PERGAMON

Modulation of spatial attention by fear-conditioned stimuli: an event-related fMRI study

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Abstract

Stimuli that signal threat can capture subjects' attention, leading to more efficient detection of, and faster responses to, events occurring in that part of the environment. In the present study we explored the behavioural and anatomical correlates of the modulation of spatial attention by emotion using a fear conditioning paradigm, combined with a covert spatial orienting task. Reaction times for the detection of a peripheral target, which was preceded by brief (50 ms) presentations of the visual conditioned stimulus (CS+) in either the same or opposite visual field, showed an interaction between stimulus emotionality and attention shifts. We used event-related functional magnetic resonance imaging (fMRI) to characterise the associated neural responses. Consistent with previous studies, conditioning-induced enhanced responses were observed in the amygdala and extrastriate visual cortex. The modulation of spatial attention by a conditioned stimulus was associated with enhanced activity in regions of frontal and parietal cortices previously implicated in spatial attention, as well as in the lateral orbitofrontal cortex (lOFC). © 2002 Elsevier Science Ltd. All rights reserved.

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1. Introduction

Detection of danger and rapid elicitation of appropriate defence reactions are crucial for survival. The fear system, highly conserved throughout evolution, operates in a rapid and efficient fashion, in some cases even without conscious awareness of an eliciting stimulus [21]. In many instances, however, once danger is detected and the initial automatic fear responses elicited, further action is necessary, requiring the redirection of attentional resources, with the engagement of flexible response repertoires, towards the threatening stimulus. This influence of emotionality on spatial attention in humans has been investigated using a variety of behavioural tasks (e.g. [3,28,38,39,54]). However, although much progress has been made in characterising neural circuits underlying fear processing (for reviews see [4,23,34]) and spatial attention (e.g. [13,14,27,37,52]), little is known about how these two systems interact in humans.

Attention and emotion can interact either by attention influencing emotional processing, or emotion modulating attentional processing. In the present study we used event-related functional magnetic resonance imaging (fMRI) to address the question of how emotion, specifically fear, influences attention, by employing a paradigm that combined discriminatory fear conditioning with a covert spatial orienting task. During scanning, subjects viewed pictures of two angry faces, one of which was paired (conditioned stimulus (CS+)), and the other not paired (CS−), with a loud burst of white noise, the unconditioned stimulus (US). We hypothesised that the CS+, having acquired aversive emotional value through conditioning, would automatically capture subjects' attention. We tested this hypothesis with a modified version of the well-known dot-probe covert attention task [47]. Subjects were instructed to detect the location of a target, appearing on either side of the central fixation location. In the critical experimental condition, the dot target was preceded by a brief presentation of a CS+ and CS− side by side, but in opposite visual fields. If attention was captured by the CS+, detection of targets on the opposite side (incongruent trials) should be slower than those on the same side (congruent trials). That is, a difference in reaction times between congruent

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Neutral/divided attention conditions

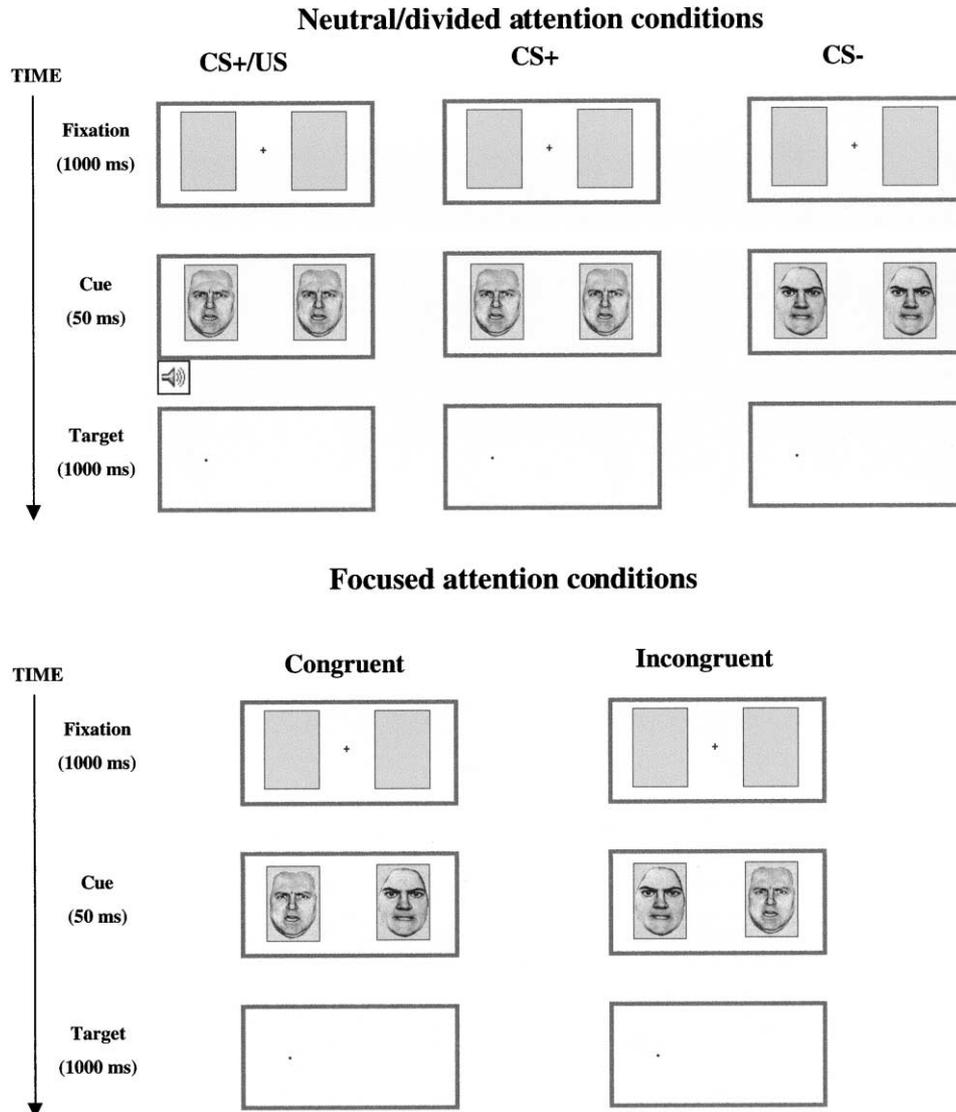## Focused attention conditions

Fig. 1. Schematic illustration of the five trial types used in the study (see Section 2 for details). The fixation cross was present for 1 s, and the face stimuli (cue) appeared for 50 ms, immediately followed by the target. In the neutral/divided attention conditions, the same stimulus (either CS+ or CS−) was presented on both sides, whereas in the focused-attention conditions the CS+ and CS− were presented together, side by side; in congruent trials the location of target was the same as that of the CS+, and opposite in the incongruent trials. In the CS+/US condition, a loud burst of white noise (200 ms) was presented in conjunction with the face stimuli.

and incongruent trials would suggest that indeed spatial attention was modulated by the affective value of the stimuli. Furthermore, by comparing neural responses between these trials where, according to our hypothesis, attention would be captured by the CS+ (henceforth, referred as *focused-attention* conditions) with trials in which the same face stimulus, either the CS+ or the CS−, was presented on both sides—therefore, attention being equally allocated to both hemifields (the *neutral/divided attention* conditions; see Fig. 1), we were able to determine which brain regions were involved in this modulation of attention by emotion.

2. Materials and methods

2.1. Subjects

Ten healthy volunteers, without a history of neurological or psychiatric impairments, participated in this study. All subjects provided written informed consent before the experiment. Data from four subjects were excluded from the analysis due to technical problems with the scanner and/or the stimulus delivery system. The results presented here correspond to data obtained form the remaining six subjects (three male, three female). All procedures were approved by

the Joint Ethics Committee of National Hospital and Institute of Neurology.

2.2. Experimental paradigm

Fig. 1 shows a schematic of the different trial types. All trials began with a fixation cross in the middle of the screen for 1 s, followed by the presentation of two faces, shown for 50 ms. Immediately after the offset of the face stimuli, a small dot was presented on either side of the visual field, coinciding with the location of one of the two previously shown faces. Subjects were required to respond, as quickly and accurately as possible, to the location of the probe, using a keypad with their right hand. Subjects were instructed to ignore the face stimuli and concentrate on the target detection task.

Two angry faces, one male and one female, taken from the Ekman and Friesen series [20] were used as CS+ and CS−. The use of angry faces as CS has been shown to provide strong conditioning responses, both at the neural [44] and autonomic [21] level, and be less susceptible to extinction than other stimuli. Because both the CS+ and CS− had similar affective value at the onset of the experiment, differential responses (CS+ > CS−) can be attributed to the effects of conditioning over and above any responses elicited by the intrinsic nature of the stimuli. Furthermore, the assignment of the two stimuli as either CS+ or CS− was counterbalanced across subjects. We used a 50% partial reinforcement schedule (i.e. only half of the presentations of the CS+ were paired with the US) to allow us to investigate the haemodynamic response to the CS+ in the absence of the US (see [5,6]). The US, a 200 ms burst of white noise, was delivered through plastic tubes, sealed by foam ear inserts and further shielded by plastic ear defenders, to minimise the influence of the gradient switching noise from the scanner. The amplitude of the US was set individually by each subject, following the instructions that it should be aversive but not painful. The final amplitude used was very similar for all the subjects (∼100 dB).

The face stimuli consisted of two faces presented side by side. There were five types of trials used during the experiment: CS+/US, CS+, CS−, incongruent, and congruent (Fig. 1). The CS+/US, CS+ and CS− presentations consisted of the same face presented on both sides. In the other two critical trial types, the CS+ and CS− were presented side by side; *congruent* trials refer to the cases when the location of the target coincided with the side where the CS+ had been presented while *incongruent* trials refer to instances where the relative position of the target and the CS+ was in opposition. During these trials, the US was never presented, in order to avoid the possibility of conditioning to the CS− (by itself or through conditioning to the CS+/CS− compound stimulus).

In total, there were 192 trials: 46 CS+ (30 paired and 16 alone), 46 CS−, 50 congruent, and 50 incongruent trials. The average trial onset asynchrony was 7 ± 2.5 s. The location of the target with respect to visual hemifield was randomised, and equally distributed within each trial type. Subjects recorded their responses using two buttons (left and right) in a keypad. For the analysis of reaction times (RTs), error trials were discarded (<3%). Median values of RTs in each condition were computed for each subject.

2.3. Image acquisition and data analysis

Images were acquired with a 2T Magnetom VISION whole-body MRI system (Siemens, Erlangen, Germany) equipped with a head volume coil. T2*-weighted echoplanar image volumes with blood oxygenation level-dependent (BOLD) contrast (echo time, 40 ms; 64×64 pixels) were acquired in an axial orientation. Each volume comprised of 32 slices (slice thickness, 3 mm), positioned to cover the whole brain. The effective repetition time (T_R) was 3.2 s/vol. To minimise head motion, subjects were restrained with bitemporal pressure pads. A total of 460 volumes were acquired for each subject, over 30 min.

Image processing and statistical analysis were performed using SPM99 (Wellcome Department of Cognitive Neurology [1]) [26,61]. The imaging time series was realigned to the first volume to correct for interscan movement. To account for the difference in sampling time of different slices, voxel time series were interpolated using sinc interpolation and resampled using the slice at the anterior–posterior commissural line as reference. Finally, the functional images were spatially normalised to a standard Talairach space [57] based on a template provided by the Montreal Neurological Institute [22] to allow group analysis. A T1-weighted anatomical MRI (1 mm × 1 mm × 1.5 mm voxel slice) was obtained for each subject and coregistered with the mean realigned functional image and normalised using the parameters determined for the functional images. A mean anatomical image was created from the subjects' individual scans, onto which activations were overlaid for anatomical localisation. Functional data were smoothed using a 8 mm (full-width at half maximum (FWHM)) isotropic Gaussian kernel to compensate for residual inter-subject variability and to allow for the application of Gaussian random field theory in the statistical analysis [26].

Data were analysed by modelling the evoked haemodynamic responses for the different stimuli as delta functions convolved with a synthetic haemodynamic function (hrf) and its temporal derivative (hrft), in the context of the fixed-effects general lineal model [25,30]. We defined five event types: CS+/US, CS+ (alone), CS−, incongruent, and congruent (Fig. 1). Differential effects were tested by applying appropriate linear contrasts to the parameter estimates for the hrf and hrft regressors of each event, resulting in a *t*-statistic for each voxel. These *t*-statistics (transformed to *Z*-statistics) constitute a statistical parametric map (SPM).

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[1] http://www.fil.ion.ucl.ac.uk.

Three contrasts were calculated. The first one, CS+ versus CS−, was aimed at detecting those areas involved in the conditioning paradigm. The second contrast involved comparing the focused-attention trials (i.e. congruent and incongruent) with the neutral/divided attention trials (CS+ and CS−). In this way, we aimed to identify areas correlated with the modulation of focused spatial attention by the CS+, while removing the influence of the presentation of the CS+ per se (hence, the inclusion of the CS+ trials in the comparison). The third contrast consisted in the comparison between incongruent and congruent trials. The corresponding *P*-values were corrected for multiple comparisons across the entire brain, except where otherwise indicated.

In the case of the amygdala, we applied a small volume correction [61] based on our a priori hypothesis of its involvement in fear conditioning. The volume of interest consisted in a 8 mm sphere centred on the amygdala coordinates reported in a previous fMRI study of fear conditioning [5]. The size and shape of this volume was the same as in previous studies from our laboratory [5,6,42,58] and based on the size of the amygdala [12,24,48] and the spatial smoothing of the functional images (8 mm FWHM Gaussian kernel).

3. Results

3.1. Fear conditioning

In order to assess the effects of fear conditioning on neural activity, we compared the responses evoked by the CS+ to those evoked by the CS− across the session. In this comparison, we excluded those trials in which the US was
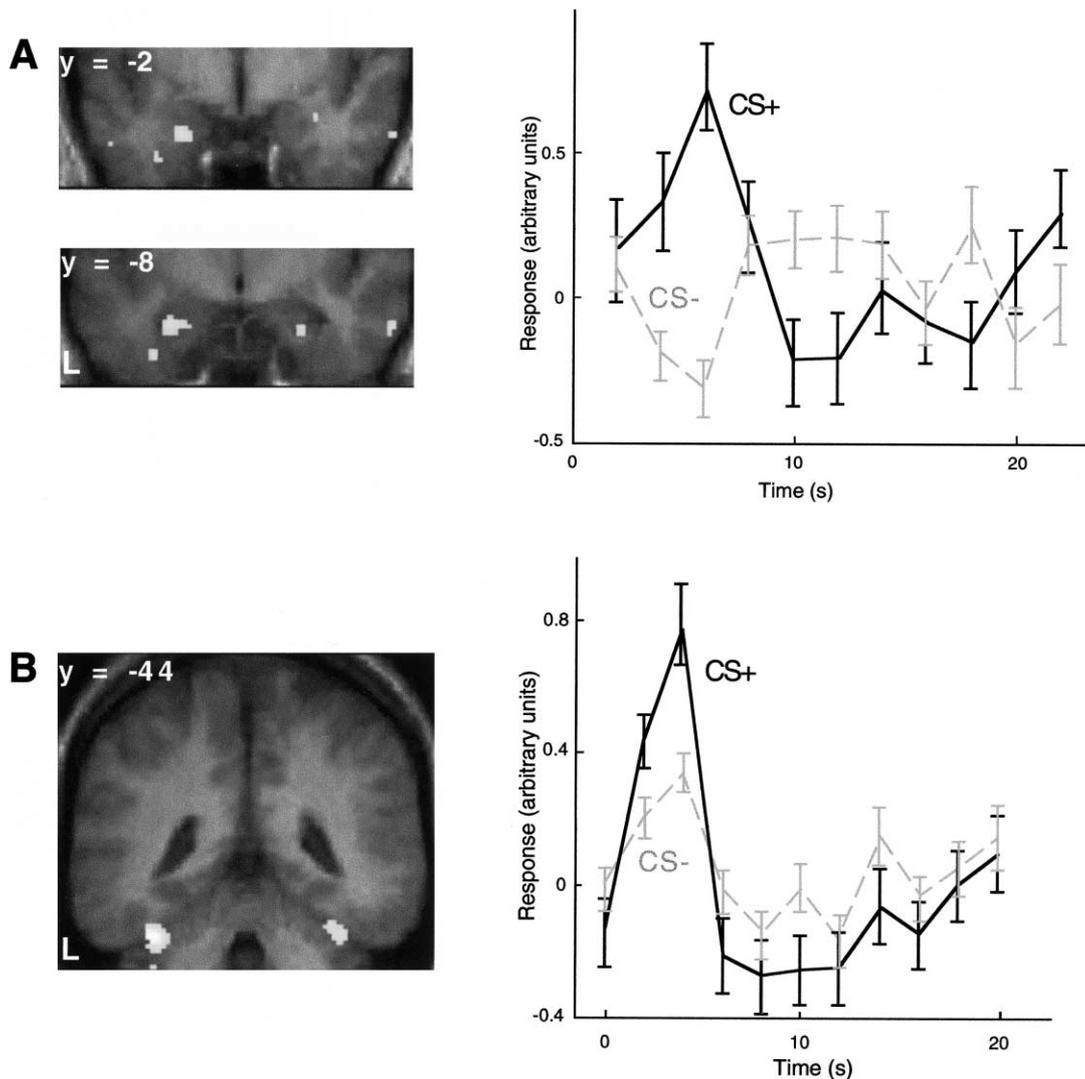

Fig. 2. Left: coronal slices depicting the activation of anterior and posterior amygdala (A) and fusiform gyrus (B) in CS+ compared to CS− trials derived from the group analysis, overlaid onto the mean anatomical MR image of all subjects, normalised to Talairach space using the MNI template. The coordinates and significance of the activations are given in Table 1. Right: group-averaged peri-stimulus time responses of the left amygdala voxel (A) and left fusiform gyrus (B) in response to the CS+ (black) and CS− (grey).

Table 1
Areas showing differential activations for the conditioned stimulus (CS+), compared to the CS−

Brain area	Coordinates (mm)	Z-score
Right inferior occipital gyrus	36, −78, −14	4.69
Left inferior occipital gyrus	−36, −62, −22	4.35
Right fusiform gyrus	40, −62, −24	4.19
Left fusiform gyrus	−38, −44, −28	4.87*
Right dorsal pons	4, −32, −42	5.10*
Right anterior amygdala	30, 0, −20	3.46**
Right posterior amygdala	26, −8, −26	3.45**
Left anterior amygdala	−24, −2, −28	4.09**

* *P*-value corrected for multiple comparisons within the entire brain volume.

** *P*-value corrected for multiple comparisons within a volume of interest based on [5].

delivered (i.e. the CS+/US trials, see Fig. 1), thus, removing the potential confound of US-elicited neural responses from the analysis (see [6]). This analysis revealed a statistically significant bilateral differential activations within the anterior amygdala and the right posterior amygdala, as well as bilateral activation in extrastriate regions centred on the inferior occipital gyrus and posterior fusiform cortex, and in the right dorsal pons (pontine tegmentum). The anatomical coordinates and significance levels of these activations are shown in Table 1, and the location of the amygdala activations is shown in Fig. 2A (left), overlaid on the subjects' mean normalised anatomical image. Fig. 2A (right) shows the peri-stimulus time courses for the CS+ and CS− for the left amygdala voxel. Fig. 2B (left) shows the anatomical locations of the activations in fusiform gyrus, whereas Fig. 2B (right) depicts the corresponding evoked responses to the

CS+ and CS− for the maximum voxel in the left fusiform gyrus.

3.2. Orienting of attention

3.2.1. Behaviour

Reaction times for target detection as a function of the event type are shown in Fig. 3. Subjects were significantly slower to respond to targets during *incongruent* trials, that is, when the CS+ and probe appeared on opposite sides of the visual display than during *congruent* trials (Wilcoxon test, $Z = 1.99$, $P < 0.05$). There was no significant difference between reaction times to the CS+ and to the CS− alone ($Z < 1$).

These results show that, as predicted, subjects' spatial attention was preferentially captured by the CS+. Given that the two stimuli used (angry faces) were equivalent in their salience and intrinsic affective value, and their assignment as CS+ or CS− counterbalanced across subjects, we can conclude that the capture of attention by the CS+ was due to its acquired aversive affective value through Pavlovian fear conditioning

3.2.2. Neuroimaging

Because we were particularly interested in the neural correlates of the modulation of spatial attention by the CS+, we collapsed, in the first instance, the congruent and incongruent trials, as in both cases subjects' attention was captured by the CS+ regardless of the location of the target. That is, we compared the two focused-attention conditions (congruent and incongruent) with the neutral/divided attention conditions (CS+ and CS−; see Fig. 1). We also analysed the neural activations associated with the comparison between congruent and incongruent trials, as described
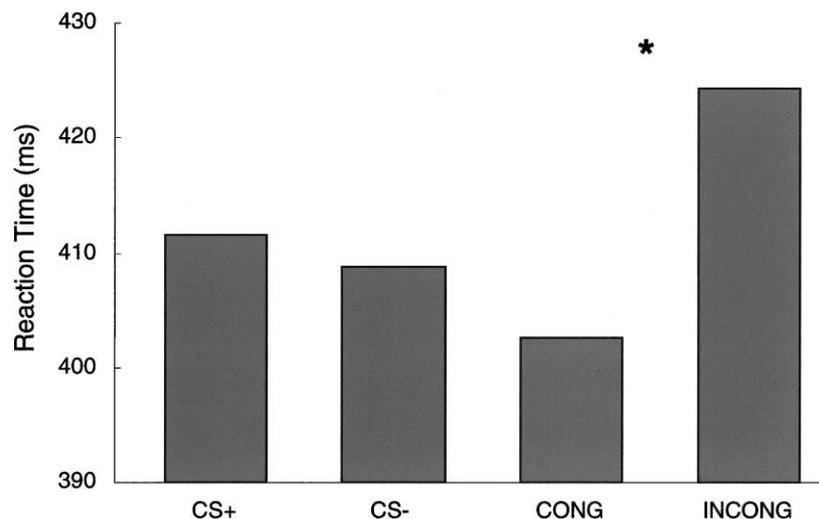

Fig. 3. Group-averaged reaction times to the peripheral target for the CS+, CS−, congruent (CS+ left, target left; CS+ right, target right) and incongruent (CS+ left, target right; CS+ right, target left) trials. Subjects were significantly slower in responding to the target in incongruent trials than in congruent ones (*P* < 0.05).

Table 2
Areas of significant differential activation during the focused-attention conditions (congruent and incongruent), compared to the neutral/divided attention conditions (CS+, CS−)[a]

Brain area	Coordinates (mm)	Z-score
Left SMA/anterior cingulate	−12, −2, 60	5.58*
Right SMA/anterior cingulate	4, 12, 58	6.18*
Left frontal eye fields	−28, −16, 62	5.20*
Right frontal eye fields	40, −2, 62	4.67
Left anterior IPS/precentral sulcus	−40, −34, 46	4.86*
Right anterior IPS/precentral sulcus	40, −32, 36	4.05
Left IPS	−32, −50, 58	5.46*
Right IPS	42, −48, 54	3.82
Left orbitofrontal cortex	−32, 46, −6	4.86*
Right orbitofrontal cortex	30, 50, −6	4.15

[a] SMA: supplementary motor area; IPS: intraparietal sulcus.

* P-value corrected for multiple comparisons within the entire brain volume.
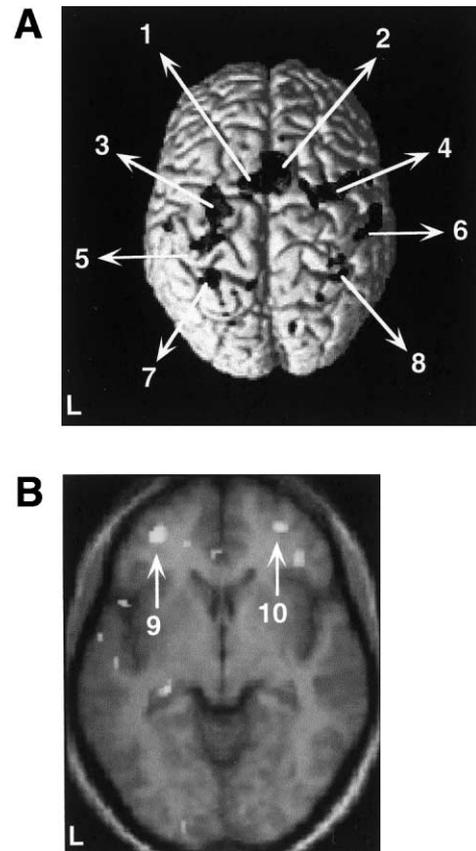

Fig. 4. (A) Dorsal view of a T1-weighted anatomical template normalised into Talairach space, showing the cortical regions displaying increased activation in the focused-attention trials, compared to the neutral/divided attention ones (see Fig. 1). (B) Differential activation of the orbitofrontal cortex in the focused-attention trials compared to the neutral/divided attention conditions. The activations are overlaid Talairach onto the average anatomical MR image of all subjects, normalised to Talairach space using the MNI template. Images are thresholded at $P < 0.001$ uncorrected for visualisation. Numbers correspond to the areas reported in Table 2.

below. Table 2 shows the anatomical locations and levels of significance in areas more active in the conditions involving focused spatial attention. The locations of these activations are shown in a rendered canonical brain in Fig. 4A. We observed differential activation of bilateral supplementary motor area (SMA)/anterior cingulate, left parietal cortex (IPS, extending into the post-central sulcus) and left frontal eye fields (extending into the precentral sulcus). There was also activation of the corresponding areas on the right hemisphere, although they did not reach the significance criterion of $P < 0.05$ corrected (all areas $P < 0.001$ uncorrected; see Table 2).

In addition, we observed significant activation of lateral orbitofrontal cortex (lOFC) in the left hemisphere and, to a lesser degree, in the right (Fig. 4B and Table 2). This activation, centred on the anterior aspects of BA11, corresponding to the anterior orbital gyrus [10,11], was specific to the focused-attention trials, and was equally expressed in the congruent and incongruent trials, as confirmed by an inspection of the corresponding parameter estimates obtained from the analysis. Furthermore, in a contrast of each of the focused-attention conditions separately (i.e. congruent and incongruent) with the neutral/divided attention trials, we obtained similar magnitudes of activations in lOFC in both cases (congruent: $Z = 4.5$, incongruent: $Z = 3.9$). A contrast of the simple main effects of the neutral/divided conditions did not reveal activation in this area, even when we adopted a less stringent significance threshold ($P < 0.01$ uncorrected).

Previous studies [14,27,46] have reported an interaction between laterality of activations and direction of attention shift, particularly in parietal cortex. Specifically, activations in a given hemisphere are more pronounced when attention is directed to the contralateral visual field, especially for the left hemisphere. We explicitly tested this prediction by dividing the focused-attention trials based

on the laterality of the CS+, independently of target position.

Trials in which the CS+ was presented on the left visual field, compared to neutral/divided attention trials, resulted in significant parietal activations in the right hemisphere ($x = −44$, $y = −38$, $z = 48$, $Z = 3.75$, $P < 0.001$ uncorrected), whereas right CS+ presentations significantly activated left and right parietal cortices (left: $x = 36$, $y = −38$, $z = 38$, $Z = 3.91$, $P < 0.001$ uncorrected; right: $x = 38$, $y = −30$, $z = 40$, $Z = 3.50$, $P < 0.001$ uncorrected).

Finally, we investigated the differences in haemodynamic responses between congruent and incongruent trials. A contrast between incongruent and congruent conditions revealed no differentially activated regions after correcting for multiple comparisons across the brain. However, given that in an fMRI study of spatial attention Nobre and co-workers [15,45] reported orbitofrontal activations associated exclusively with incongruent trials, we specifically explored the possibility of similar activations in our study. Consistent with

their findings, we observed activation in left lateral OFC ($x = -24$, $y = 30$, $z = -18$; $Z = 3.32$, $P < 0.001$), close to the location ($x = -30$, $y = 30$, $z = -18$) reported by Coull et al. [15]. It is important to point out that the anatomical location of this activation, located in the posterior orbital gyrus [10], is distinct from the ones associated with the focused-attention trials (Table 2 and Fig. 4B), which were present in both congruent and incongruent trials (see earlier sections).

4. Discussion

4.1. Conditioning-induced differential responses

The differential amygdala activation, extending into neighbouring perirhinal and entorhinal cortices, in response to the CS+ observed in this study is in agreement with previous human functional neuroimaging studies [5,6,33,44] and single-unit recordings in rodents (e.g. [49,50]) during fear conditioning.

Unlike some previous fMRI conditioning studies [5,6,33], the activations elicited by the CS+ did not decrease over the course of the experiment. This finding is consistent with a recent study by Morris et al. [42], showing a possible dissociation in the temporal patterns of CS-related activations within the amygdala. Specifically, Morris et al. found that responses in the ventral amygdala, in a location close to the one found in our study, did not show time-related decreases, whereas such time changes were observed in the dorsal amygdala. Although the reasons for the differences between studies are yet not clear, Morris et al. suggested that the discrepancy could be related to the nature of the conditioned stimuli. In their study, they used angry faces, which have been shown to facilitate the acquisition and maintenance of conditioned responses [21]. In contrast, the previous studies used either neutral faces [6] or colour patches [33]. The present findings are consistent with this hypothesis, as we also used angry faces as conditioned stimuli. Other explanations, based on task-related differences, are also possible. Whereas in previous studies, subjects were passively exposed to the CSs, in our study they were asked to perform a reaction time task, which demanded sustained attention, and could, thus, have altered the level of general arousal. It is important to point out, however, that the coexistence of time-dependent and time-independent amygdala conditioning-induced increased responses to the CS+ is in agreement with single-unit studies in rodents, showing distinct population of lateral amygdala cells with differential time courses of responses [49–51].

The differential activation associated with CS+ trials observed in the dorsal pons, in what appears to be the caudal pontine reticular nucleus (PnC), is consistent with its role in the acoustic startle reflex (for reviews see [18–31]). In the present study, the visual CS+ was associated with the expectation of a loud burst of white noise, the US, whereas the CS− was not. Previous studies have shown that the startle reflex can be potentiated by the presence of a visual conditioned stimulus, by way of direct projections of the central nucleus of the amygdala to the PnC (see [19]). Thus, the activation observed here may be associated with the preparation of motor responses in response to an aversive stimulus. Although no auditory US was presented in the trials analysed in this contrast, expectation of its presentation could lead to an enhanced response of the reticular formation, by way of direct projections from the central nucleus of the amygdala [53].

Finally, the differential activation in sensory cortical areas (e.g. fusiform gyrus) in response to the CS+ is consistent with previous neuroimaging [6,43] and electrophysiological [2,49,59] studies, supporting the notion that fear conditioning can modulate the cortical processing of sensory information, probably by way of direct and indirect feedback projections from the amygdala [1,2,35].

4.2. Modulation of spatial attention by conditioned fear stimuli

The main objective of the present study was to assess, both behaviourally and neurophysiologically, whether stimuli that acquire aversive value, through classical conditioning, modulate spatial attention. The behavioural results, shown in Fig. 3, demonstrate that conditioned stimuli can indeed capture subjects' attention. Our findings are entirely consistent with previous behavioural studies showing similar effects employing naturally threatening stimuli, such as angry faces (compared to neutral ones) [38]. This study, however, has the advantage that the stimuli used had an intrinsically equivalent affective value prior to the experiment; the only difference was that one of them was consistently associated with an unconditioned aversive stimulus. Because of this, we can rule out the possibility that the attention effects were due to physical differences between the stimuli, rather than their emotional value.

The lack of a significant difference in reaction times between the CS+ and CS− trials is perhaps somewhat surprising. It could be argued that the presentation of the CS+ in both hemifields should have resulted in an enhancement in divided attention and, thus, result in faster response times to the target than in the case of CS− presentations. One possible explanation for the negative finding is that because all trials were preceded by a fixation cross alerting the subjects to be ready to detect the presence of a target, their attention would be already allocated equally to both hemifields, and thus, the presentation of the same stimulus on both sides, regardless of its affective value, would have no further effect on the distribution of attentional resources. This could also account for the lack of significant activation of the attention network in the comparison between CS+ and CS−. Another possibility is that a putative reduction in RTs to the CS+, due to enhanced attention, was counterbalanced by an interference effect. It has been shown that the presentation

of stimuli with aversive value can interfere with an ongoing unrelated task, resulting in longer response times to the task (e.g. [60]). The experimental paradigm used in the present study does not allow us to argue for either of these, or other, possible interpretations.

Stormark and co-workers [55,56], employing a similar procedure as the one used here, reported a *reduced* cost of processing targets invalidly cued by a CS+. This result appears to contradict our findings. However, a major difference between the two studies was the duration of the CS+: in the Stormark and co-workers study the CS+ was shown for 600 ms, whereas in the present study the duration was only 50 ms. Previous studies have shown that when the cue is present for longer than 300–500 ms, reaction times to stimuli in the same location are actually slower, a phenomenon known as inhibition of return (IOR) [47]. It is, thus, possible that the results obtained by Stormark et al. reflect an IOR elicited by the conditioned stimulus. However, other reasons for the discrepancy between the two studies are possible and more studies (for example, varying in a parametric fashion the duration of the CS+) would be necessary to further elucidate this issue.

The modulation of attention by the CS+ observed in the behavioural responses was associated with the activation of a distributed neural network that largely overlaps with the fronto-parietal network consistently proposed as having a key role in spatial attention and reported in previous neuroimaging studies (e.g. [13,14,16,27,29,46,52]), as well as bilateral activation of lateral OFC (see following sections). This pattern of activations provides direct support to the hypothesis that attention can be captured by stimuli that signal threat, such as the CS+ in this study, in an automatic fashion. It is important to note that in all trials, regardless of the attention condition, subjects were performing the same target detection task, for which the face stimuli were irrelevant. The key difference between experimental conditions was that in the case of neutral or divided attention condition (same stimulus in both hemifields), there was no further modulation of spatial attention by the face stimuli, whereas in the congruent and incongruent trials, subjects' spatial attention was shifted towards the location of the CS+ as demonstrated by the reaction times described above. Thus, the activations reported in Table 2 correspond to neural activity above and beyond that associated with target detection and motor responses.

The activation of the anterior aspect of the IPS (see Table 2) extended into the post-central sulcus. The spatial resolution of our images does not allow us to assess whether this activation lies entirely within the parietal lobe or in fact it also reflects some somatosensory activity. This latter possibility is particularly interesting given the suggested role of somatosensory cortex in emotional evaluation (e.g. [17]), and should be the focus of future investigation.

The orbitofrontal activation observed when attention was influenced by an emotional stimulus is intriguing, as activation of this region of prefrontal cortex has not been previously reported in neuroimaging studies of attention (for review see [7]) or fear conditioning [5,6,44]. Lateral OFC is ideally placed to provide an interface between these two processes, as projections from the amygdala to the lateral OFC are well documented in several species [8,32,36,40], and important connections exist between the OFC, particularly the anterior lateral region, and the posterior parietal cortex and frontal eye fields [9,40,41]. Therefore, cells in the OFC can relay information about the affective value of a given stimulus in the environment from the amygdala to cortical areas subserving attention. Future studies may help to further elucidate the role of lateral OFC in the modulation of attention by emotional stimuli.

4.3. Congruent versus incongruent trials

The event-related nature of our experiment allowed us to separate the attention trials between congruent and incongruent. Such analysis revealed a significant activation in orbitofrontal cortex during incongruent trials, consistent with previous studies [15,45]. As mentioned above, this activation occurred in an area of OFC different, more ventral and posterior, from that activated in the focused-attention conditions, putatively in the posterior orbital gyrus (see [10]). Thus, it appears that different regions within lOFC are involved in the capture of attention by emotional stimuli and the "breaches of expectation" [45] that may subsequently occur.

In summary, we have shown that stimuli which acquired aversive value through fear conditioning can capture subjects' attention to their location. Furthermore, our study demonstrates that this modulation of attention by conditioned stimuli engages the fronto-parietal neural network thought to underlie the control of spatial attention, as well as the anterior lOFC.

Acknowledgements

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