively” the movie was (1—a little, 2—quite, 3—very much).

The average rating of the five emotions expressed by faces was 1.4, which corresponds to a judgment of expressivity between “a little” and “quite”, while ratings of the liveliness of Neutral faces was 2.2. Likewise, the average rating of the five emotions expressed by bodies was 1.4, also corresponding to a judgment of expressivity between “a little” and “quite”, while the liveliness of Neutral bodies were rated 1.4. These results suggest that PS generally perceived emotional expressions from both faces and bodies.

(ii) Localizer experiment: PS was also scanned on two runs of an experiment previously shown to reliably localize face- and body-selective areas in visual cortex (Peelen and Downing, 2005a, 2005b). Each run consisted of 21 15 s blocks. Of these 21 blocks, five were fixation-only baseline conditions, occurring on blocks 1, 6, 11, 16 and 21. The other 16 blocks consisted of pictures of faces, headless bodies, tools, or scenes. Forty full-color exemplars of each category were tested. Each image was presented for 300 ms, followed by a blank screen for 450 ms. Twice during each block, the same image was repeated in immediate succession. The task was to detect these immediate repetitions by button press (1-back task). The position of the image was jittered slightly on alternate presentations, in order to disrupt attempts to perform the 1-back task using low-level visual transients. Two different versions were used, counterbalancing for the order of stimulus category. In both versions, assignment of category to block was counterbalanced, so that the mean serial position in the scan of each condition was equated.

Data acquisition. Scanning was performed on a 3T Siemens Trio Tim MRI scanner at Geneva University

Hospital, Center for Bio-Medical Imaging. For functional imaging, a single shot EPI sequence was used (T_2^* -weighted, gradient echo sequence). Scanning parameters were: TR = 2490 ms, TE = 30 ms, 36 off-axial slices, voxel dimensions: 1.8×1.8 mm, 3.6 mm slice thickness (no gap). Anatomical images were acquired using a T_1 -weighted sequence. Scanning parameters were: TR/TE: 2200 ms/3.45 ms; slice thickness = 1 mm; in-plane resolution: 1×1 mm.

Pre-processing. Pre-processing and statistical analysis of MRI data was performed using BrainVoyager QX (Brain Innovation, Maastricht, The Netherlands). Functional data were motion corrected, slice-time corrected, spatially smoothed with a Gaussian kernel (4 mm FWHM), and low-frequency drifts were removed with a temporal high-pass filter (cut-off 0.006 Hz). Functional data were manually co-registered with a 3D anatomical T_1 scan ($1 \times 1 \times 1$ mm³ resolution). The 3D anatomical scan was transformed into Talairach space, and the parameters from this transformation were subsequently applied to the co-registered functional data.

ROI analyses. The right fusiform face area (FFA; Kanwisher *et al.*, 1997) was defined by contrasting activation during face blocks with the average activation during blocks of scenes and tools from the localizer experiment. Likewise, the right fusiform body area (FBA; Peelen and Downing, 2005a) and bilateral extrastriate body area (EBA; Downing *et al.*, 2001) were defined by contrasting activation during body blocks vs blocks with scenes and tools. For both fusiform ROIs, the most significantly activated voxel in the fusiform gyrus was first identified. Each ROI was then defined as the set of contiguous voxels that were significantly activated ($P < 0.0001$, uncorrected) within a 10 mm cube surrounding (and including) the peak voxel. Within these ROIs a further general linear model was then applied, modeling the response of the voxels in the ROI (in aggregate) to the conditions of the emotion experiment.

Bilateral amygdala ROIs were also defined to measure responses in this region to different conditions in the main experiment. Because direct contrasts between emotion and neutral stimuli did not show reliable activation at conventional thresholds, we defined *a priori* ROIs as a $3 \times 3 \times 3$ mm³ around previously published coordinates for both sides (left amygdala: -18, -5, -9; right amygdala: 21, -5, -9; e.g. Pessoa *et al.*, 2002; Peelen *et al.*, 2007).

Whole-brain analyses. Whole-brain analyses were conducted on data from the main experiment. Events were defined as the 4 s period between onset of the movie and onset of the response window. These events were convolved with a standard model of the HRF (Boynton *et al.*, 1996). A general linear model was created with one predictor for each condition of interest. Regressors of no interest were also included to account for differences in the mean MR signal across scans. Regressors were fitted to the MR time-series in each voxel and the resulting beta parameter estimates

were used to estimate the magnitude of response to the experimental conditions.

RESULTS

Experiment 1: Visual search task

Results of normal controls. Figure 1 gives mean reaction times and percent correct for the four target conditions (Fearful, Happy, Neutral, Red). Detection of target faces was highly accurate (mean 96.4% correct), without a significant difference between the four conditions [$F(3, 33) = 0.45$, $P = 0.72$].

The latency of correct detections was strongly modulated by the target type [$F(1, 33) = 40.7$, $P < 0.001$]. As shown in Figure 1, search was faster for fearful faces [mean 1743 ms, 95% confidence interval (CI) = 1465–2022; $t = 3.45$, $P < 0.005$] and faster for happy faces (mean 1722 ms, CI = 1414–2029; $t = 3.57$, $P < 0.005$) relative to neutral faces (mean 1968 ms, CI = 1630–2305), and also faster for red-colored faces (mean 1273 ms, CI = 1073–1473) relative to both emotional and neutral faces (both t values > 7.6 , P -values < 0.001).

Results of PS. PS correctly reported the gender of the face target on 90.3% of the trials across all conditions (Figure 1), indicating that she was able to discriminate a single face among others with a different identity (same/different judgment, see Rossion *et al.*, 2003), even though she was much slower than normal controls (see below).

There was no significant effect of target condition on percent correct ($\chi^2 = 0.26$, $P = 1$).

The latencies for correct responses varied significantly between conditions. A Kruskal–Wallis test on reaction times showed a highly significant effect of Condition ($H = 57.5$, $P < 0.001$). PS was particularly slow for neutral trials, on which the target face differed from the distracter faces only by identity (mean 9317 ms). Similar to normal controls, PS's performance improved dramatically when the target face was uniquely colored red (2606 ms, $P < 0.05$). Importantly, PS's performance also improved when the target face was emotional (Happy = 3279 ms, Fearful = 4455 ms), with both emotions being significantly different from Neutral ($P < 0.05$, for both tests). Furthermore, there was a significant difference between Fearful and Red ($P < 0.05$), but no significant differences between Happy and Red or between Fearful and Happy.

Comparison between results of PS and normal controls. PS was significantly slower than normal controls for all conditions ($P < 0.001$, for all tests). This difference was expected given that the target face was always defined by a different identity relative to the distracter faces, information that is not readily available to PS because of her prosopagnosia. To take into account this general slowing across all conditions, we then also computed a ratio of relative facilitation by emotion and color compared to the Neutral condition (e.g. $[RT_{Neutral} - RT_{Happy}] / RT_{Neutral}$).

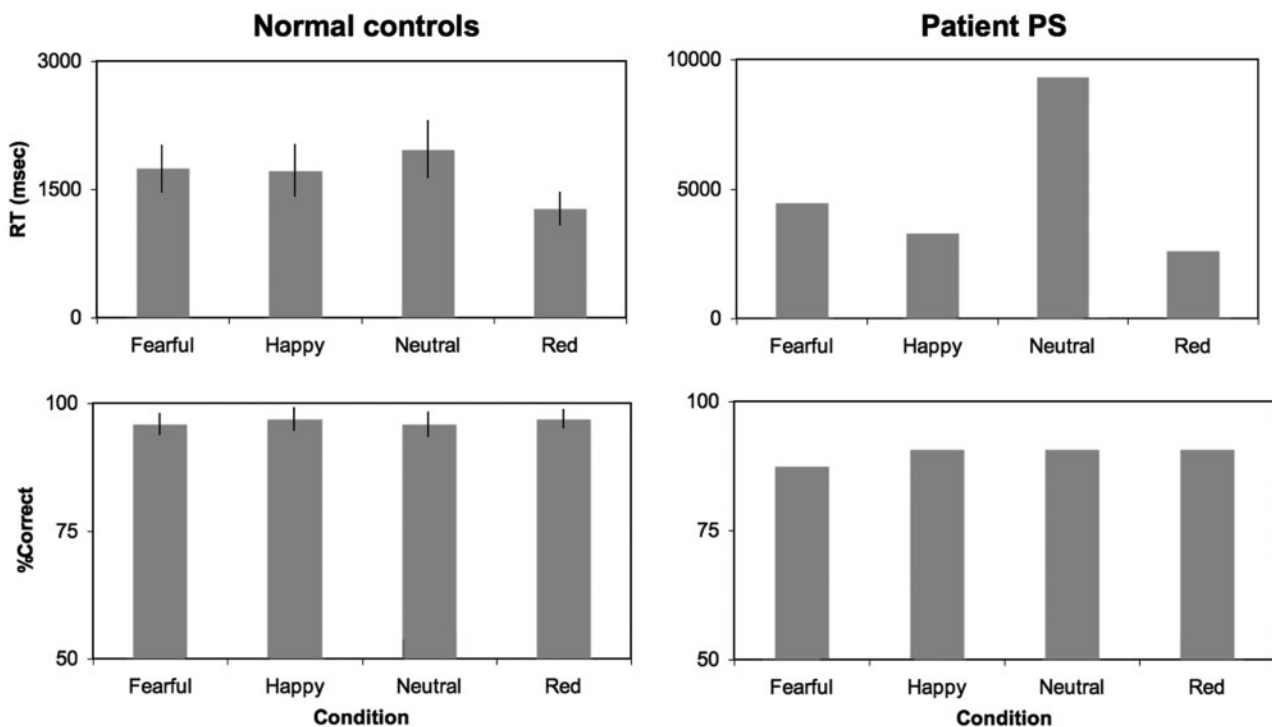


Fig. 1 Mean reaction times and percent correct for the four target conditions (Fearful, Happy, Neutral, Red) in the visual search task. The left panels show the results for normal controls, and the right panels show the results for patient PS. Search was significantly faster (top panels) for red-colored and emotional faces compared with neutral faces, for both normal controls and patient PS. There were no significant differences in accuracy (bottom panels). Error bars indicate 95% confidence intervals.

This analysis revealed that PS showed a stronger relative facilitation than normal controls for Happy (ratio PS: 0.65, vs mean from normals: 0.12; $P < 0.001$), Fearful (PS: 0.52, normals: 0.11; $P < 0.001$), and Red (PS: 0.72, normals: 0.35; $P < 0.001$). This indicates that emotional and color cues were relatively more beneficial for PS in finding the target face than they were for normal controls, which likely reflects the difficulty of PS in finding the target when it differs from distracters by identity alone (i.e. the Neutral condition). Importantly, these facilitation ratios show again that, despite her severe face recognition deficits, PS's search performance was still strongly influenced by emotional cues, and (at least in the current experimental design) even more so than for normal controls.

Experiment 2: change detection task

Results of normal controls. Figure 2 gives the percentage of detected changes for Fearful faces, Neutral faces, and Houses. Detection of changes was generally higher for faces (mean 71.7% correct) than houses [45.3% correct, 95% CI = 37.6–53.1; $F(1, 14) = 26.3$, $P < 0.001$]. In addition, correct detection rates were significantly higher for fearful (74.3%, CI = 66.1–82.5) than neutral faces [69.0%, CI = 60.1–77.9; $F(1, 14) = 5.98$, $P < 0.05$]. This pattern shows a systematic detection advantage for faces over houses, as well as for emotional faces over neutral faces.

Results of PS. As shown in Figure 2, the percentage of detected changes was generally much lower for faces in PS (27%) as compared with normals (72%), but comparable for houses (PS: 52%; normals: 45.3%). A chi-square test on the total number of detections (across all runs in the two sessions) revealed a significant difference between the three change conditions ($\chi^2 = 18.1$, $P < 0.001$). Unlike in normal controls, changes occurring on the houses were detected significantly more often (52%) than changes on neutral faces (16%; $\chi^2 = 18.0$, $P < 0.001$). There was no difference in detection rate between houses and fearful faces (38%; $\chi^2 = 2.6$, $P = 0.2$). Importantly, and similar to normal controls, changes occurring on fearful faces were detected more

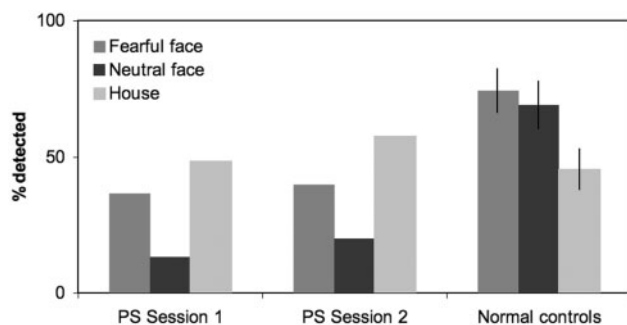


Fig. 2 Percent detected changes in the change detection task for two testing sessions of patient PS and normal controls. Both normal controls and patient PS detected significantly more changes on fearful faces than neutral faces. Error bars indicate 95% confidence intervals.

often (38%) than changes on neutral faces (16%; $\chi^2 = 6.1$, $P < 0.05$), suggesting that attention was drawn more efficiently to the faces when they were fearful.

Here again, the results suggest that emotional expression could facilitate detection of face changes, despite prosopagnosia. By contrast, changes of neutral faces were poorly detected and actually yielded worse performance than the detection of changes in houses.

Comparison between results of PS and normal controls. PS was significantly less accurate than normal controls in detecting changes on fearful and neutral faces ($P < 0.001$, for both tests). By contrast, PS did not differ from normal controls in detecting changes on house stimuli ($P > 0.1$). This result again confirms PS's impairment in performing tasks involving face identity judgments. When comparing the ratio of relative facilitation by fearful faces relative to neutral faces [(Fearful – Neutral)/Neutral], PS showed stronger effects than normal controls (ratio PS: 1.38, normal: 0.08; $P < 0.001$). This marked difference in ratio was driven by the low performance of PS for neutral faces, and clearly indicates that PS's detection rates were still strongly facilitated by fearful expressions.

It should be noted that the large overall difference between normal controls and PS in the ability to detect changes on the face stimuli makes a direct comparison of the magnitude of these emotional facilitation effects somewhat difficult. For example, it could be that normal controls were already close to their optimal performance in the neutral condition, and therefore had less possibility for facilitation by fearful expressions than PS. Nevertheless, the most critical point here concerns the residual advantage for emotional over neutral faces in PS, despite a loss of a general advantage for faces over houses. Moreover, PS's performance for houses was similar to the performance of normal subjects, indicating that her pattern could not be accounted for by more global difficulty factors.

Experiment 3: fMRI responses to emotional faces and bodies in patient PS

Localizer experiment. In the localizer task, PS showed reliable activation of category-selective visual regions. When contrasting responses to images of faces with images of scenes and tools, we observed significant activation in the right fusiform gyrus, at the typical location of the rFFA (Talairach coordinates of peak: $x = 36$, $y = -52$, $z = -20$; $t = 10.2$; Figure 3a), confirming a previous report on this patient (Rossion *et al.*, 2003).

When contrasting images of headless bodies with images of scenes and tools, we also found strong activation in the fusiform gyrus, adjacent to the rFFA (Talairach coordinates of peak: $x = 42$, $y = -49$, $z = -20$; $t = 6.6$; Figure 3a). The latter body-selective activation abutting (and partly overlapping) the rFFA is consistent with similar effects observed in normal subjects, and corresponds to the previously identified fusiform body area (FBA; Peelen and Downing, 2005a).

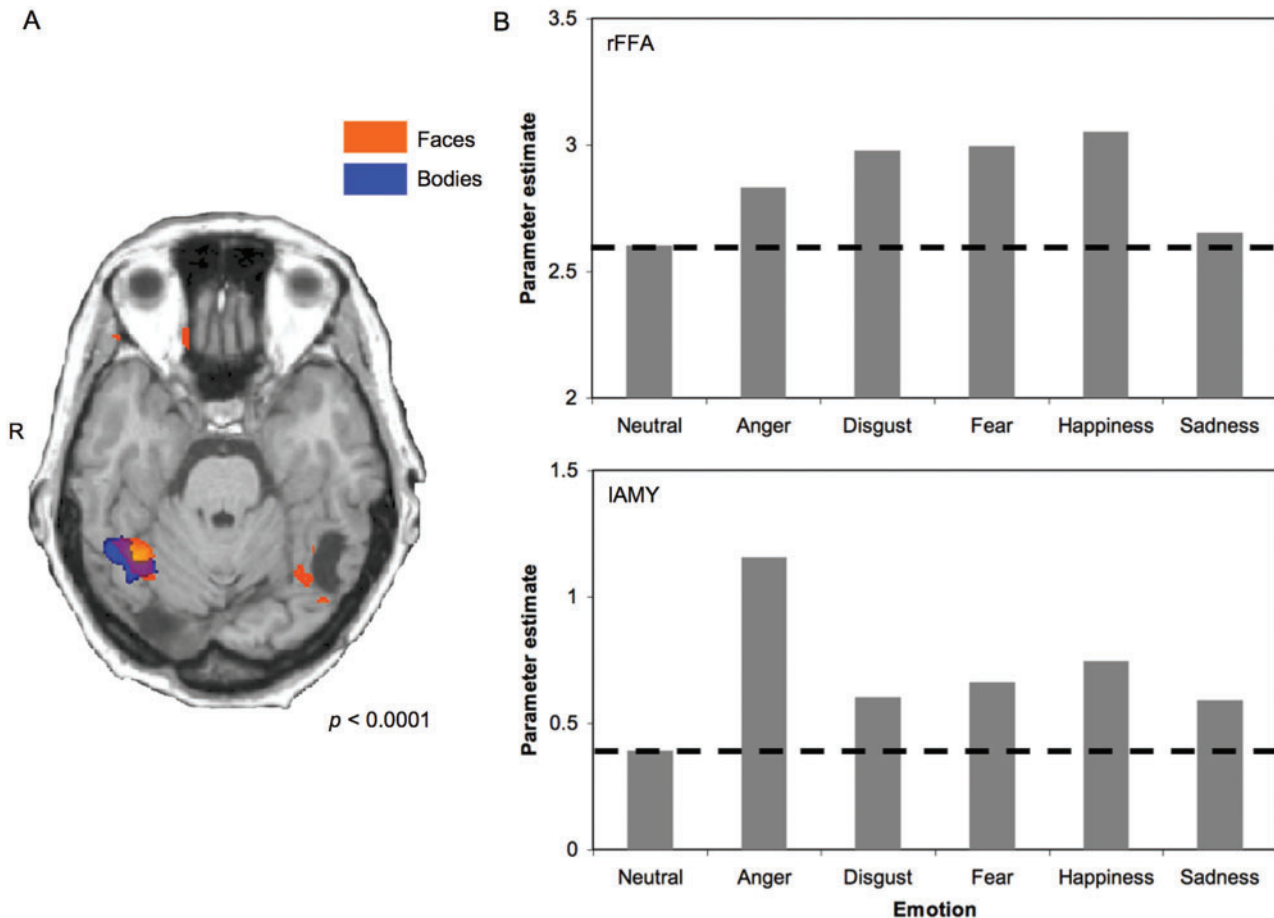


Fig. 3 (A) Face- and body-selective activations in the localizer experiment ($z = -22$), at $P < 0.0001$ (uncorrected). Both faces (orange) and bodies (blue) strongly activated right fusiform gyrus, relative to tools and scenes. These face- and body-selective activations correspond to areas rFFA and rFBA, respectively. (B) The top panel shows activation in rFFA (as defined by the localizer) for emotional and neutral faces. The dashed line indicates the activation level of neutral faces. The bottom panel shows activation in left amygdala (anatomically defined) for emotional and neutral faces. The dashed line indicates the activation level of neutral faces.

Strong body-selective activation was also observed at the location of the extrastriate body area (Downing *et al.*, 2001). Left EBA: $x = 48$, $y = -67$, $z = -8$, $t = 12.7$; right EBA: $x = -39$, $y = -76$, $z = 7$; $t = 10.6$.

Emotion experiment. In the whole-brain analysis, contrasting all emotional faces (averaged across the different emotions) with neutral faces showed significant ($P < 0.0005$, uncorrected) activation in right premotor cortex ($x = 42$, $y = -19$, $z = 40$; $t = 3.8$), left anterior temporal lobe ($x = -42$, $y = 17$, $z = -23$; $t = 3.7$), and right cerebellum ($x = 30$, $y = -58$, $z = -38$; $t = 3.8$). At slightly lower threshold ($P < 0.005$, uncorrected), this contrast also activated right fusiform gyrus at the location of the rFFA ($x = 36$, $y = -52$, $z = -26$; $t = 2.9$).

To test whether this latter activation cluster overlapped with the rFFA as functionally defined, parameter estimates for different stimulus conditions in the localizer were extracted from the same voxels. The cluster was indeed significantly face-selective. Faces ($\beta = 1.3$) gave significantly more activation than Bodies ($\beta = 0.8$, $P < 0.005$), Scenes ($\beta = 0.7$, $P < 0.0005$), and Tools ($\beta = 0.8$, $P < 0.005$) in this

cluster. Figure 3b shows the response to all emotion categories in the rFFA. Emotional increases in rFFA were comparable to previous reports [e.g. fear increased responses by about 15% relative to neutral faces, which is similar to results in healthy adults (Vuilleumier *et al.*, 2001)].

Finally, we performed an ROI analysis for bilateral amygdalae (anatomically defined, see Methods section). Results showed that the left amygdala response was higher for all emotional face conditions (average $\beta = 0.8$) than the neutral condition ($\beta = 0.4$; Figure 3b), although these differences did not reach significance ($P > 0.05$, for all tests). Activation in right amygdala was similar for emotional (average $\beta = 0.5$) and neutral face conditions ($\beta = 0.6$).

Contrasting emotional bodies (averaged across the different emotions) with neutral bodies gave significant ($P < 0.0005$, uncorrected) activation in right premotor cortex ($x = 45$, $y = -22$, $z = 37$; $t = 4.5$), right anterior temporal lobe ($x = 39$, $y = 17$, $z = -29$; $t = 4.5$), left orbitofrontal cortex ($x = -9$, $y = 57$, $z = -14$; $t = 3.5$), and right fusiform gyrus close to the rFBA ($x = 42$, $y = -37$, $z = -26$; $t = 3.8$). Emotional bodies modulated activity in functionally defined

rFBA, with stronger responses to the emotional body conditions (average $\beta=3.0$) relative to the neutral body conditions ($\beta=2.8$), although these differences did not reach significance ($P>0.05$, for all tests). No emotional modulation for bodies was found in EBA or amygdala.

DISCUSSION

The present results show that, similar to healthy adults, emotional expression can guide visual attention to faces and modulate fMRI activity in right fusiform gyrus in a rare patient with acquired prosopagnosia. Our findings provide evidence for a distinction between brain systems responsible for attentional orienting to facial expressions and brain systems underlying face identification.

In our first behavioral experiment, the visual search task, PS's performance improved dramatically when the target face was emotional. For happy faces this improvement was of the same magnitude as when the target face was colored in red. Note that the target stimulus was a different face than the distracter faces in all conditions, such that there were few additional low-level differences between target and distracters in the emotion conditions. These data are consistent with previous studies on visual search in healthy subjects, showing facilitation for the detection of emotional faces in a crowd of neutral faces (Eastwood *et al.*, 2001; Fox, 2002). However, our new data also go beyond these results by showing for the first time that such effects are preserved despite the severe impairment in face recognition mechanisms leading to prosopagnosia.

A previous study, using the exact same search task, found normal attention orienting to emotional faces in the contralesional hemifield of neglect patients (Lucas and Vuilleumier, 2008). Neglect patients have difficulty orienting attention voluntarily to contralesional space, but several studies have shown that their attention can still be captured by emotional stimuli, including emotional faces (Vuilleumier and Schwartz, 2001; Fox, 2002). These studies therefore provide converging evidence for a dissociation of attentional orienting based on top-down, voluntary attention (mediated by cortical fronto-parietal systems) and more reflexive, involuntary orienting driven by emotional stimuli (presumably mediated by distinct emotion-specific systems). Our results of a strong emotional advantage during face search in prosopagnosia suggest that the brain systems mediating these effects are also distinct from those responsible for face identification.

Results from the change detection task provide further evidence for this hypothesis. Similar to the visual search task, PS showed a marked facilitation in change detection performance when the changes occurred on emotional (fearful) faces as compared with neutral faces. Changes in both the emotional and the neutral condition consisted of changes in the identity of the face. As PS is severely impaired at discerning face identity, it was not surprising that her performance was better for the house than the face stimuli,

which is different from normal controls, who were more sensitive to changes occurring on face stimuli than on other categories (Mack and Rock, 1998; Ro *et al.*, 2001). Although it might seem somewhat surprising that she was able to detect changes in face identity at all, given her dense prosopagnosia, it is likely that she performed the change detection task by relying on differences in local features rather than a higher-level representation of facial identity (Rossion *et al.*, 2003; Caldara *et al.*, 2005). Note, however, that the changes in local features between the two presentations within a trial were comparable for the emotional and the neutral condition, as emotion was held constant between the two successive images. Therefore, we suggest that the improvement in change detection for emotional faces was due to a facilitation of attention towards these stimuli due to their emotional significance. When the two stimuli (a face and a house) are presented simultaneously, they competed for attention; but if the emotional face was more efficient than the neutral face in attracting attention, this would then lead to increased sensitivity to a subsequent change of the stimulus, and thus promote detection rates.

Such attentional benefits produced by emotional faces are in accordance with studies finding increased sensitivity for detecting low-contrast stimuli following valid emotional cues (Phelps *et al.*, 2006), as well as increased occipital responses in evoked potentials (Pourtois *et al.*, 2004) and fMRI studies (Pourtois *et al.*, 2006b) of spatial orienting to emotional stimuli. Finally, an increase in attention to fearful faces may have not only enhanced the detection of local changes, but may have also increased configural processing, thereby facilitating face identification more directly (de Gelder *et al.*, 2003).

Taken together, our behavioral results indicate that the ability to identify faces is not critical for orienting to emotionally expressive faces. Thus, the brain mechanisms of these two processes must, at least in part, be distinct. Furthermore, we can conclude from the present data that the lesioned brain areas in PS, namely the IFFA and rOFA, are not critically involved in emotional attentional orienting (while conversely they presumably play a pivotal role in face identification pathways, see Rossion *et al.*, 2003). Previous studies of emotion processing have implicated the amygdala as a possible source for enhanced visual perception of emotionally salient events, by showing that intact amygdalae are necessary for enhanced perception in attentional blink paradigms (Anderson and Phelps, 2001). Several imaging and lesion studies have also implicated the amygdala in such emotional modulation of activity in sensory cortical regions. For example, a PET imaging study showed that amygdala activation is correlated with modulation to emotional faces in right fusiform gyrus (Morris *et al.*, 1998), and a subsequent combined lesion/fMRI study provided direct evidence that the emotional modulation in FFA is dependent on intact amygdala, with no such visual enhancement in patients with damage to the amygdala

(Vuilleumier *et al.*, 2004). In line with this, neuroanatomical studies in monkeys have shown projections from amygdala neurons to discrete regions of visual cortex (Amaral *et al.*, 2003), and thus suggest a critical role for these projections in the emotional modulation of cortical areas. We therefore hypothesize that improved detection and discrimination of emotional faces, as observed in the present study, might be a result of increased activation in visual cortex, due to amygdala influences on visual cortex.

Accordingly, in the present study, we could demonstrate an increased activation in the right face-selective fusiform gyrus in PS. This increased activation may underlie the improvement in performance with these stimuli, although the present study alone does not provide direct evidence linking behavior and fMRI responses. This residual enhancement of rFFA to emotional faces in PS accords well with the consistent effects observed in healthy subjects in a wide range of imaging studies (for review, see Vuilleumier, 2005).

Despite increases in visual areas in response to emotional faces, no significant amygdala activation was found in PS in the whole-brain analysis. A subsequent ROI analysis revealed increased responses in left (but not right) amygdala to all emotional face conditions, although these increases did not reach statistical significance. This lack of significant amygdala response could be due to signal dropout related to differences in magnetic susceptibility in this region, which is a well-known problem in fMRI (Robinson *et al.*, 2004; Stocker *et al.*, 2006). It may also be due to a lack of power, as instead of having a group of subjects (as in previous studies showing amygdala activation) we could scan PS only on a few runs of the experiment.

In line with our fMRI study, another recent study tested brain responses to emotional and neutral faces and bodies in three developmental prosopagnosics and four normal controls (Van den Stock *et al.*, 2008). This study found that right fusiform activation to fearful faces was normal in developmental prosopagnosics, whereas there was a trend for activity to neutral faces to be reduced in the latter cases relative to normal controls (but see Avidan *et al.*, 2005). However, contrary to typical findings and our present results, none of the two groups showed a clear emotional modulation in right fusiform (if anything, activity in normal controls was higher for neutral than emotional faces). The absence of emotional modulation in normal controls in this study makes it difficult to draw strong conclusions regarding the emotional effects in developmental prosopagnosia, and their relation to the present findings in acquired prosopagnosia. Unlike PS, who had normal face recognition mechanisms until her lesion, individuals with developmental prosopagnosia might learn to process (and attend to) faces and expressions in a different manner than normals. To directly compare the two forms of prosopagnosia would require testing both types of patients on the same experimental paradigm (e.g. Barton *et al.*, 2001; Humphreys *et al.*, 2007).

Although this was not the main focus of the study, we also localized body-selective FBA to further investigate the functional organization of the intact right fusiform gyrus in PS. In healthy adults, this region partly overlaps the face-selective FFA (Peelen and Downing, 2005a). Like normals, PS showed strong activation in both rFFA and rFBA, with partial overlap of these two regions. Furthermore, fusiform cortex also showed a preserved modulation by emotional body expressions, as previously observed in normal subjects (Hadjikhani and de Gelder, 2003; Peelen *et al.*, 2007). Taken together, these findings suggest a normal functional organization of the right fusiform gyrus in PS, at least with respect to face and body selectivity, and with respect to increased responses to emotional stimuli. Of interest, however, a recent study reported that the rFFA of patient PS, despite showing normal absolute activation levels to face images, did not show adaptation to face identity (Schiltz *et al.*, 2006). Thus, contrary to normal controls, her rFFA response was equally strong for blocks of identical and distinct faces. Given that PS does not report difficulties in recognizing bodies, and no deficits in body identification were found in preliminary tests, future experiments could test whether PS shows normal adaptation to body identity in rFBA. Such a finding would provide further evidence for a normally functioning fusiform gyrus, and would thus support the claim that intact fusiform gyrus is not sufficient for face identification (Rossion *et al.*, 2003).

To conclude, we found an interaction of emotion and attention in a case of acquired prosopagnosia, with attention preferentially directed towards emotionally expressive faces. We also found emotional modulation in right fusiform gyrus, which may underlie the observed behavioral effects. Together these results suggest that mechanisms underlying the orienting towards facial expressions can operate without mechanisms involved in face identification.

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