Brain (2001), **124,** 1241–1252

Differential extrageniculostriate and amygdala responses to presentation of emotional faces in a cortically blind field

J. S. Morris,[1] B. DeGelder,[4] L.Weiskrantz[3] and R. J. Dolan[1,2]

[1]*Wellcome Department of Cognitive Neurology,* [2]*Royal Free and University College Hospitals School of Medicine, London,* [3]*Department of Experimental Psychology, University of Oxford, UK and* [4]*Cognitive Neuroscience Laboratory, Tilburg University, The Netherlands*

Correspondence to: R. J. Dolan, Wellcome Department of Cognitive Neurology, Queen Square, London WC1N BG, UK
E-mail: r.dolan@fil.ion.ucl.ac.uk

Summary

Patient G.Y. is able to discriminate emotional facial expressions presented in his blind (right) hemifield despite an extensive lesion of the corresponding (left) striate cortex. One proposal is that this residual ability (affective 'blindsight') depends on a subcortical visual pathway comprising the superior colliculus, posterior (extrageniculate) thalamus and amygdala. Here we report differential amygdala responses in G.Y. to presentation of fearful and fear-conditioned faces in his blind (right) hemifield. These amygdala responses exhibited condition-dependent covariation with neural activity in the posterior thalamus and superior colliculus. Our results provide further evidence that an extrageniculostriate (colliculo-thalamo-amygdala) neural pathway can process fear-related stimuli independently of both the striate cortex and normal phenomenal visual awareness.

Keywords: blindsight; consciousness; amygdala; fear; neuroimaging

Abbreviations: BOLD = blood oxygenation level dependent; CS = conditioned stimulus; fMRI = functional magnetic resonance imaging; SPM = statistical parametric map

Introduction

Damage to the human striate cortex (V1) produces blindness in the corresponding visual field (Holmes *et al.*, 1918). However, in appropriate experimental contexts some patients with striate cortex lesions demonstrate remarkable residual visual abilities ('blindsight'), e.g. accurately 'guessing' the location or identity of stimuli presented in their blind field (Weiskrantz *et al.*, 1974; Barbur *et al.*, 1980). Recent studies with G.Y., a blindsight patient with a long-standing right hemianopia (Fig. 1), indicate that he is able to discriminate (by guessing) different emotional facial expressions in his blind hemifield (de Gelder *et al.*, 1999). This residual ability in G.Y. is notable in that it parallels the ability of healthy subjects to discriminate backwardly masked ('unseen') emotional expressions by means of involuntary skin conductance changes and brain activations (Esteves *et al.*, 1994; Morris *et al.*, 1998*a*; Whalen *et al.*, 1998). Given that the superior colliculus is implicated in non-striatal visual function in both monkeys (Mohler *et al.*, 1977; Miller *et al.*, 1980; Rodman *et al.*, 1989) and humans (Sahraie *et al.*, 1997) and that the posterior visual thalamus (pulvinar) is activated by visual stimulation in the blind hemifield of V1-lesioned patients (Ptito *et al.*, 1999), it has been proposed that the residual visual abilities of blindsight patients depend on an extrageniculate colliculothalamic visual pathway (Weiskrantz *et al.*, 1974; Barbur *et al.*, 1980). It has also been suggested that G.Y.'s blind hemifield discrimination of emotional expression is amygdala-dependent (de Gelder *et al.*, 1999). Although the superior colliculus, posterior thalamus and amygdala have been implicated in mediating differential responses to masked 'unseen' emotional faces in intact subjects (Morris *et al.*, 1999*a*), evidence that these subcortical structures can mediate emotional discrimination in blindsight (i.e. in the absence of the striate cortex) has been lacking. Neuroimaging of patients with striate cortex damage, therefore, allows a direct test of the conjecture that subcortical visual pathways are sufficient for visual discrimination of salient, emotional stimuli.

We conducted two functional neuroimaging experiments with G.Y. involving blind hemifield presentation of emotional facial expressions. In the first experiment, fearful and happy faces were presented in both right (blind) and left visual hemifields. In the second experiment, lateralized presentations

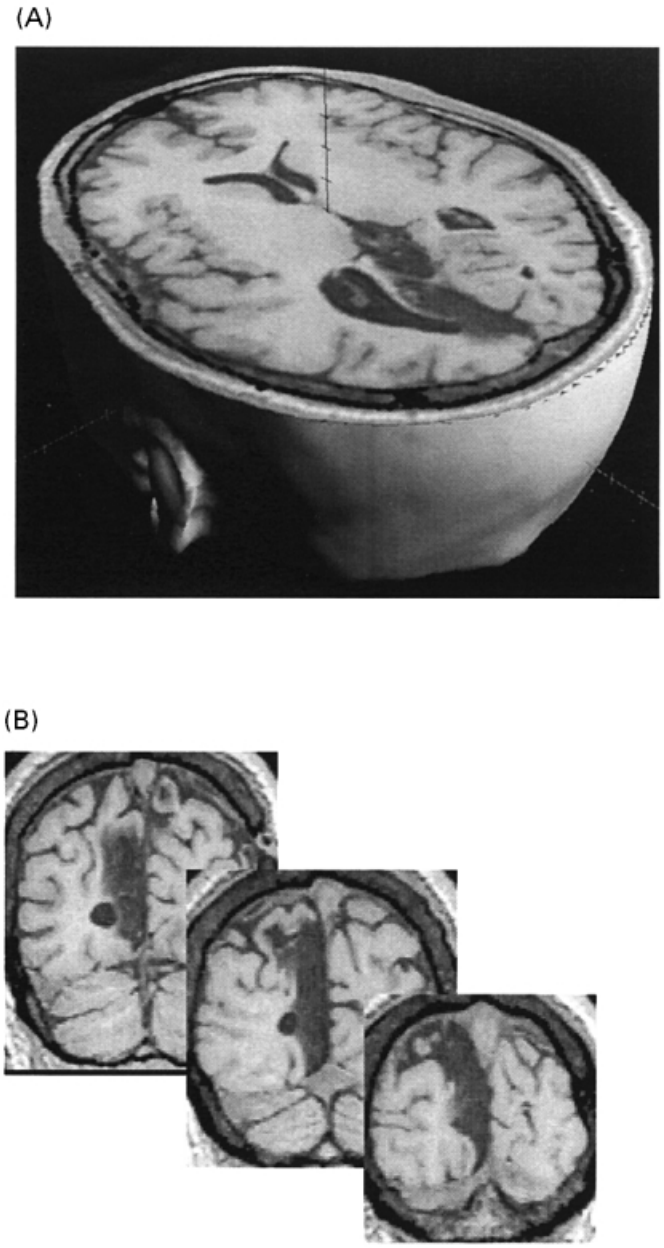

Fig. 1 G.Y.'s left occipital lesion. (**A**) 3D structural MRI of G.Y.'s brain, illustrating left occipital damage. A horizontal cutaway 6 mm above the anterior–posterior commissure axis is shown. (**B**) Coronal sections of G.Y.'s structural MRI, showing the extent of the striate cortex lesion (74, 78 and 82 mm posterior to the anterior commissure).

of angry faces (one male and one female) were made. The female angry face was always immediately followed by a loud (>90 dB) white noise when presented in the left (intact) hemifield in order to produce aversive conditioning. The male angry face was never followed by noise, nor were right (blind) hemifield presentations of the female angry face. In both experiments, G.Y. was instructed to indicate the sex of each presented face (by button presses) while maintaining fixation on a central cross. Eye movements were monitored continually using laser eye-tracking equipment. G.Y. was not informed that emotion was a variable of interest. Previous neuroimaging studies in healthy subjects have shown specific amygdala responses to backwardly masked, 'unseen' fearful faces (Whalen *et al.*, 1998), and on this basis we predicted enhanced amygdala responses to right (blind) hemifield presentation of fearful faces. Aversively conditioned faces also elicit enhanced amygdala responses in healthy subjects (Buchel *et al.*, 1998) even when masked (Morris *et al.*, 1998*a*), and therefore we also predicted enhanced amygdala responses to right-sided, 'unseen' presentations of the aversively conditioned female face.

Methods

Subject

G.Y. is a 44-year-old left-handed male who has a right homonymous hemianopia following damage to his left occipital lobe at the age of 8 years in a motor car accident (Fig. 1). He has macular sparing extending 3° into his right (blind) hemifield. G.Y. gave informed consent to the present study, which was approved by the combined Ethics Committee of the National Hospital for Neurology and Neurosurgery and the Institute of Neurology, London.

Experimental design

G.Y. performed two experimental tasks while being scanned with functional MRI (fMRI). In Experiment 1, G.Y. was shown static grey-scale images of fearful and happy expressions from 10 individuals (five male and five female) taken from a standard set of pictures of facial affect (Ekman and Friesen, 1975). Faces (6.6 × 4.4° in size) were shown singly for 1 s in either the right (blind) hemifield or left (intact) hemifield while G.Y. fixated a permanent central cross. The face images and fixation cross were projected on to a screen placed above the head volume coil of the fMRI scanner. The horizontal separation between the central fixation point and the outer edge of the face was 5.5°, for the outer eye it was 6.7° and for the centre of the face it was 7.7°. Mean luminance of the fearful faces was 4.397 cd/m^2 (SD 0.065); mean luminance of the happy faces was 4.378 cd/m^2 (SD 0.047). There was no significant difference in overall luminance between the fearful and happy face sets ($P > 0.3$ in a two-sample t test). The interstimulus interval varied randomly between 11.28 and 15.78 s. Stimulus onset was indicated by a circle appearing around the central fixation cross. G.Y.'s explicit task was to decide the sex of each face, making responses by button presses with his right hand. There were four conditions: (i) fearful left; (ii) happy left; (iii) fearful right; and (iv) happy right. Stimuli were presented in a single experimental session of 104 trials, with a randomized condition order.

In Experiment 2, G.Y. was shown two static grey-scale images of angry expressions from two individuals (one male and one female) taken from a standard set of pictures of facial

effect (Ekman and Friesen, 1975). The overall luminance of the male face was 4.52 cd/m^2 and that of the female face was 4.48 cd/m^2. The faces were shown singly in either the right (blind) field or left (intact) field while G.Y. fixated a permanent central cross. Stimulus sizes, positions, durations, cues, interstimulus intervals and mode of presentation were the same as for Experiment 1. Every presentation of the female angry face in the intact (left) hemifield was immediately followed by a loud (>90 dB), aversive, white noise burst. The aversive noise, which constituted the unconditioned stimulus, was never paired with the male face or with blind hemifield presentations of either face. As a consequence of this discriminatory classical conditioning process, the female face became the positive conditioned stimulus (CS^+) and the male face became the negative conditioned stimulus (CS^-). There were four conditions: (i) female face (CS^+) plus noise in the left field (unconditioned stimulus); (ii) male face (CS^-) in the left field; (iii) female face (CS^+) in the right field; and (iv) male face (CS^-) in the right field. Stimuli were presented in a single experimental session of 104 trials, with a randomized order of conditions. G.Y.'s explicit task was the same as in Experiment 1. A behavioural measure of differential conditioning was provided by recording reaction times. We also monitored G.Y.'s skin conductance responses to index autonomic conditioning, but a poor signal-to-noise ratio in the recording prevented meaningful analysis of the data.

Data acquisition

Functional neuroimaging data were acquired with a 2 T Magnetom Vision whole-body MRI system equipped with a head volume coil. Contiguous multislice T_2*-weighted echoplanar images were obtained using a sequence that enhanced blood oxygenation level-dependent (BOLD) contrast. Volumes covering the whole brain (48 slices, slice thickness 2 mm) were obtained every 4.3 s. A T_1-weighted anatomical MRI ($1 \times 1 \times 1.5$ mm) was also acquired. In each experiment a total of 320 whole-brain echoplanar images were acquired during a single session, of which the first eight volumes were discarded to allow for T_1 equilibration effects.

Data analysis

The fMRI data were analysed by statistical parametric mapping (Friston *et al.*, 1995; see also http://www.fil.ion.ucl.ac.uk/spm). Following realignment of all the functional (T_2*-weighted) volumes to the first volume in each session, the structural (T_1-weighted) MRI was co-registered into the same space. The functional data were then smoothed using a 6 mm (full width at half maximum) isotropic Gaussian kernel to allow corrected statistical inference. The evoked responses for the different stimulus events were modelled by convolving a series of delta (or stick) functions with a synthetic haemodynamic response function. These functions were used as covariates in a general linear model, together with a constant term and a basis set of cosine functions with a cut-off period of 512 s to remove low-frequency drifts in the BOLD signal. Specific effects (e.g. blind fear versus blind happy) were tested by applying linear contrasts to the parameter estimates for each event type. The resulting *t* statistic at every voxel constituted a statistical parametric map (SPM). Reported *P* values were corrected for the search volume of regions of interest: e.g. an 8 mm radius sphere for the amygdala, a 10 mm radius sphere for the posterior thalamus and a 6 mm radius sphere for the superior colliculus. The significance of activations outside our regions of interest was corrected for multiple comparisons across the entire brain volume.

In a separate analysis of the neuroimaging data, we tested for psychophysiological interactions, i.e. condition-dependent changes in the covariation of response between the amygdala and other brain regions (Friston *et al.*, 1997). Values of adjusted responses were extracted from maximal voxels in the right and left amygdalae for the following contrasts: 'unseen' fearful minus 'unseen' happy (in Experiment 1) and 'unseen' CS^+ minus 'unseen' CS^- (in Experiment 2). Using a specially developed routine in SPM, the adjusted data in each session were first deconvolved and amygdala activity at the time of trials of one of the conditions was extracted. The resulting condition-specific estimate of neuronal activity was then reconvolved with a synthetic haemodynamic response function. This procedure was repeated for the other conditions of interest. The resulting regressors were entered as variables of interest into separate analyses. Linear contrasts were applied to the parameter estimates for the regressors in order to identify regions where responses exhibited significant condition-dependent interactions with amygdala activity.

Results

Throughout testing, G.Y. denied any perception of faces presented in his right (blind) field. In the first experiment, however, he reported non-visual awareness that 'something happened' during right hemifield (blind) trials. This 'event awareness' during right hemifield presentations also occurred in the second experiment, although less frequently. G.Y. has reported this blindfield awareness in previous studies and distinguishes the experience from normal visual perception (Weiskrantz *et al.*, 1995). Despite the absence of normal vision in his blind hemifield, G.Y. was significantly above chance ($P < 0.001$) in the first experiment in identifying the sex of 'unseen' faces: left side 63.5% correct, right (blind) side 76.5% correct. In the second experiment, the female (CS^+) face was assigned the correct sex on 90.5% of left hemifield ('seen') trials but on only 34.4% of right hemifield (blind) trials, i.e. G.Y. was significantly more likely ($P < 0.05$) to categorize the 'unseen' aversively conditioned female face as male. The male (CS^-) face was correctly identified on 62.1% of left hemifield trials, and on 43.1% of right hemifield (blind) trials. Reaction time data from the second conditioning experiment show that responses to the 'unseen' CS^+

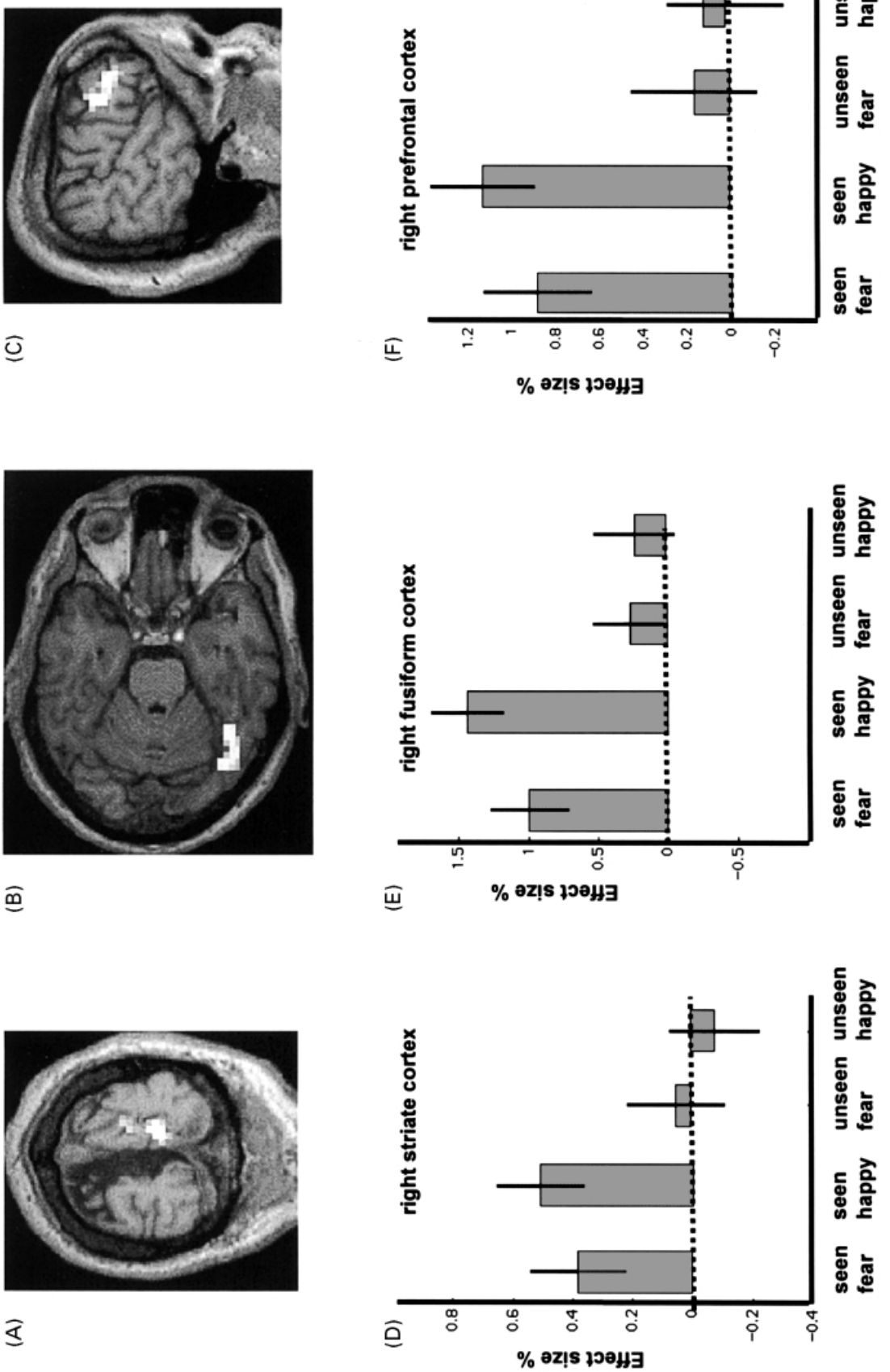

Fig. 2 Neural responses to 'seen' faces. (**A**) Right striate cortex activation by face presentation in the left hemifield. Activation is displayed on a coronal section of G.Y.'s structural MRI, 84 mm posterior to the anterior commissure. (**B**) Right fusiform activation by face presentation in the left hemifield. Activation is displayed on a transverse section of G.Y.'s structural MRI, 18 mm inferior to the anterior–posterior commissure (AC–PC) axis. (**C**) Right prefrontal activation by face presentation on left hemifield. Activation is displayed on a sagittal section of G.Y.'s structural MRI, 54 mm right of the AC–PC axis. A threshold of $P < 0.01$ (uncorrected) was used to display the contrasts in panels **A**–**C**. (**D**–**F**) Graphical displays of parameter estimates in all experimental conditions for activations shown in **A**–**C**, respectively.

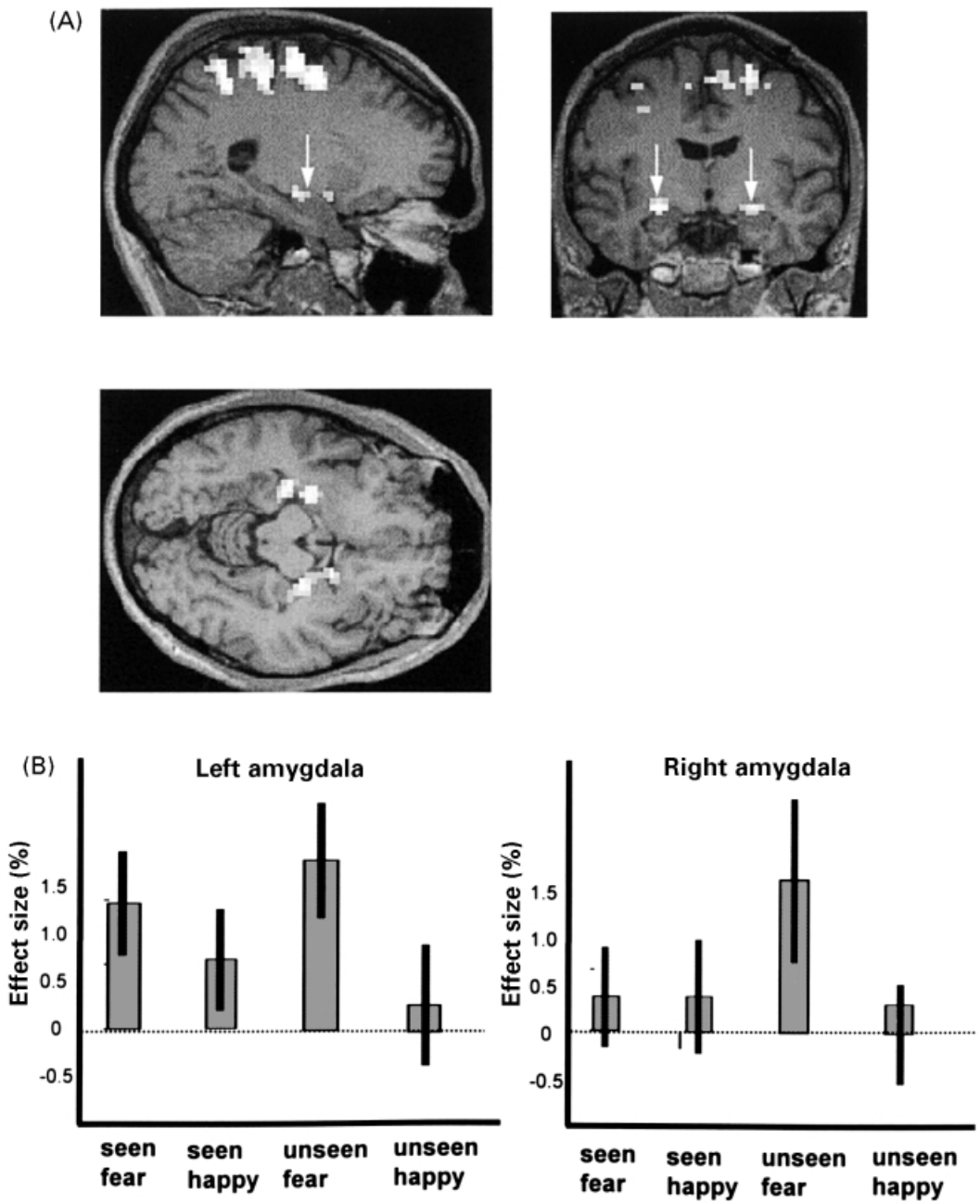

Fig. 3 (**A**) An SPM showing bilateral increased amygdala responses (indicated by arrows) to fearful faces (compared with happy faces) presented in the right (blind) hemifield. Amygdala activations are projected on to orthogonal sections of G.Y.'s structural MRI centred on the maximal voxel in the right amygdala (located 22 mm to the right of the midline, 0 mm posterior and 10 mm inferior to the anterior commissure). A threshold of $P < 0.01$ (uncorrected) was used to display the contrast. (**B**) Graphical display of parameter estimates for right and left amygdala responses to the four event types in Experiment 1.

(compared with 'unseen' CS^-) became faster as the learning session progressed, indicating learning-dependent facilitation of processing (Fig. 4C).

In the first experiment, explicitly seen faces (i.e. all left hemifield compared with all right hemifield stimuli, regardless of emotional expression) evoked enhanced responses in the striate, fusiform and dorsolateral prefrontal cortices ($P < 0.05$, corrected) (Fig. 2). These data accord with previous reports in healthy subjects of enhanced fusiform responses to explicitly seen faces (Haxby *et al*., 1994; Morris *et al.*, 1999*a*). However, face stimuli presented in the right (blind) hemifield did not evoke increased striate, fusiform or dorsolateral prefrontal responses. Blind hemifield presentation of fearful faces evoked increased responses (compared with

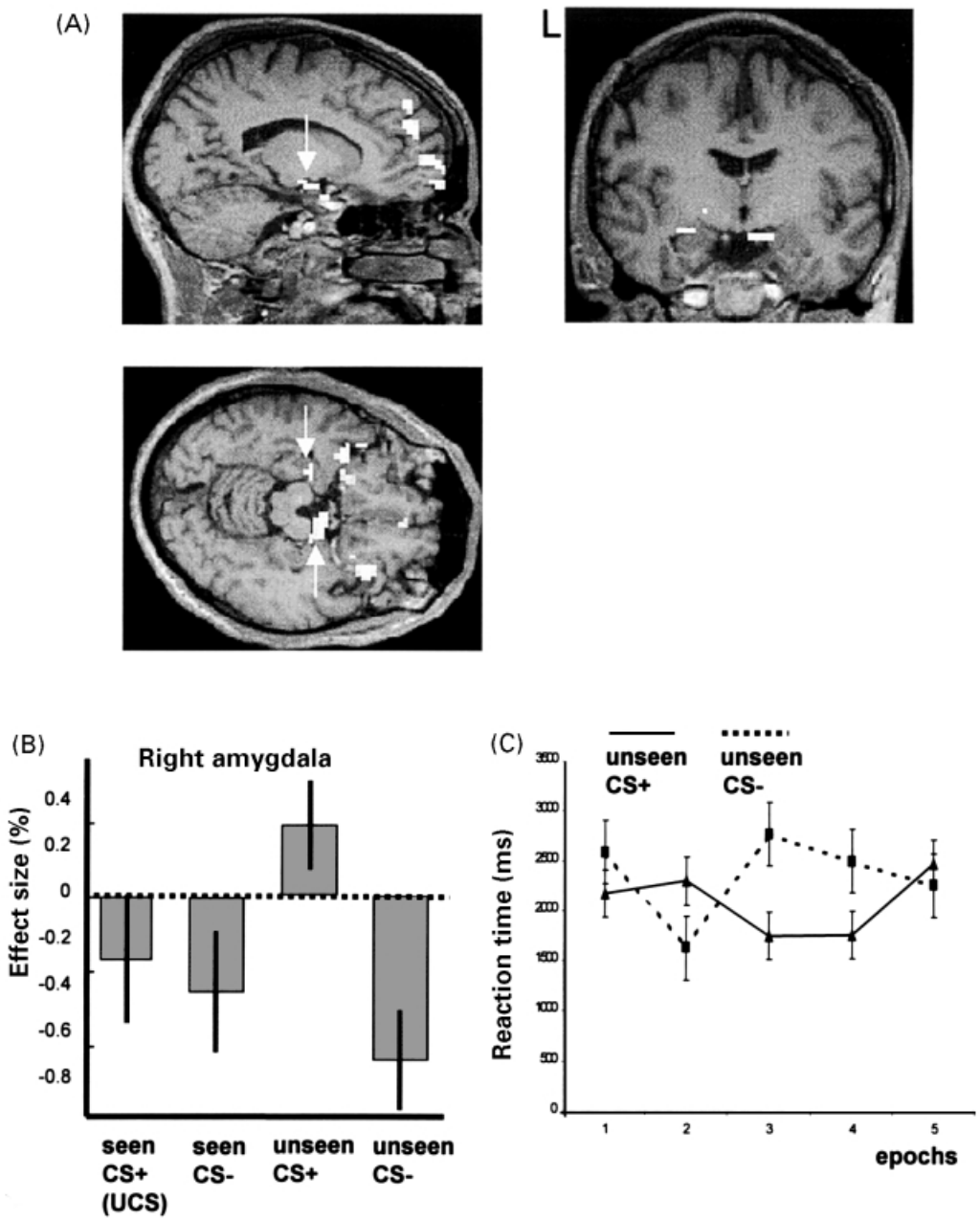

Fig. 4 Amygdala responses in G.Y. to 'unseen' conditioned faces. (**A**) An SPM showing bilateral increased amygdala responses (indicated by arrows) to CS^+ faces (compared with CS^- faces) presented in the right (blind) hemifield. Amygdala activations are projected on to orthogonal sections of G.Y.'s structural MRI centred on the maximal voxel in right amygdala (located 14 mm to the right of the midline, 2 mm posterior and 14 mm inferior to the anterior commissure). A threshold of $P < 0.01$ (uncorrected) was used to display the contrast. (**B**) Graphical representation of parameter estimates for right amygdala responses to the four event types in Experiment 2. (**C**) Plot of reaction times in the 'unseen' CS^+ and 'unseen' CS^- conditions in Experiment 2. The session was divided into five equal epochs. Mean reaction times are shown for each epoch. Bars represent 2 SE.

happy faces) in bilateral regions of the amygdala (left, $P < 0.05$, corrected; right, $P < 0.01$, corrected) (Fig. 3). Left hemifield fearful faces elicited significantly increased responses (compared with left-sided happy faces) in the left but not the right amygdala ($P < 0.05$, corrected). In the second experiment, right (blind) hemifield presentation of the CS^+ face elicited greater responses than the CS^- face in bilateral regions of the amygdala (left, $P < 0.01$, corrected; right, $P < 0.001$, corrected) (Fig. 4), as well as in the superior colliculus ($P < 0.001$, corrected) (Fig. 5). The significance of activations in other, unpredicted regions (e.g. somatosensory cortex as shown in Fig. 3A) did not survive correction for multiple comparisons across the whole brain.

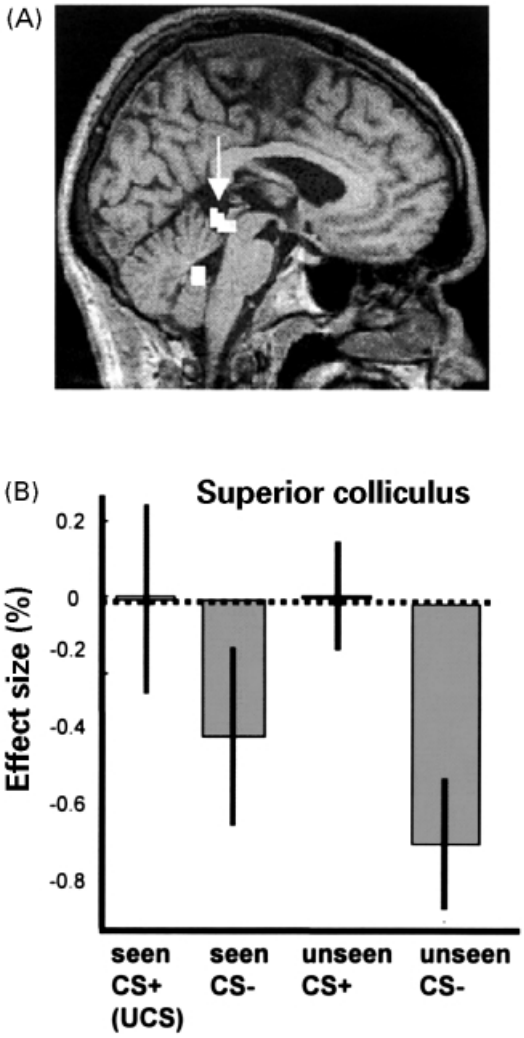

Fig. 5 Superior colliculus responses in Experiment 2. (**A**) An SPM showing a region of the superior colliculus with greater responses to 'unseen' CS^+ than 'unseen' CS^- faces. The SPM is displayed on a midline sagittal section of G.Y.'s structural MRI. A threshold of $P < 0.01$ (uncorrected) was used to display the contrast. (**B**) Graphical display of parameter estimates for superior colliculus responses to the four event types in Experiment 2.

Given the nature of G.Y.'s occipital lesion (Fig. 1), visual signals mediating discriminatory blind field responses to fear-related faces must access the amygdala via pathways that bypass the striate cortex. To determine the nature of these alternative pathways, we conducted additional analyses using measures of amygdala activity as condition-specific regressors (Friston *et al.*, 1997). In the first experiment, this regression analysis showed that the emotional content of faces presented in the right (blind) field influenced the covariation of response between the amygdala (bilaterally) and the superior colliculus (Fig. 6). A positive covariation was found during presentation of 'unseen' fearful faces, whereas a negative covariation was evident with 'unseen' happy faces (Fig. 6B and C). A similar bilateral pattern of condition-dependent response covariation ($P < 0.001$, corrected) was observed between the amygdala and a ventrolateral region of the posterior thalamus (Fig. 7).

In the second experiment, responses in the right amygdala exhibited a positive covariation with responses in posteromedial thalamus during presentation of right hemifield ('unseen') CS^+ faces, while a negative covariation of response between these regions was observed for 'unseen' CS^- faces ($P < 0.05$, corrected) (Fig. 8). Negative covariation of right amygdala and posteromedial thalamic responses was also observed during presentation of left hemifield ('seen') CS^+ faces. No condition-dependent covariation of responses between the left amygdala and the posterior thalamus was observed. Also, unlike the first experiment, no condition-dependent response covariation between amygdala and superior colliculus was identified in the second experiment. However, both amygdala and superior colliculus exhibited increased mean responses to 'unseen' CS^+ faces compared with 'unseen' CS^- (Figs 4 and 5).

Discussion

These results obtained in patient G.Y. show striking parallels with previous neuroimaging data from healthy volunteers when masking procedures were used (Morris *et al.*, 1998*a*, *b*, 1999*a*; Whalen *et al.*, 1998). In both G.Y. and normal subjects, 'unseen' fearful and fear-conditioned faces elicit increased amygdala responses (Figs 3 and 4) (Morris *et al.*, 1998*a*; Whalen *et al.*, 1998). One difference, however, is that whereas masked CS^+ faces elicited bilateral amygdala responses in G.Y., only right amygdala responses were seen in healthy subjects (Morris *et al.*, 1998*a*). This divergence of results may arise from methodological differences between studies, or from indirect effects of G.Y.'s striate cortex lesion. Nevertheless, it is notable that in G.Y. right amygdala responses to masked CS^+ faces were more spatially extensive (Fig. 4) and that, as in intact subjects (Morris *et al.*, 1999*a*) the right (but not left) amygdala showed fear-dependent covariation with pulvinar activity during 'unseen' presentations (Fig. 8).

G.Y. also showed some differences from healthy subjects in the response of the superior colliculus to masked CS^+ faces. In normal subjects, increased condition-specific covariation of colliculo-amygdala responses to masked CS^+ faces was observed without any significant change in mean collicular responses (Morris *et al.*, 1998*a*). In G.Y., on the other hand, increased mean responses to masked CS^+ faces were observed in both the amygdala and the superior colliculus (Figs 4 and 5). There are several crucial methodological differences between the studies that may explain these divergent findings. In the previous PET experiment on normal subjects (Morris *et al.*, 1998*a*) the stimuli were always presented centrally, in blocked conditions, whereas in the present event-related fMRI study the stimuli were presented in different lateralized locations,

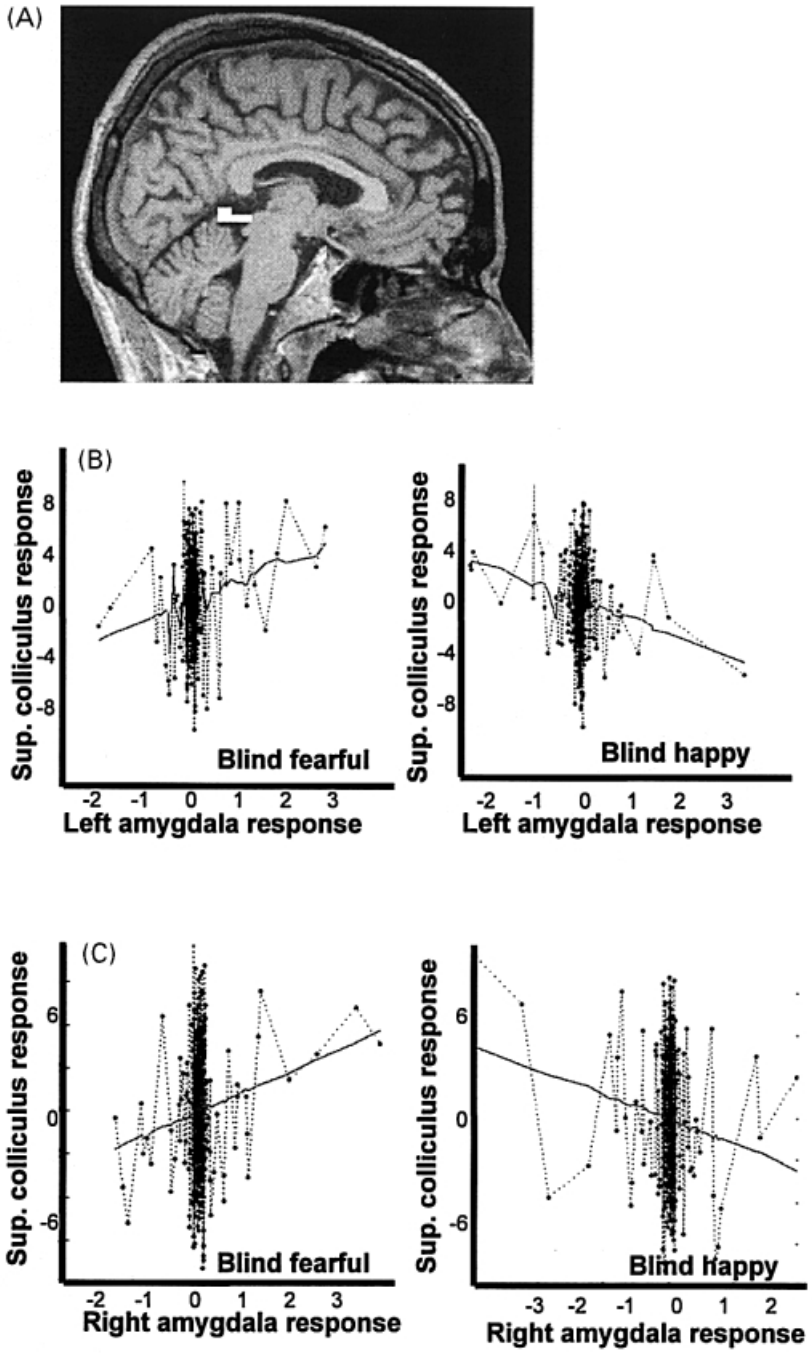

Fig. 6 Amygdalocollicular covariation in Experiment 1. (**A**) An SPM showing a region of the superior colliculus where response covariation with the left and right amygdala was more positive during presentation of 'unseen' fearful than 'unseen' happy faces. The SPM is displayed on a sagittal section of G.Y.'s structural MRI (2 mm right of the midline). A threshold of $P < 0.01$ (uncorrected) was used to display the contrast. (**B** and **C**) Graphical displays showing bivariate plots of event-related amygdala and superior colliculus responses in the 'unseen' fearful and 'unseen' happy conditions. The solid lines represent predicted (i.e. fitted) collicular responses in relation to amygdala activity. The broken lines represent fitted values plus residuals.

with central fixation, in a randomized, mixed trial paradigm. These differences in stimulus presentation may account for the contrasting patterns of superior colliculus activation. However, it is also possible that G.Y.'s occipital lesion has produced experience-dependent changes in collicular function. Experiments on monkeys indicate that the number

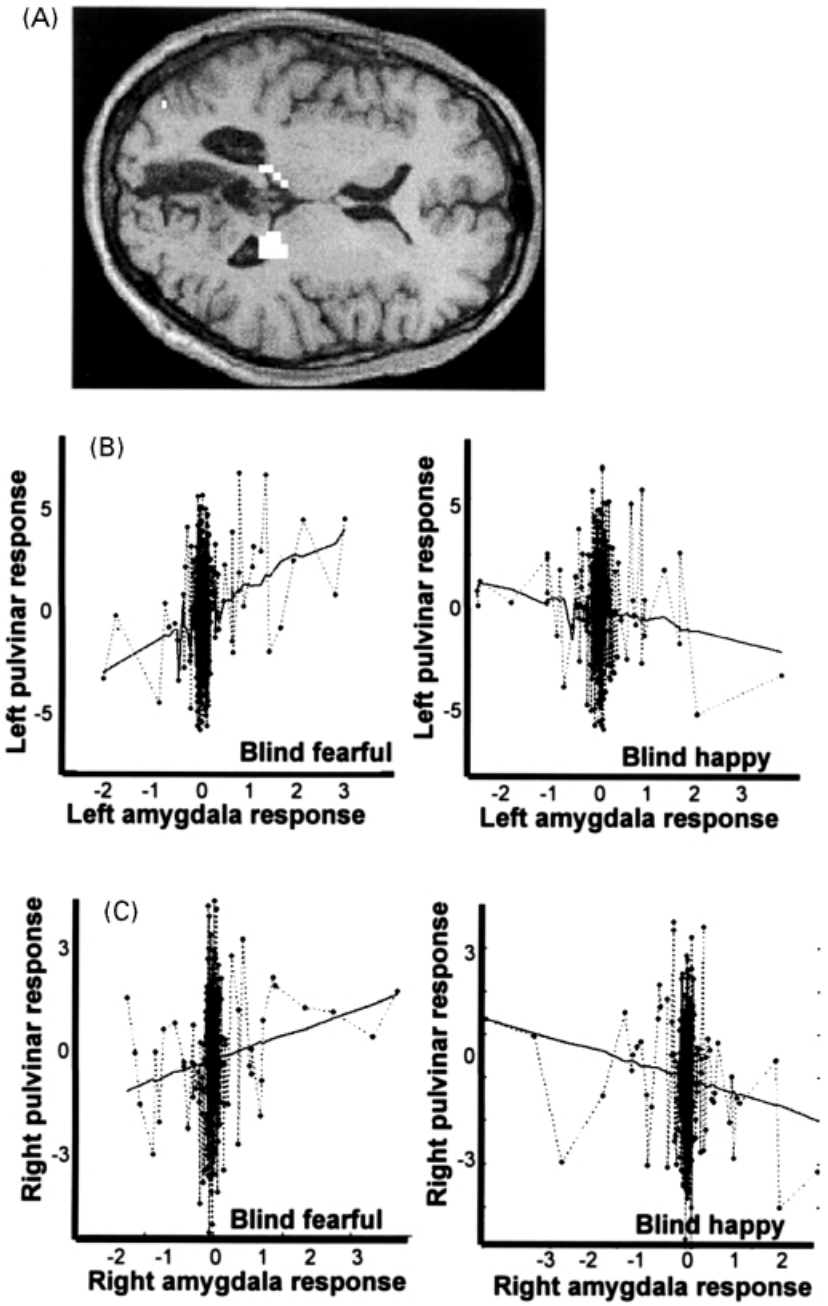

Fig. 7 (**A**) An SPM showing a bilateral region of the pulvinar where response covariation with the left and right amygdala was more positive during presentation of 'unseen' fearful than of 'unseen' happy faces. The SPM is displayed on a transverse section of G.Y.'s structural MRI (8 mm above the anterior–posterior commissure axis). A threshold of $P < 0.01$ (uncorrected) was used to display the contrast. (**B** and **C**) Graphical displays showing bivariate plots of event-related amygdala and pulvinar responses in 'unseen' fearful and 'unseen' happy conditions. See also legend to Fig. 6B.

of collicular cells with enhanced responses to visual targets increases significantly following striate cortex lesions (Mohler and Wurtz, 1977). Similar plasticity in G.Y.'s superior colliculus may explain the gradual changes in his blindsight performance that have been observed during repeated testing over the years (Weiskrantz, 2000).

Despite changes in G.Y.'s blindsight sensitivity over time (Weiskrantz, 2000), he continues to deny visual perception in his blind field (as distinct from event awareness). Irreversible damage to the striate cortex, therefore, appears to have produced a long-lasting (and perhaps permanent) loss of normal phenomenal visual

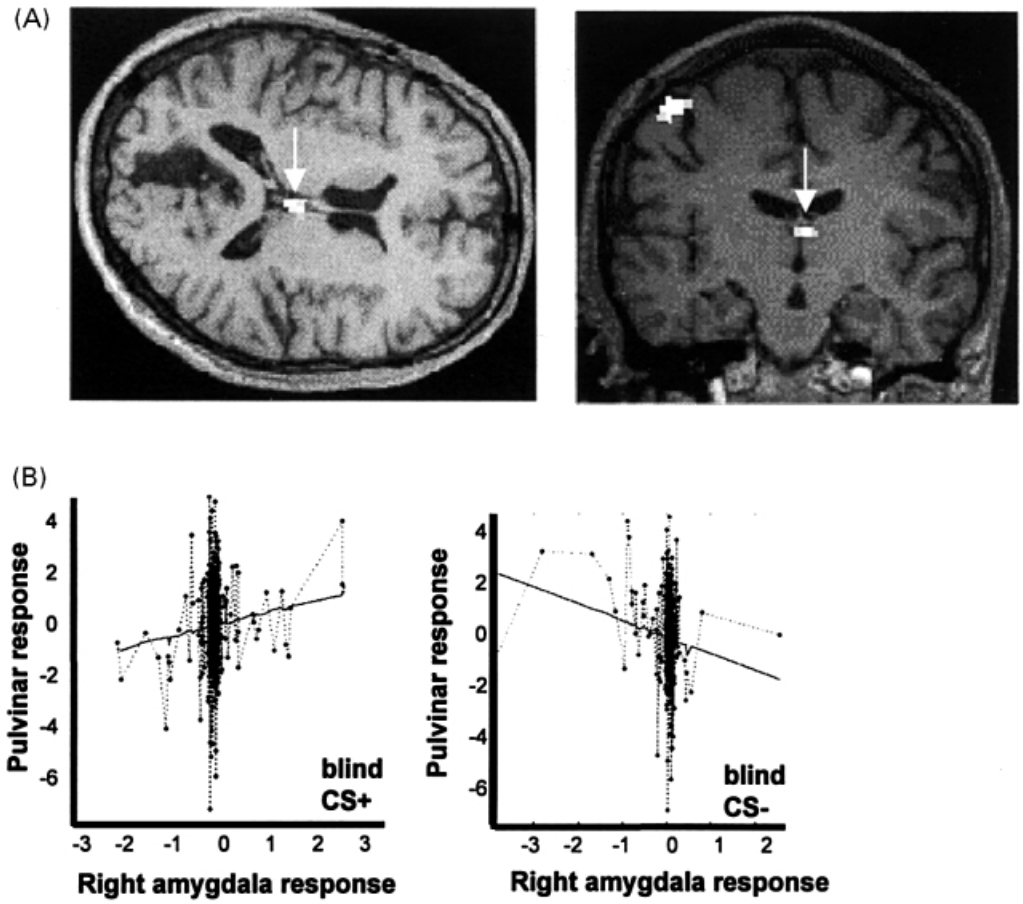

Fig. 8 (**A**) An SPM showing a region of the right medial pulvinar where response covariation with the amygdala was more positive during presentation of 'unseen' CS^+ than of 'unseen' CS^- faces. The SPM is displayed on a transverse section (10 mm above the anterior–posterior commissure axis) and a coronal section (20 mm posterior to the anterior commissure) from G.Y.'s structural MRI. A threshold of $P < 0.01$ (uncorrected) was used to display the contrast. (**B**) Graphical displays showing bivariate plots of event-related amygdala and pulvinar responses in 'unseen' CS^+ and 'unseen' CS^- conditions. See also legend to Fig. 6B.

awareness. By contrast, transient disruption of striate responses produced by backward masking (Macknik and Livingstone, 1998) produces temporary interference with visual awareness. It is notable, however, that, despite these differences in mechanism and time course, both blindsight and backward masking are associated with residual (non-conscious) visual abilities (Weiskrantz *et al.*, 1974; Esteves *et al.*, 1994). These data suggest, therefore, that, although the striate cortex may be critically important for conscious visual perception, including detailed discrimination and verbal (semantic) categorization of stimuli, a number of implicit visual processes, including differential responses to emotional facial expressions, do not require the primary visual cortex.

Although an intact striate cortex may not be necessary for implicit visual processing, the present results indicate that several subcortical visual structures (i.e. the superior colliculus and posterior thalamic nuclei) are involved in processing 'unseen' emotional faces (Figs 5–8). The anatomical connectivity and functions of these subcortical structures are consistent with such an implicit visual role. The superior colliculus in the midbrain tectum receives direct visual input from the retina and is critical for the guidance of eye movements (Wurtz and Goldberg, 1971; Schiller and Mallpeli, 1977). Intriguingly, the deep layer of the superior colliculus in the rat is also implicated in the expression of fear-related behaviour (Sahibzada *et al.*, 1986; Coimbra *et al.*, 1996). Efferent axons from the superior colliculus terminate in several nuclei in the posterior thalamus: neurones in the superficial layer project to the lateral pulvinar, inferior pulvinar and suprageniculate nuclei; deep-layer cells project to the medial pulvinar, posterior intralaminar nuclei, the peripeduncular nucleus and the medial division of the medial geniculate nucleus (Benevento and Fallon, 1975; Linke *et al.*, 1999; Grieve *et al.*, 2000). Experiments in monkeys indicate that this 'secondary' extrageniculostriate visual system via the superior colliculus is able to mediate visual discriminatory

responses, albeit at a lower spatial resolution than the geniculostriate system (Miller *et al.*, 1980; Rodman *et al.*, 1989).

The pulvinar in the posterior thalamus comprises several retinotopically organized subnuclei that have greatly expanded in the primate to occupy a third of the entire thalamus (Robinson and Petersen, 1992). The pulvinar has extensive reciprocal connections with many brain regions (Robinson and Petersen, 1992) and is implicated in processing behaviourally salient visual targets (Petersen *et al.*, 1985; Grieve *et al*., 2000). Both the medial pulvinar and the suprageniculate nucleus in the posterolateral thalamus have direct projections to the lateral amygdala (Jones and Burton, 1976; Linke *et al*., 1999). It is notable, therefore, that in the present study we observed amygdala-dependent covariation of response in two distinct regions of posterior thalamus (Figs 7 and 8). The current resolution of our neuroimaging data, however, prevents identification of these regions as specific subnuclei of the pulvinar or the posterior thalamus.

The direct anatomical connections between the posterior thalamic visual subnuclei and lateral amygdala (Jones and Burton, 1976; Linke *et al*., 1999) provide support for the proposal that the amygdala forms part of a secondary extrageniculostriate visual system (Morris *et al*., 1999*a*). The present neuroimaging data obtained in G.Y., showing condition-dependent colliculo-amygdala and thalamo-amygdala response covariation (Figs 6–8), add further support to this proposal. Processing in this extrageniculostriate visual system appears to be selective for fear-related stimuli and not to involve normal phenomenal awareness, although the development of some awareness might be possible with specialized training programmes (Cowey and Stoerig, 1995; Moore *et al.*, 1995; Sahraie *et al.*, 1997; Whalen *et al.*, 1998; Morris *et al.*, 1999*a*; Ptito *et al.*, 1999; Weiskrantz, 2000).

An amygdala-based fear system is present in many different species, including mammals, birds and reptiles, testifying to its long evolutionary history and its importance for survival. Our results obtained with G.Y. provide evidence that this phylogenetically ancient fear system can function independently of the more recently evolved geniculostriate visual system and without normal visual awareness. In this regard, fear may be distinct from other emotions in the degree of processing autonomy it exhibits. The presence of parallel visual systems in the human brain (one subserving automatic, non-conscious fear processing, the other subserving conscious identification and discrimination) suggests the need for mechanisms to overcome conflicts and to integrate both inputs and outputs for coordinated behavioural responses. Our results, together with other data obtained in subjects with an intact brain (Morris *et al.*, 1998*b*; Whalen *et al.*, 1998; Morris *et al.*, 1999*a*, *b*) are consistent with the view (LeDoux, 1996) that the amygdala, a structure with extensive reciprocal connections to both visual systems, may be crucial in this integrative process.

References

Barbur JL, Ruddock KH, Waterfield VA. Human visual responses in the absence of the geniculo-calcarine projection. Brain 1980; 103: 905–28.

Benevento LA, Fallon JH. The ascending projections of the superior colliculus in the rhesus monkey (Macaca mulatta). J Comp Neurol 1975; 160: 339–61.

Buchel C, Morris J, Dolan RJ, Friston KJ. Brain systems mediating aversive conditioning: an event-related fMRI study. Neuron 1998; 20: 947–57.

Coimbra NC, Eichenberger GC, Gorchinski RT, Maisonnette S. Effects of the blockade of opioid receptor on defensive reactions elicited by electrical stimulation within the deep layers of the superior colliculus and DPAG. Brain Res 1996; 736: 348–52.

Cowey A, Stoerig P. Blindsight in monkeys. Nature 1995; 373: 247–9.

de Gelder B, Vroomen J, Pourtois G, Weiskrantz L. Non-conscious recognition of affect in the absence of striate cortex. Neuroreport 1999; 10: 3759–63.

Ekman P, Friesen WV. Pictures of facial affect. Palo Alto (CA): Consulting Psychologists Press; 1975.

Esteves F, Dimberg U, Öhman A. Automatically elicited fear: conditioned skin conductance responses to masked facial expressions. Cogn Emotion 1994; 8: 99–108.

Friston KJ, Holmes, AP, Worsley KJ, Poline J-B, Frith CD, Frackowiak RSJ. Statistical parametric maps in functional imaging: a general linear approach. Hum Brain Mapp 1995; 2: 189–210.

Friston KJ, Buechel C, Fink GR, Morris J, Rolls E, Dolan RJ. Psychophysiological and modulatory interactions in neuroimaging. Neuroimage 1997; 6: 218–29.

Grieve KL, Acuna C, Cudeiro J. The primate pulvinar nuclei: vision and action. [Review]. Trends Neurosci 2000; 23: 35–9.

Haxby JV, Horwitz B, Ungerleider LG, Maisog JM, Pietrini P, Grady CL. The functional organization of human extrastriate cortex: a PET–rCBF study of selective attention to faces and locations. J Neurosci 1994; 14: 6336–53.

Holmes G. Disturbances of vision by cerebral lesions. Brit J Ophthal 1918; 2: 353–84.

Jones EG, Burton H. A projection from the medial pulvinar to the amygdala in primates. Brain Res 1976; 104: 142–7.

LeDoux JE. The emotional brain. New York: Simon & Shuster; 1996.

Linke R, De Lima AD, Schwegler H, Pape H-C. Direct synaptic connections of axons from superior colliculus with identified thalamo-amygdaloid projection neurons in the rat: possible substrates of a subcortical visual pathway to the amygdala. J Comp Neurol 1999; 403: 158–70.

Macknik SL, Livingstone MS. Neuronal correlates of visibility and invisibility in the primate visual system. Nat Neurosci 1998; 1: 144–9.

Miller M, Pasik P, Pasik T. Extrageniculostriate vision in the monkey. VII. Contrast sensitivity functions. J Neurophysiol 1980; 43: 1510–26.

Mohler CW, Wurtz RH. Role of striate cortex and superior colliculus in visual guidance of saccadic eye movements in monkeys. J Neurophysiol 1977; 40: 74–94.

Moore T, Rodman HR, Repp AB, Gross CG. Localization of visual stimuli after striate cortex damage in monkeys: parallels with human blindsight. Proc Natl Acad Sci USA 1995; 92: 8215–8.

Morris JS, Öhman A, Dolan RJ. Conscious and unconscious emotional learning in the human amygdala. Nature 1998a; 393: 467–70.

Morris JS, Friston KJ, Buchel C, Frith CD, Young AW, Calder, AJ, et al. A neuromodulatory role for the human amygdala in processing emotional facial expressions. Brain 1998b; 121: 47–57.

Morris JS, Ohman A, Dolan RJ. A subcortical pathway to the right amygdala mediating 'unseen' fear. Proc Natl Acad Sci USA 1999a; 96: 1680–5.

Morris JS, Scott SK, Dolan RJ. Saying it with feeling: neural responses to emotional vocalizations. Neuropsychologia 1999b; 37: 1155–63.

Petersen SE, Robinson DL, Keys W. Pulvinar nuclei of the behaving rhesus monkey: visual responses and their modulation. J Neurophysiol 1985; 54: 867–86.

Ptito M, Johannsen P, Faubert J, Gjedde A. Activation of human extrageniculostriate pathways after damage to area V1. Neuroimage 1999; 9: 97–107.

Robinson DL, Petersen SE. The pulvinar and visual salience. [Review]. Trends Neurosci 1992; 15: 127–32.

Rodman, HR Gross, CG, Albright TD. Afferent basis of visual response properties in area MT of the macaque. I. Effects of striate cortex removal. J Neurosci 1989; 9: 2033–50.

Sahibzada N, Dean P, Redgrave P. Movements resembling orientation or avoidance elicited by electrical stimulation of the superior colliculus in rats. J Neurosci 1986; 6: 723–33.

Sahraie A, Weiskrantz L, Barbur JL, Simmons A, Williams SC, Brammer MJ. Pattern of neuronal activity associated with conscious and unconscious processing of visual signals. Proc Natl Acad Sci USA 1997; 94: 9406–11.

Schiller PH, Malpeli JG. Properties and tectal projections of monkey retinal ganglion cells. J Neurophysiol 1977; 40: 428–45.

Weiskrantz L. Blindsight: implications for the conscious experience of emotion. In: Lane RD, Nadel L, editors. Cognitive neuroscience of emotion. New York: Oxford University Press; 2000. p. 277–95.

Weiskrantz L, Warrington EK, Sanders MD, Marshall J. Visual capacity in the hemianopic field following a restricted occipital ablation. Brain 1974; 97: 709–28.

Weiskrantz L, Barbur JL Sahraie A. Parameters affecting conscious versus unconscious visual discrimination with damage to the visual cortex (V1). Proc Natl Acad Sci USA 1995; 92: 6122–6.

Whalen PJ, Rauch SL, Etcoff NL, McInerney SC, Lee MB, Jenike MA. Masked presentations of emotional facial expressions modulate amygdala activity without explicit knowledge. J Neurosci 1998; 18: 411–8.

Wurtz RH, Goldberg ME. Superior colliculus cell responses related to eye movements in awake monkeys. Science 1971; 171: 82–4.

Received September 28, 2000. Revised January 25, 2001. Accepted February 15, 2001