CHAPTER 4

Dynamics of emotional effects on spatial attention in the human visual cortex

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Abstract: An efficient detection of threat is crucial for survival and requires an appropriate allocation of attentional resources toward the location of potential danger. Recent neuroimaging studies have begun to uncover the brain machinery underlying the reflexive prioritization of spatial attention to locations of threat-related stimuli. Here, we review functional brain imaging experiments using event-related potentials (ERPs) and functional magnetic resonance imaging (fMRI) in a dot-probe paradigm with emotional face cues, in which we investigated the spatio-temporal dynamics of attentional orienting to a visual target when the latter is preceded by either a fearful or happy face, at the same (valid) location or at a different (invalid) location in visual periphery. ERP results indicate that fearful faces can bias spatial attention toward threat-related location, and enhance the amplitude of the early exogenous visual P1 activity generated within the extrastriate cortex in response to a target following a valid rather than invalid fearful face. Furthermore, this gain control mechanism in extrastriate cortex (at 130-150 ms) is preceded by an earlier modulation of activity in posterior parietal regions (at 40-80 ms) that may provide a critical source of top-down signals on visual cortex. Happy faces produced no modulation of ERPs in extrastriate and parietal cortex. fMRI data also show increased responses in the occipital visual cortex for valid relative to invalid targets following fearful faces, but in addition reveal significant decreases in intraparietal cortex and increases in orbitofrontal cortex when targets are preceded by an invalid fearful face, suggesting that negative emotional stimuli may not only draw but also hold spatial attention more strongly than neutral or positive stimuli. These data confirm that threat may act as a powerful exogenous cue and trigger reflexive shifts in spatial attention toward its location, through a rapid temporal sequence of neural events in parietal and temporal-occipital areas, with dissociable neural substrates for engagement benefits in attention affecting activity in extrastriate occipital areas and increased disengagement costs affecting intraparietal cortex. These brain-imaging results reveal how emotional signals related to threat can play an important role in modulating spatial attention to afford flexible perception and action.

Introduction

Negative emotions such as fear or anger imply both the appraisal of the presence of some nuisance, and the elicitation of appropriate behavioral reactions. Accordingly, emotional processes may be intimately linked to action tendencies (Lang, 1979; Frijda, 1986) that can be mapped onto either a defensive motivational system (for negative emotions) or an appetitive motivational system (for pleasant emotions). Heightened vigilance and enhanced allocation of cognitive resources toward motivationally relevant information in the environment,
particularly when potentially threatening, is certainly among the most crucial adaptive aspects of emotional processing (Frijsda, 1986; Eysenck, 1992; Cacioppo and Gardner, 1999), presumably shaped during evolution across many species to promote adequate actions and behaviors in the service of survival (Ohman and Mineka, 2001). In humans, abundant empirical evidence has converged from different fields in clinical psychology and cognitive sciences to indicate that processing of threat-related stimuli can exert strong influences on attentional mechanisms (Fox, 2002; Vuilleumier et al., 2004a), which constitute one of the most central cognitive abilities controlling perception and action. Furthermore, some of these interactions of emotions with attentional and cognitive functions are liable to important modulations by individual or contextual factors, including for instance anxiety, personality traits, learning, or goals and values. Thus, studies of emotion and attention interactions can provide many precious insights into the basic functional architecture of the human mind and more subtle individual differences.

Here, we review our recent brain imaging work using event-related potentials (ERPs) and functional resonance imaging (fMRI) that has attempted to uncover the neuroanatomical substrates and temporal dynamics underlying the regulation of attentional resources by emotional processes. In particular, we will review recent data concerning the networks and time-course of neural activity in the healthy human brain that may control the spatial distribution of visual attention in response to threat-related cues in the peripheral visual field (Fox, 2002; Vuilleumier, 2002). We used electrical and hemodynamic brain-imaging approaches during a very simple, well-standardized experimental paradigm (i.e., the dot-probe task, Bradley et al., 2000), allowing us to explore the sequence of neural events at stake during the different processing stages necessary to orient spatial attention toward behaviorally relevant stimuli (e.g., shift, engage, and disengage Posner et al., 1980), and thus enabling us to examine how emotional signals of threat might influence these different attentional mechanisms.

In this classical dot-probe paradigm (Fig. 1A), derived from the spatial orienting task originally designed by Posner et al. (Posner et al., 1980; Navon and Margalit, 1983), subjects are required to detect a neutral visual target (i.e., a dot or probe) whose location is uncertain from trial to trial but unpredictably preceded by another emotionally significant stimulus (i.e., a cue). Critically, this emotional cue can appear at either the same location as the subsequent target (valid trial) or at another location in the visual field (invalid trials), such that if the emotional value of the cue can exert some capture on the spatial distribution of attention, it will lead to a facilitation of target processing in the former (valid) situation and/or to a distraction from target processing in the latter (invalid) situation (Mogg and Bradley, 1999b). Accordingly, such effects on spatial orienting have been documented by several behavioral studies using a variety of threat-related cues including pictures of aversive scenes (Mogg and Bradley, 1998; Mogg et al., 2000), aversive words (MacLeod et al., 1986; Mogg et al., 1994), emotionally negative faces (Mogg and Bradley, 1999b; Bradley et al., 2000), or averringly conditioned stimuli (Armony and Dolan, 2002; Koster et al., 2004b, 2005). Moreover, these effects have often been found to vary as a function of individual anxiety levels, even in people without clinical manifestations (Fox et al., 2001; Koster et al., 2004b). However, behavioral studies have provided somewhat conflicting results as to whether the emotional effects on spatial attention in the dot-probe task (and the influence of anxiety on these processes) might primarily result from a facilitation of orienting to the targets following valid emotional cues (i.e., via shifting and engaging processes), or conversely from an interference on reorienting to the targets following invalid emotional cues (i.e., on disengaging processes) (Fox et al., 2001; Koster et al., 2004a; Mathews et al., 2004; see Fig. 1B).

In our studies, by combining ERPs and fMRI during the dot-probe task, we could distinguish between brain responses to the cues themselves and their potential effect on the subsequent target as a function of cue validity, and thus show distinct emotional influences on orienting and reorienting stages in attention (Fox et al., 2001). While ERPs provide brain-imaging measures with a high temporal resolution allowing the registration of
neural activity from the scalp on a millisecond time-scale, which is optimal to separate cue and target processing. fMRI provides a measure with a much poorer temporal resolution of the order of 1–4 s but with excellent millimetric anatomical resolution. In addition, we also used modern source localization techniques allowing us to assess the temporal dynamics of the cascade of successive stages implicated during spatial orienting. Taken together, our imaging data converge to suggest (i) that the deployment of spatial attention toward threat signals (here conveyed by fearful faces) can occur rapidly and produce an enhanced sensory response to targets within the extrastriate
visual cortex (at <200 ms); (ii) that this effect might result from a direct modulation of visual cortex by emotional inputs which can facilitate spatial orienting toward the target, through mechanisms controlled by the posterior parietal cortex and activated prior to the enhancement of target processing (at <100 ms); and (iii) that activation of these neural circuits by invalid emotional cues can produce a cost in disengaging attention toward a target presented at another location, by reducing the activity of orienting mechanisms within posterior parietal cortex, but at the same time inducing concomitant increases in the response of other brain regions within the ventromedial prefrontal cortex. These data therefore indicate that neural mechanisms responsible for orienting spatial attention toward threat-related stimuli may partly overlap with those controlling shifts of spatial attention through nonemotional (neutral) cues, but also involve partly distinct mechanisms. We discuss these brain-imaging observations in a more general framework (Vuilleumier, 2005) proposing that emotion and attention may operate through parallel neural pathways that can exert additive modulatory influences on sensory processing in the visual cortex.

Emotion and spatial attention

A facilitation of spatial attentional orienting by threat signals has been documented in a variety of behavioral tasks (for review see Vuilleumier, 2002), including not only covert orienting in dot-probe tasks where emotional stimuli can act as exogenous spatial cues (MacLeod et al., 1986; Mogg and Bradley, 1999b; Bradley et al., 2000; Fox et al., 2001), but also visual search tasks where emotionally negative targets are detected faster than neutral or positive targets (Hansen and Hansen, 1988; Fox et al., 2000; Eastwood et al., 2001; Ohman et al., 2001). In many studies, these emotional effects on attention were obtained with negative stimuli, such as fearful or angry faces, whereas positive stimuli produced less consistent effects, suggesting a special role of threat-related cues in neural systems governing emotion and attention interactions. Moreover, some effects of positive emotional cues on attention might be more frequently found in visual search tasks (Juth et al., 2005; Williams et al., 2005) than in dot-probe orienting tasks, possibly reflecting some intrinsic differences in attentional processes engaged in these two situations. Orienting to dot probes typically involves a single and rapid shift of attention toward brief stimuli that are presented in peripheral visual field; whereas visual search requires serial shifts of attention among stimuli that can be processed by foveal vision and remain visible throughout the task, potentially recruiting other exploratory strategies, including eye movement control.

In the dot-probe task, emotional stimuli are generally irrelevant to the task, and subjects are instructed to respond only to the dot-probe target that can unpredictably appear at one of two possible locations (Fig. 1A), either replacing the location previously occupied by the emotional stimulus (the so-called valid) or replacing another neutral position (the so-called invalid). In the initial study using this paradigm (MacLeod et al., 1986), words (one threatening, one neutral) were presented at two separated spatial locations (in the upper and lower visual field) and followed after a short-time interval by a small dot probe at the spatial location of one of the two words. Participants were asked to respond as fast as possible to the dot probe. Results indicated that people with higher anxiety level directed their attention more readily to the location of threat-related words, suggesting a facilitated detection of threat with anxiety (Eysenck, 1992). Subsequent variants of this paradigm (Fox, 1993; Bradley et al., 1997) have used different types of cues to examine emotional influences on spatial attention in both (subclinical) anxious and nonanxious individuals (see Fox, 2002 for an overview). In many studies, stimuli have been presented laterally in either visual hemifield (rather than vertically), but only a few have found reliable differences between hemifields (Mogg and Bradley, 1999a; Hartikainen et al., 2000; Fox, 2002). Remarkably, similar emotional biases in spatial attention have been observed with different types of targets and tasks, including simple detection or more complex discrimination tasks (see Mogg and Bradley, 1999b; Bradley et al., 2000).
The dot-probe task can thus provide a useful snapshot of attentional allocation toward emotional stimuli by computing the difference in reaction times and/or accuracy rate for dot-probe targets appearing at invalid minus valid locations (Bradley et al., 2000). Note, however, that the “attentional bias” measure obtained by this invalid–valid difference might in principle reflect either faster orienting to targets at valid locations, or slower reorienting to targets at invalid locations, or both (Fox et al., 2001; see Fig. 1B). In several studies (Fox et al., 2001; Koster et al., 2004a; Mathews et al., 2004), target detection was found to be slowed by threat cues more than by neutral or positive cues presented at an invalid location, even though threat produced no advantage over neutral or positive cues when the targets were presented at valid locations, suggesting that threat stimuli may not necessarily act by attracting attention to their own location, but rather by influencing the disengagement of attention from current fixation. However, other findings demonstrate a substantial facilitation in visual processing for targets presented at locations validly cued by an emotionally negative stimulus (Phelps et al., 2006). Furthermore, the fact that such attentional biases can arise in response to task-irrelevant emotional stimuli also suggests that these effects may operate in a remarkably involuntary manner, even when potentially harmful for optimal performance (e.g., on invalid trials). Some studies reported significant biases under conditions where emotional cues (faces) were masked and rendered invisible (Mogg et al., 1994, 1995; Mogg and Bradley, 1999a). In our own experiments, similar effects were often observed in subjects who failed to note any emotional features in facial cues presented in their visual periphery (Pourtotis et al., 2004). Further behavioral studies are needed to investigate whether some changes in the strategic set to respond to peripheral events vs. to focus on central stimuli may affect the degree of involuntary spatial orienting to emotional cues. However, some studies have reported significant interference by peripheral emotional flankers in tasks where subjects always responded to central stimuli only (Fenske and Eastwood, 2003).

Similarly, neuropsychological studies in brain-damaged patients with impaired spatial attention and hemi-neglect following parietal-lobe lesions have shown that their detection of stimuli in the contralesional (neglected) visual field is better for emotional than for neutral pictures (Vuilleumier and Schwartz, 2001a,b; Vuilleumier et al., 2002; Fox, 2002). Note that contralesional deficits in these patients were reduced but not abolished for emotional stimuli, indicating that spatial attention was facilitated toward these contralesional events, yet still necessary and clearly compromised to afford normal awareness. Importantly, these results suggest that spatial attention can be captured by contralesional emotional stimuli despite a profound impairment in directing attention toward that side. This may already indicate at least a partial dissociation between brain mechanisms responsible for controlling spatial attention in response to emotional vs. nonemotional cues, such that damage to spatial attention networks in fronto-parietal areas leading to neglect (see Driver and Vuilleumier, 2001; Kerkhoff, 2001; Corbetta and Shulman, 2002) may still leave intact some effects on attention that are triggered by emotionally charged cues (through their valence and/or arousal properties, see Lang et al., 1998; Sabatinelli et al., 2005).

Emotional signals may also influence attention during Stroop tasks (Pratto and John, 1991; Williams et al., 1996) and attentional blink experiments (Anderson, 2005). These nonspatial effects are beyond the scope of the present review (see Vuilleumier et al., 2004a), but also indicate a prioritization of processing for emotionally relevant information.

Time-course of spatial orienting to threat locations

In a recent ERP study (Pourtois et al., 2004), we used a modified version of the dot-probe task (adapted from Mogg et al., 1994) in normal (non-anxious) adult participants while we recorded high-density EEG (Fig. 2B) to track the time-course of spatial orienting toward the location of emotional stimuli. Cues were faces with fearful, happy, or neutral expression, appearing briefly prior to a single neutral target presented at the same location as one of these faces (see Fig. 2A). On each trial, two faces were first shown together,
for a duration of 100 ms, one in the left visual field (LVF) and one in the right visual field (RVF), one neutral and one with an emotional expression (fearful or happy, Ekman and Friesen, 1976). The faces were then replaced by a small bar-probe (duration of 150 ms), oriented either vertically or horizontally, appearing at the position just occupied by one of the faces (Fig. 2A). All stimuli (faces and bar-probe) were presented in the upper visual field to allow us to measure early retinotopic responses in ERPs (Jeffreys and Axford, 1972; Clark et al., 1995). Participants were asked to perform a go/no-go matching task in which they had to judge, on each trial, whether the orientation of
the bar-probe (in the LVR or RFV) matched that of the thicker line-segment within the fixation cross. The task was to press a button only when the bar orientation was the same as the thicker line of the cross (infrequent go trials), but to withhold responses otherwise (more frequent no-go trials). This task ensured that participants maintained their gaze on the central fixation cross (as confirmed subsequently by eye-tracking data, see below) and that all visual inputs were indeed restricted to the upper (peripheral) visual field. This also allowed us to record ERPs uncontaminated by any motor-related activity, since only ERPs for no-go trials were analyzed (Fig. 2C, D).

Critically, the bar-probe could appear either on the side of the emotional face (valid condition) or on the side of the neutral face (invalid condition), in an unpredictable (50% valid and 50% invalid) and randomized manner. However, faces were entirely irrelevant to the participants' task. Thus, spatial validity of the target-bar was arbitrarily defined by the position of the preceding emotion face expression. Moreover, since participants had to fixate the central cross, emotional cues appeared in a truly unattended location, which allowed us to properly assess any spatial biases in distribution of attention to peripherally presented probes (see Fox et al., 2001). We used only short-time intervals between the face pair and the bar onset (100–300 ms, systematically randomized) to tap exogenous mechanisms of spatial orienting (Egeth and Yantis, 1997).

Our main question was whether sensory responses to the peripheral bar-probes would be enhanced when replacing an emotional (valid) face, rather than a neutral (invalid) face, as predicted if spatial attention was involuntarily oriented toward that particular location (see Bradley et al., 2000; Armony and Dolan, 2002; Vuilleumier, 2002); and whether such attentional bias would differ between negative (fearful) and positive (happy) emotional cues. Our main comparison therefore concerned the amplitude or latency of ERP generated by the exact same bar-probe as a function on the different emotional values of the preceding face context (Fig. 2D). We predicted that any spatial orienting of attention should affect early visual processing stages activated by the target-bar, consistent with sensory gain or enhanced vigilance mechanisms (Heinze et al., 1990; Luck, 1995; Hopfinger and Mangun, 1998; Hillyard et al., 1998; Carrasco et al., 2000; Keil et al., 2005).

Behaviorally, our modified version of the dot-probe paradigm was successful to trigger exogenous shifts of spatial attention toward the side of the negative face cues (Mogg et al., 1994; Mogg and Bradley, 1999b; Bradley et al., 2000). Participants showed a better discrimination of bar orientation when the latter appeared in valid rather than invalid locations, as demonstrated by higher $d'$ values from signal detection theory (Green and Swets, 1966), and this spatial validity effect was significantly greater for fearful than happy faces (see Mogg and Bradley, 1999b).

Conventional analyses (Picton et al., 2000) on the exogenous visual ERPs confirmed that fearful faces (but not happy faces) significantly modulated the early sensory processing of bar-probes appearing at the same location. The lateral occipital P1 component peaking at 135 ms post-stimulus onset (Heinze et al., 1990; Luck et al., 1990) was significantly enhanced when the target-bar replaced a valid fearful face as compared with an invalid neutral face (Fig. 3A–C), even though the bars were always physically identical but differed only due to the preceding emotional face. This effect on P1 was equally present for bar probes shown in the upper LVF or RFV, in agreement with our behavioral results that did not show any hemispheric asymmetry in spatial orienting to threat faces (but see Mogg and Bradley, 1999b; Fox, 2002 for greater facilitation of RTs in the LVF in a similar paradigm). Source estimation methods (Pascual-Marqui et al., 1994) further confirmed that the P1 component was generated in the extrastriate visual cortex (Fig. 3D), including the middle occipital gyrus and inferior temporal gyrus (Pourtois et al., 2004). Such neural sources are consistent with previous ERP studies on P1 responses that were found to be modulated by spatial attention in tasks using nonemotional stimuli (Clark et al., 1995; Martinez et al., 1999; Di Russo et al., 2002, 2003).

These results therefore suggest an amplification of sensory responses to a neutral visual stimulus (bar-probes) taking place at early processing stages
Fig. 3. (A) Grand average waveforms in the fear condition (electrode PO8). The black vertical line bar indicates the onset of the bar probe (target). The P1 (area highlighted by an orange shaded area) was larger for fear valid compared to fear invalid trials, although the target stimulus was the exact same in these two conditions. (B) Mean global field power (GFP, see Lehmann and Skrandies, 1980) recorded 130–140 ms post bar-probe onset (corresponding to a temporal window where P1 amplitude was maximal) across the different experimental conditions. A signal increase is observed in the fear valid condition relative to the three other conditions (fear invalid, happy valid, and happy invalid), as indicated by a significant validity x emotion interaction. (C) Voltage maps for the P1 in the fear valid and fear invalid conditions (in the same 130–140 ms time interval following bar-probe onset) showing a more prominent P1 scalp topography in the former than the latter condition but without any qualitative change in the dipolar configuration of this map across conditions (amplitude modulation only). (D) Inverse solution by LAURA (Grave de Peralta Menendez et al., 2004) for the P1 revealing distributed brain sources in the extrastriate occipital cortex including the middle occipital gyrus (red line) and inferior temporal gyrus (blue line).

within extrastriate visual cortex, induced by the preceding emotional face presented at the same location. A greater amplitude of P1 activity in extrastriate visual cortex in response to bar probes following a fearful face also extend the related ERP findings by Stormark et al. (1995) who used emotion words (rather than facial expressions) and found enhanced P1 and P3 components for invalid trials, but with a longer SOA between the cue and the target (600 ms) as compared with the present study. In our study, we found no effect on the latency of ERPs (Pourtois et al., 2004). The effect of threat signals on visual processing is therefore strikingly similar to the effect previously obtained with explicit manipulations of spatial attention (Heinze et al., 1990; Hillyard et al., 1998).
which is usually thought to operate by gain control mechanisms imposed on visual pathways through top-down signals from parietal and frontal areas. Such boosting of visual cortical processing may thus provide a neural substrate for recent psychophysical findings showing that the presence of a fearful (as opposed to neutral) face can enhance contrast sensitivity and reduce detection threshold for a following visual stimulus (Gabor patch), an effect that is also magnified with transient covert attention (Phelps et al., 2006). By contrast, we found that positive emotional cues conveyed by happy faces did not produce any effect on P1 responses to bar-probes appearing at valid vs. invalid locations (Fig. 3B).

Importantly, in a control ERP experiment in a different group of participants, we could further ascertain that amplitude increases for P1 responses to bar-probe following fearful vs. neutral or happy faces was truly driven by the preceding facial expression rather than any low-level pictorial differences in the facial cues. Thus, no modulation of P1 was found when we used inverted (as opposed to upright) faces, which are known to impair the normal recognition of emotional expression in faces (Searcy and Bartlett, 1996). Moreover, a quantitative analysis of our face stimuli showed no significant difference in mean luminance, contrast, surface or central spatial frequency content between fearful, happy, and neutral faces (Pourtois et al., 2004).

Noteworthy, the effect of fearful faces on ERPs to subsequent target-bars was selective for the lateral occipital P1 component, but did not affect other exogenous visual components, such as the earlier C1 component arising from the primary visual cortex (see Clark et al., 1995) or the subsequent N1 component presumably generated by higher extrastriate areas within occipito-parietal cortex (Vogel and Luck, 2000; Fig. 3A). Spatial validity effects produced by nonemotional exogenous cues (e.g., light flash or abrupt onset) have also been found to affect predominantly the lateral occipital P1 component on valid trials (see Clark and Hillyard, 1996; van der Lubbe and Woestenburg, 1997; Hopfinger and Mangun, 1998), whereas the N1 component is classically not affected by exogenous cues (Hopfinger and Mangun, 1998) and is more sensitive to attentional manipulations requiring feature discrimination rather than detection (Vogel and Luck, 2000). Likewise, C1 component is thought to reflect initial processing in primary visual cortex that is not affected by spatial attention (Martinez et al., 1999; Di Russo et al., 2003), although primary visual cortex might be modulated at a later delay through feedback mechanisms from higher cortical areas (Martinez et al., 1999; Noesselt et al., 2002). Thus, our results suggest that the spatial orienting induced by fearful faces may operate through a modulation of early exogenous visual response in extrastriate areas, and act on the same processing pathways as traditional influences of spatial attention controlled by fronto-parietal mechanisms.

Early responses to emotional faces preceding visual targets

One limitation of behavioral measures in the dot-probe task is that the attentional biases can only be measured at the time when the target-probe is presented, while any effect triggered by emotional cues themselves, prior to the subsequent attentional consequence on target processing, cannot directly be registered since behavioral measures provide only a snapshot of attentional focus by comparing the different responses to targets (Mogg and Bradley, 1999b). In our ERP study, however, continuous EEG recordings could be obtained not only in response to the bar-probe (as described above) but also in response to the preceding face pair (Fig. 2C). This allowed us to assess whether fearful or happy faces in the initial cue display actually produced any differential brain response already prior to the onset of the target (bar-probe).

Thus, although our main question concerned how the location of emotional faces in the cue display affected ERPs time-locked to the subsequent bar-probe (see above), we also analyzed ERPs time-locked to the face pairs (Pourtois et al., 2004). This analysis revealed a striking effect of emotion on very early visual responses to faces, affecting the C1 component (Clark et al., 1995), which was selectively enhanced by fearful expressions. Thus,
C1 had a significantly higher amplitude for displays with a fearful face than a happy face, irrespective of the visual hemifield in which the fearful face was presented, with mean latency of 90 ms post onset. The scalp topography of this effect showed a negative polarity that corresponded to the expected response to visual stimulations (bilateral face display) presented in the upper visual field (Clark et al., 1995). A distributed source localization estimate also confirmed that this C1 response was evoked by main generators in two regions of the occipital visual cortex, including the cuneus and lingual gyrus, corresponding to early striate cortex (see Pourtois et al., 2004).

This early valence effect of face expressions on ERPs to the cue display was not observed for the subsequent P1 or N170 components elicited by these faces. Moreover, this also allowed us to rule out the possibility that the modulation of P1 amplitude to targets could reflect a mere carry over effect, for example, due to some slow potential wave following emotional faces that would persist and contaminate subsequent ERPs to bar-probes (see Walter et al., 1964) despite our carefully randomized SOAs between faces and targets. Furthermore, analysis of low-level visual features in faces did not suggest any difference that could have caused early C1 increases (see above), and our control experiment with inverted faces did not produce a similar effect.

Such early effects of emotional expression have not been previously reported for ERPs to fearful faces, which usually evoke later modulations in the P1, N170, and/or subsequent components (Pizzagalli et al., 1999, 2002; Krolak-Salmon et al., 2001; Eimer and Holmes, 2002; Batty and Taylor, 2003; Ashley et al., 2004; see Vuilleumier and Pourtois, in press for a recent overview). However, most studies on emotional faces have always presented stimuli only centrally or aligned on the horizontal meridian, which may prevent a reliable C1 component evoked by more peripheral stimulation in upper or lower visual fields (see Jeffreys and Axford, 1972; Clark et al., 1995). However, a previous MEG study (Halgren et al., 2000) has already reported a similar early visual effect for centrally presented emotional faces (sad vs. happy faces) arising in the occipital striate cortex. The early latency (∼110 ms) of this emotion effect was puzzling, given that the authors only found a reliable difference between faces and scramble faces (i.e., basic categorical effect) at a later latency, around 165 ms post-stimulus onset, with sources located more anteriorly within the fusiform gyrus. According to Halgren et al. (2000), this early differential response to emotional face expression in early visual areas (V1) could serve to rapidly decode these socially relevant stimuli in distant regions such as the amygdala, which begins to respond to faces at ∼120 ms (Halgren et al., 1994) and which receives projections from early visual areas (Amaral et al., 2003). This could explain the preserved emotional processing of faces sometimes reported in prosopagnosic patients with occiptotemporal damage (Tranel et al., 1988). The nature of this C1 effect remains unclear and needs further replications; but it might also reflect a rapid modulation of primary visual cortex by reentrant feedback from emotion-related areas such as the amygdala (Anderson and Phelps, 2001; Amaral et al., 2003; Vuilleumier et al., 2004b), possibly activated at similar or even earlier latencies (Krolak-Salmon et al., 2004; Halgren et al., 1994; see Kawasaki et al., 2001 for early visual responses to emotional stimuli in the ventral prefrontal cortex), or alternatively reflect some other deeper sources activated at the same latency and contributing to a similar occipito-parietal scalp topography as the classic C1 component.

We further asked whether this early effect of fearful faces on C1 responses might be functionally related to the subsequent enhancement of responses to the bar-probes. To indirectly address this issue, we examined whether there was any relationship between the amplitude of the C1 evoked by the face cues, and the magnitude of the validity effect on amplitude of P1 evoked by the bar target (Pourtois et al., 2004). Strikingly, we found a significant positive correlation between C1 time-locked to faces and enhancement of P1 time-locked to subsequent bar-probe, selectively arising in the fear condition, whereas there was no significant correlation in the happy condition. This correlation suggests that, even though the time interval between the two stimuli varied randomly, the larger the C1 response to a fearful face in the
peripheral visual field, the larger the subsequent validity effect on the occipital P1 evoked by a bar-probe appearing at the same location. These data provide indirect support for the idea that direct feedback from amygdala on early visual cortex might induce a sustained boosting of sensory processing and attention to visual stimuli (Amaral et al., 2003; Vuilleumier et al., 2004b); and it raises further questions about whether such boosting can be retinotopic or hemifield/hemispheric-specific.

In keeping with this idea, several previous fMRI studies have shown that fearful faces can induce a greater activation of face-sensitive regions in fusiform cortex as compared with neutral stimuli (Morris et al., 1998; Vuilleumier et al., 2001; Armony and Dolan, 2002; Surguladze et al., 2003; see Sabatinelli et al., 2005 with emotional scenes), but similar emotional enhancements were also found in primary visual cortex (Vuilleumier et al., 2001; Pessoa et al., 2002) and in more lateral occipital areas (Lane et al., 1998). These fusiform and occipital increases to emotional faces are likely to depend on direct feedback from the amygdala because they are abolished in patients with amygdala lesions (Vuilleumier et al., 2004b) but persist in patients with parietal lesions (Vuilleumier et al., 2002). Moreover, such effects of emotion in early visual cortex may interact with selective attention and be further augmented when emotional stimuli appear in task-relevant location (Vuilleumier et al., 2001; Pessoa et al., 2002). It remains, however, unclear to what extent these increases can only affect the processing of emotional stimuli themselves, or also affect the processing of neutral stimuli following emotional cues as in our dot-probe paradigm.

Importantly, in these studies, the enhancement of P1 amplitude for attended relative to unattended stimuli was not associated with any concomitant change in latency, waveform, or scalp voltage topography of this component, suggesting that the effect of spatial attention on target processing may primarily correspond to a gain control mechanism arising in identical visual pathways (Luck, 1995; Hillyard et al., 1998; Carrasco et al., 2002). According to this model, spatial attention is thought to operate as an amplification of visual processing via top-down signals from fronto-parietal areas, which are activated prior to target onset in the case of preparatory/endogenous attention or at an earlier latency post-stimulus onset in the case of reflexive/exogenous attention. These fronto-parietal areas can then in turn enhance the neural responses in extrastriate cortex (see Kastner and Ungerleider, 2000; Hopfinger et al., 2000; Corbetta and Shulman, 2002).

In a follow-up study using our dot-probe paradigm (Pourtois et al., 2005), we therefore, tested whether any differential neural activity (e.g., within the fronto-parietal network) might precede the amplitude modulation of P1 responses to bar-probes and thus correspond to a possible source of attentional biases in spatial attention. To this aim, we employed a different approach than our previous waveform analysis and turned to topographical segmentation methods (Lehmann and Skrandies, 1980; Michel et al., 1999) that allowed the identification of subtle changes in the topographic configuration of scalp EEG over time. Such topographic changes can arise independently of component waveforms and independently of differences in field strength (i.e., the amplitude of waveforms; see Lehmann and Skrandies, 1980). A standard topographic analysis (Lehmann and Skrandies, 1980; Michel et al., 1999) was performed on ERP data from the same dot-probe task as used previously (Pourtois et al., 2004), which provides a spatio-temporal segmentation of the successive field configurations activated during the sequence of stimulus processing (usually referred to as "microstate". Lehmann and Skrandies, 1980). The rationale of this approach is to identify a series of statistically distinct topographic configurations (i.e., activity maps) over the

Cascade of neural events and source of sensory gain in extrastriate visual cortex

Our findings of increased P1 amplitude (without any change in the latency) for visual targets cued by fearful faces converge with similar effects observed in electrophysiological studies of spatial attention using nonemotional cues (van der Lubbe and Woestenburg, 1997; Hopfinger and Mangun, 1998; Hillyard and Anllo-Vento, 1998).
time-course of the evoked neural responses, reflecting the succession of different functional states engaged by stimulus processing, with the underlying assumption that topographic changes may denote the activation of distinct neural sources (Brandeis and Lehmann, 1986). Given that only landscape or topographic differences are of interest in this spatio-temporal cluster analysis, dominant maps are normalized to unitary strength values by dividing the voltage at each electrode by a measure of the global field power (Lehmann and Skrandies, 1980). Here again, we focused on responses evoked by the bar-probes, as a function of the preceding emotional face context.

This new analysis (Pourtois et al., 2005) first showed that EEG activity during the time-range of the P1 component evoked by bar-probes (120–160 ms) did not exhibit any differences in topographic configuration across the different emotion and validity conditions of preceding face cues, whereas there was a significant increase in the strength of this P1 topography (as indicated by a higher global field power, Lehmann and Skrandies, 1980) for targets following a valid fearful face as compared with an invalid fearful face (Fig. 3C). This pattern fully agrees with our hypothesis of a gain control mechanism enhancing visual target processing subsequent to orienting of spatial attention toward threat-related cues (Pourtois et al., 2004), as typically found with attentional orienting based on nonemotional cues (Hillyard et al., 1998).

More importantly, this analysis revealed the existence of an early (<100 ms post bar-probe onset) and stable (40–80 ms) topographical map that reliably distinguished valid from invalid target trials during the fear condition (Fig. 4A, B), just preceding the topographical maps corresponding to P1. No differential activity was seen for valid vs. invalid trials in the happy condition, although the same map was also present prior to P1. The neural sources estimated for this map were clearly distinct from extrastrate occipital sources associated with P1, and involved cortical generators in posterior temporal and posterior parietal regions instead (Fig. 4C). In other words, these data indicate that an early topographic microstate (at 40–80 ms post-target onset) was differentially activated when targets appeared at the same vs. different location as a fearful face; and that this distinctive configuration of neural activity preceded another subsequent microstate (at 120–160 ms) corresponding to P1, whose generators did not differ but whose amplitude was enhanced for valid vs. invalid targets following fearful cues (Pourtois et al., 2005). These results are consistent with the idea that a first sweep of activity in posterior temporal and parietal regions might take place rapidly after a visual target onset (Bullier, 2001; Foxe and Simpson, 2002) and possibly provide the signal for subsequent top-down control of target processing (Hopfinger et al., 2000; Kastner and Ungerleider, 2000; Bullier, 2001).

Remarkably, we also found that these two consecutive neural events were positively correlated (Pourtois et al., 2005; Fig. 4E), suggesting some functional coupling between the early posterior parietal activity (40–80 ms) and subsequent P1 activity (120–160 ms). The variance of the early 40–80 ms map (indexing the strength of its expression across subjects) showed a significant positive linear correlation with the variance of the next

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**Fig. 4.** (A) Grand average waveforms in the fear condition (electrode PO8) time-locked to the onset of the bar probe (valid and invalid trials collapsed). Before the onset of the P1 (area highlighted by an orange shaded area), there was a significant topography difference between valid and invalid trials in the fear condition, although no exogenous electric component was detectable at this specific lateral occipito-temporal site (PO8) during this early time-period (40–80 ms post bar probe onset). (B) Voltage maps in the fear valid and fearful invalid conditions in the 40–80 ms post bar probe showing a significant modulation of the global scalp configuration (with no change in amplitude). (C) Statistical parametric mapping provided by LAURA indicated that brain regions that were more activated by fear valid than fear invalid trials in the 40–80 ms post-bar-probe onset were mainly located in the left posterior parietal cortex (p < 0.001, uncorrected). (D) Conversely, fear invalid trials evoked more activation than fear valid trials in medial frontal regions (corresponding to rostral anterior cingulate cortex (ACC; p < 0.01, uncorrected) during the same time interval (40–80 ms post bar-probe onset). (E) There was an enhanced positive correlation between this early scalp map (40–80 ms post stimulus onset) and the directly following P1 map in the fear valid condition (r = 0.55, p = 0.03) but a clear attenuation of this correlation in the fear invalid condition (r = 0.004, p = 0.50), suggesting an enhanced coupling between these two successive functional microstates in the fear valid condition.
120–160 ms P1 map, which was present across all conditions but selectively enhanced for valid targets following fearful faces, and selectively suppressed for invalid targets following fearful faces (Fig. 4E). This enhanced coupling between parietal and extrastriate activity might provide a plausible neural mechanism underlying the facilitation in orienting spatial attention toward targets appearing at the location of threat-related cues (Fox, 2002; Vuilleumier, 2002). If early activity in posterior parietal and temporal regions following target onset (<100 ms) is implicated in the generation of top-down signals to influence ongoing visual processing in occipito-temporal areas (120–200 ms) (Kastner and Ungerleider, 2000; Bullier, 2001), then these functional influences appear to be enhanced for targets at valid conditions and disrupted for targets at invalid locations following fearful faces, with no such effect for happy faces.

Conversely, our topographical analyses revealed that ERPs to bar-probes invalidly cued by fearful faces were associated with a distinctive pattern of activity at the same early latency (40–80 ms), re-placing the posterior parietal and temporal activation related to spatial orienting (Fig. 4B, D). Neural sources for this distinct map were located within ventromedial prefrontal areas, including the rostral anterior cingulate cortex (ACC) (Fig. 4D). Such activation in rostral ACC may be consistent with a role in controlling attention in conflict situations (MacDonald et al., 2000) and error processing (Carter et al., 1999), particularly based on affective or motivational signals (Bush et al., 2000; Bishop et al., 2004a) or related to breaches in implicit expectation generated by invalid cues (Nobre et al., 1999). If spatial attention was reflexively oriented toward the location of the threat-relevant stimulus in face display, then a target appearing on the opposite side might require resolving a potential conflict between responding to the task-relevant stimulus and disengaging from the emotionally alerting stimulus. This selective invalidity effect of fearful faces in ERPs also converge with behavioral findings suggesting that negative stimuli may not only draw more easily, but also hold spatial attention more strongly than neutral stimuli, and thus lead to greater invalidity cost rather than greater validity benefit in covert orienting task (see Fox et al., 2001; Koster et al., 2004b). Problems in disengaging from threat signals might be particularly important in people with higher anxiety (even at subclinical level, see Fox et al., 2001; Mathews et al., 2004). Accordingly, increases in rostral ACC activity when ignoring emotional stimuli (Vuilleumier et al., 2001) have been found to be greater in anxious than nonanxious individuals (Bishop et al., 2004a).

Taken together, our ERP data (Pourtois et al., 2004, 2005) reveal a precise cascade of neural events involved during spatial orienting to peripheral visual targets, with selective influences of emotional cues conveyed by fearful faces. Targets following valid fearful faces evoked an enhanced exogenous visual response in extrastriate cortex (presumably through gain control mechanism), proceeded by specific enhancement of activity in posterior parietal cortex and posterior temporal regions; whereas the same targets appearing on the side opposite to a fearful face evoke no differential visual responses but greater activation of medial prefrontal regions. Collectively, these results have begun to provide novel insights into brain mechanisms by which fear-related signals can mobilize processing resources (Ohman and Mineka, 2001) and trigger a prioritization of spatial attention toward their location (Vuilleumier, 2002, 2005). In a follow-up fMRI study, we identified brain regions underlying this capture of spatial attention by threat-related stimuli.

**fMRI correlates for benefits and cost in spatial attention produced by threat cues**

Converging neurophysiological, neuropsychological, and neuroimaging studies (see Driver and Vuilleumier, 2001; Kanwisher, 2001) have now clearly established how nonemotional (neutral) exogenous (e.g., light flash or abrupt onset/offset) or endogenous/symbolic cues recruit specific brain regions associated with visual spatial attention in a variety of paradigms (Gitelman et al., 1999; Corbetta et al., 2000; Hopfinger et al., 2000; Woldorff et al., 2004). A distributed cortical network of dorsal regions in fronto-parietal cortex
directly participating to the control of spatial attention, including the intraparietal sulcus (IPS) and frontal eye field (FEF), is crucially involved in the voluntary or endogenous control of spatial attention (Mesulam, 1998; Kastner and Ungerleider, 2000), whereas a more ventral cortical network in the ventrolateral prefrontal cortex (VLPFC) and temporoparietal junction (TPJ) contributes to the detection of unexpected, behaviorally relevant or salient stimuli, with the latter ventral system interacting with the dorsal system during involuntary or exogenous shifts in attention (Downar et al., 2000; Corbetta and Shulman, 2002). Moreover, the more dorsal areas (FEF and IPS) may be rapidly activated following stimulus onset (see Bullier, 2001; Foxe and Simpson, 2002) to act as a regulatory source and directly contribute to the top-down selection of stimuli and responses in distant brain areas located within the temporal, frontal, and occipital lobe. In this perspective, this dorsal network plays a crucial role during the deployment of spatial attention and can bias activity in remote visual areas to narrow sensory processing onto relevant visual targets (Hopfinger et al., 2000). Posterior parietal regions are then responsible for imposing feedback signals on sensory areas to enhance processing of behaviorally relevant, attended events (Kastner et al., 1999). Moreover, when attention is oriented reflexively toward behaviorally relevant or salient (but emotionally neutral) stimuli, the same dorsal fronto-parietal network can be activated together with the TPJ and VLPFC, to promote a shift of processing resources toward the new events (Downar et al., 2000; Corbetta and Shulman, 2002; Peelen et al., 2004).

However, very few PET or fMRI studies have investigated whether the same fronto-parietal areas are also differentially activated during shifts of spatial attention in response to emotionally threatening stimuli. In a pioneer study, Fredrikson et al. (1995) found increased activation in superior parietal and frontal regions for fear-conditioned stimuli and suggested that such effects might reflect increased attention toward these stimuli. Another brain imaging study by Armony and Dolan (2002) was the first to use a dot-probe task in which averively conditioned faces served as cues and were presented in either visual field in an event-related manner, preceding the dot probe at either a valid or invalid location. Armony and Dolan (2002) reported an activation of fronto-parietal areas during shifts of attention toward a unilateral dot probe when the averively conditioned face stimulus (CS+) was briefly presented at a different location in the visual field prior to the target onset (see Mogg et al., 1994; Bradley et al., 2000), suggesting an involuntary capture of attention by the aversive face.

We recently conducted an event-related fMRI study (Poursots et al., 2006) using the same dot-probe paradigm as in our previous ERP work (Poursots et al., 2004; Fig. 2A) to identify neural substrates responsible for a spatially selective modulation of attention when threat cues were conveyed by fearful expression in faces, rather than by prior explicit conditioning (unlike prior studies, see Fredrikson et al., 1995; Armony and Dolan, 2002). Our aims were to determine how brain responses to a neutral visual target might be altered when preceded by emotional signals at valid or invalid locations, as previously investigated by the modulation of visual ERP components recorded on the scalp (Poursots et al., 2004). However, given the slow temporal resolution of fMRI (Bandettini, 1999), it was not directly possible to separate neural effects related to the processing of emotion in face pairs (cue) from those related to the processing of subsequent bar-probes (target). Moreover, in our ERP study, we used short temporal intervals between faces and targets (100–300 ms) to assess purely reflexive orienting mechanisms (Egeth and Yantis, 1997), such that any fMRI activation in this context could only correspond to a compound of neural responses to both the face pair (cue) and bar-probe (target). For this reason, to identify a true modulation of target processing, distinct from the effect of emotional faces by themselves, we designed a slightly modified version of the dot-probe paradigm during fMRI and introduced ‘cue-only’ trials (face pairs with no subsequent target) that were unpredictably intermingled with the “cue-plus-target” trials (face pairs followed by a unilateral target at valid or invalid location, similarly to our ERP study, see Poursots et al., 2004). A similar approach has been used in neuroimaging studies of spatial
attention during typical, nonemotional version of Posner orienting task (see Corbetta et al., 2000; Shulman et al., 2002; Woldorff et al., 2004), allowing a clear distinction of brain activity related to cueing effects from target processing. A second change in this fMRI experiment as compared with our initial ERP study (Pourtois et al., 2004) concerned the task: in the fMRI experiment, subjects were asked to respond on each “cue-plus-target” trial and to judge whether the orientation of the bar-probe matched (50%) or did not match (50%) the orientation of the thicker line-segment of the fixation cross on that particular trials (by pressing two different keys; see Pourtois et al., 2006). Recall that in our earlier ERP study, subjects were required to press a button only in a minority of trials where the peripheral bar’s orientation matched the thick fixation-cross segment (see Pourtois et al., 2004). Thus, in our fMRI experiment, the dual task requirement and the frequent withdrawal of responses did not provide a pure measure for spatially selective orienting effects in valid trials, even though different detection or discrimination judgments have been reported to produce similar attentional biases in emotional dot-probe tasks (Mogg and Bradley, 1999b). Otherwise, all stimuli and conditions were similar in this fMRI study as in our previous ERP study (with fearful and happy emotional expressions, unpredictably shown at valid and invalid locations, equally probable and randomized).

Critically, fMRI results in our modified dot-probe task disclosed a pattern of brain activation clearly indicating that fearful faces again had a unique impact on spatial orienting of attention toward the subsequent bar-probe target, whereas happy faces did not produce similar effects. First, following cue displays with a fearful face, bar-probes appearing at valid locations were found to produce an increased neural response in lateral occipital cortex, as compared with bar-probes appearing at invalid locations (Fig. 5). There was no difference in activation of the lateral occipital cortex when comparing fearful and happy faces on “cue-only” trials, indicating that this occipital activation reflected target processing, not face processing. Thus, consistent with previous ERPs showing enhanced P3 response in extrastriate regions, fMRI showed that occipital responses to visual targets were enhanced by their presentation on the same (valid) rather than the opposite (invalid) side as a preceding fearful face, even though the bars and their orientation were otherwise identical across these two conditions, and faces always task-irrelevant. The lateral occipital cortex is known to be critically involved in visual shape recognition (Grill-Spector et al., 2001; Kourtzi and Kanwisher, 2001), and might therefore be enhanced by perceived threat signals (see also Lane et al., 1998). Note, however, that we found no difference in these occipital responses as a function of the side of fearful faces, and no effect of emotion or validity in early visual areas within the lingual gyrus that exhibited different retinotopic responses to targets in LVF or RVF. These data do not seem to support the idea that fearful stimuli may produce retinotopic increases in early visual areas.

More importantly, the comparison of event-related fMRI responses to valid vs. invalid targets following fearful faces showed a unique pattern of spatially selective effects in the IPS in both hemispheres — an area playing a major role in spatial attention (Corbetta and Shulman, 2002). Right IPS was unresponsive to targets in the RVF after an invalid fearful face presented contralaterally on the left side, whereas the left IPS was conversely unresponsive to targets in the LVF after an invalid fearful face in the contralateral RVF, even though both IPS could respond to targets on either side in other conditions (see Fig. 6). IPS responses to peripheral targets were selectively reduced when targets were presented in the ipsilateral visual field after a fearful face in the contralateral (invalid) hemifield (Fig. 6). These data therefore suggest some suppression in the processing of ipsilateral targets when attention was focused on the contralateral side during invalid fear trials. By contrast, IPS was strongly activated by targets in the ipsilateral hemifield when preceded by a fearful face at the same (valid) location. In other words, for both hemispheres, attentional processing in IPS was apparently restricted to contralateral targets following a fearful face on that same side, but more bilaterally responsive to targets on either side in the other conditions. These fear-dependent spatial invalidity effects led to a significant emotion ×
validity interaction in IPS and found symmetrically in both hemispheres. These spatially selective effects on target processing in IPS are highly consistent with the idea that the presentation of a fearful face in visual periphery might lead to a transient focusing of attentional resources mediated by contralateral parietal areas toward that side, with a relative suppression of responses to visual events occurring at other locations (Fig. 6). Moreover, no such effect was found in IPS when comparing contralateral and ipsilateral fearful faces in “cue-only” trials, suggesting a spatially selective modulation of IPS responses to targets by invalid fearful cues (see Kincade et al., 2005) rather than a response to emotional faces alone. Again, we found no effect of happy faces (valid or invalid) in IPS. Furthermore, eye-tracking data during fMRI allowed us to ensure that our subjects made no systematic eye movement toward either the left or right upper visual field across the different stimulus conditions, but correctly maintained fixation on the central cross, ruling out the possibility that IPS activity may reflect different saccadic behavior during the task (Pourtois et al., 2006).

These brain-imaging data clearly show that threat-related cues may not only draw covert
attention more efficiently than neutral or positive cues, and thus produce benefits in visual (i.e., occipital) responses to targets presented at the same/valid location; but may also hold attention more strongly and produce greater cost on reorienting (i.e., IPS) when targets are presented at a different/invalid location ("disengage" effect, see Fox et al., 2001; Koster et al., 2004b for behavioral evidence).

In addition, we also found that bar-probes invalidly cued by fearful faces also increased activation in the left lateral orbitofrontal cortex, as compared with validly cued trials. This may be consistent with a role of this region in regulating the allocation of processing resources during breaches of expectation implicitly generated by emotional cues (Nobre et al., 1999), or in the presence of affective or motivational conflicts (Vuilleumier et al., 2001; Bishop et al., 2004a).

This activation of orbitofrontal regions on trials where a fearful face called for attention on one side and a visual target subsequently appeared on the opposite side converges with a similar effect in our previous ERP study (Pourtois et al., 2005), in which neural sources in ventro-medial prefrontal areas were found (Fig. 4D) in the early phase of the orienting response to invalid bar-probes, again following fearful but not happy faces.

**fMRI responses to peripheral faces alone**

All fear-selective effects in our fMRI study described above were identified by examining brain activations for "cue-plus-target" trials, but not "cue-only" trials, indicating that these likely resulted from a spatially selective modulation of
target processing by the position of the preceding fearful faces, but not just emotional face processing. However, as in our ERP study (Pourtois et al., 2004) in which we could examine ERPs time-locked to the target onset, as well as ERPs time-locked to the face cues, here we could test for fMRI responses not only during “cue-plus-target” trials but also during “cue-only” trials to determine any effect of peripheral faces alone. Our analysis of “cue-only” trials showed that fearful but not happy faces produced an increased response of the right precuneus in medial occipito-parietal cortex, regardless of the side of fearful faces but with a contralateral predominance. This medial occipital response to fearful face might be consistent with the previous EEG (Pourtois et al., 2004) and MEG (Halgren et al., 2000) results showing increased activity for occipital sources arising at an early latency post face onset, corresponding to C1 time-range (see above), and potentially reflecting some general alerting or arousal effect triggered by fearful faces (Lang et al., 1998; Thiel et al., 2004).

On the other hand, we found that peripheral fearful faces in “cue-only” trials produce a selective activation of the inferior temporo-parieto-occipital junction on the side opposite to the fearful faces (with no effect of happy faces). These increases might be consistent with a role of ventral cortical regions within the attentional networks, more critically concerned with the detection of behaviorally relevant or unexpected stimuli, rather than with top-down selection or focusing as controlled by the more dorsal IPS (Corbetta and Shulman, 2002). However, unlike a study using similar displays with bilateral faces presented in peripheral visual field (Noesselt et al., 2005), we found no significant increases in fusiform cortex or amygdala in the hemisphere contralateral to fearful faces. Nevertheless, several previous findings suggest that the amygdala (and fusiform) is consistently activated by fearful faces (see Vuilleumier et al., 2004a), and that such amygdala activation might play an important role in triggering subsequent visual orienting of attention to threat locations (Amaral et al., 2003; Vuilleumier, 2005). We believe that this lack of amygdala effects might result from a number of methodological factors, including an habituation due to repetition of the same faces (Breiter et al., 1996; Phillips et al., 2001; Fischer et al., 2003) and the presence of one fearful or happy face in all bilateral cue displays (Pessoa et al., 2002; Zald, 2003), but amygdala responses to fearful faces is likely to play a crucial role in eliciting attentional orienting behaviors toward threat (Holland and Gallagher, 1999).

Taken together, these fMRI data have provided us with a valuable refinement concerning a wide network of brain areas within extrastriate occipital cortex, superior and inferior parietal cortex, and ventromedial prefrontal regions, implicated in attentional biases and spatially selective modulations of target processing induced by emotional cues such as fearful faces. More generally, our brain-imaging results show how emotional stimuli may act as exogenous cues on spatial attention by modulating activity in a network of brain areas that partly overlap with cortical systems previously associated with the control of attention for non-emotional stimuli (see Corbetta and Shulman, 2002), but also partly involve distinct neural systems.

Role of anxiety in emotion–attention interactions

Many behavioral studies (e.g., Fox et al., 2001; Koster et al., 2004b) have shown that attentional biases induced by emotionally threatening cues in dot-probe tasks can be significantly exaggerated in people with higher anxiety levels, even below clinical levels. Whereas some findings suggest that anxiety may facilitate orienting or engaging attention toward emotional cues (Mogg and Bradley, 1998), other findings indicate a greater difficulty to reorient away or disengage from threat cues (Fox et al., 2001; Koster et al., 2004b; Mathews et al., 2004). However, the neural correlates of these effects of anxiety remain unclear. A number of recent fMRI studies have pointed to heightened responses to negative emotional stimuli in highly anxious subjects in various regions including the amygdala (Bishop et al., 2004b; Etkin et al., 2004; Sabatinelli et al., 2005) or ACC (Bishop et al., 2004a). However, in our own studies, we have found no reliable modulation of amygdala responses to fearful faces in relation to general scores.
of anxiety trait or state in similar tasks (Vuilleumier et al., 2001, unpublished data), but we observed more consistent effects in ventromedial prefrontal regions (e.g., see Sander et al., 2005).

Moreover, in the current series of ERPs and fMRI studies using the dot-probe paradigm, we systematically recorded anxiety scores in our participants. But our preliminary analysis failed to identify straightforward correlations between anxiety levels and ERPs indices related to P1 amplitude or fMRI indices related to validity effects. As a tentative explanation, this might be caused by the weak variation and low score in state and trait anxiety levels (Spielberger, 1983) across our non preselected participants. In any case, further research is therefore needed to explore more systematically the anatomical substrate and time-course of emotional biases in perception and attention, contrasting large but preselected (and representative) samples of anxious/fearful vs. non-anxious participants (based on a careful selection of more extreme anxiety scores in either the subclinical or clinical range) and using well controlled tasks that may provide more sensitive measures for different attentional subprocesses.

Conclusions

Selective attention is an essential cognitive mechanism governing the capacity-limited processing resources of our brains (Marois and Ivanoff, 2005) and promoting an efficient selection of salient or goal-related information in the environment (Posner et al., 1980). Until recently, attention has mainly been studied in conditions where such selection was based on relatively simple bottom-up sensory-driven mechanisms (e.g., pop-out) or higher-level top-down influences (Egeth and Yantis, 1997; Kastner and Ungerleider, 2000). Here we have reviewed recent neuroimaging data (ERP and fMRI) indicating that emotional values, such as threat signals conveyed by fearful faces, can also influence the spatial distribution of selective attention (Mogg and Bradley, 1998; Vuilleumier et al., 2001, 2004a; Fox, 2002; Dolan and Vuilleumier, 2003). Using the classical dot-probe paradigm (Bradley et al., 2000), we could show that healthy (nonanxious) participants may orient covertly and reflexively to the position briefly occupied by an irrelevant and nonpredictive fearful face in the (upper) visual field, such that this will modify their behavioral performance and brain responses to a subsequent target appearing at the same location. These results suggest that fearful faces may act as powerful exogenous cues and produce a transient involuntary capture of spatial attention, somehow similar to an abrupt onset or offset, or a sudden luminance change (Egeth and Yantis, 1997). By contrast, happy faces do not seem to produce similar effects, suggesting a special role of threat cues in such interactions with mechanisms of covert spatial attention.

More specifically, brain imaging data obtained by both ERPs (Stormark et al., 1995; Pourtois et al., 2004, 2005) and fMRI (Armony and Dolan, 2002; Pourtois et al., 2006) during the dot-probe task (Posner et al., 1980; Bradley et al., 2000) are now converging to delineate the precise brain pathways and spatio-temporal dynamics underlying emotional biases in spatial attention. We suggest a current working model that implicates both direct effects of emotional signals from amygdala on sensory processing and indirect effects on attentional systems subserved by parietal cortical areas (Vuilleumier, 2005). Taken together, the extant fMRI results (Vuilleumier et al., 2004b; Noesselt et al., 2005; Pourtois et al., 2006) combined with ERPs results (Pourtois et al., 2004, 2005) indicate that a fearful face cue in peripheral visual field may not only activate the amygdala but also induce rapid feedback to visual cortex to enhance face-sensitive areas as well as earlier occipital areas, possibly within less than 100 ms post-onset for the latter region (and probably within 170–200 ms for the former). The effect of direct feedback to occipital areas may then outlast the presentation of the facial threat cue, to reduce sensory threshold in retinotopic or nonretinotopic regions of early occipital cortex during a brief period (e.g., see Phelps et al., 2006), leading to a subsequent facilitation of spatial selection mechanisms directing attention to the same location (or same side), and thus to an enhanced activation of posterior parietal and posterior temporal regions implicated in orienting to a subsequent visual
target (through processes presumably activated at <80 ms post-target onset, see Bullier, 2001). This may in turn lead to enhanced sensory processing of the target in the lateral extrastriate occipital cortex, and generate enhanced P1 responses to the target (at <130–150 ms post-target onset), in a similar manner as the result of preparatory baseline shifts of activity imposed by endogenous top-down biases or by other exogenous signals in attention (Hillyard et al., 1998; Kastner et al., 1999; Super et al., 2003; Tallon-Baudry et al., 2005; Liu et al., 2005). This amplitude modulation of early sensory responses to visual targets following a valid emotional cue seems compatible with a gain control mechanism (Hillyard et al., 1998). The electrophysiological properties (i.e., latency, polarity, topography and neural sources in the extrastriate cortex) are entirely consistent with those previously reported by ERP studies of spatial attention using nonemotional exogenous cues (e.g., Hopfinger and Mangun, 1998; Hillyard and Anllo-Vento, 1998; Van der Lubbe and Woestenberg, 2000), suggesting a similar substrate and time-course but distinct sources for the top-down bias signal (Pourtois et al., 2004).

On the other hand, when a target follows a threat cue at another location, posterior parietal responses to the target are reduced in the ipsilateral hemisphere, disclosing a spatially selective restriction of attention to the location invalidly cued by the preceding threat, which is consistent with behavioral observations that fearful stimuli do not only draw spatial attention more readily than neutral or positive stimuli, but also hold attention more durably (Fox et al., 2001). In ERPs, this corresponds to a relative suppression of an early microstate in posterior parietal and posterior temporal cortex (<80 ms post-onset) associated with orienting attention to the target. These results reveal dissociable neural substrates for the engage and disengage components of spatial attention with threat-related cues. Concomitantly, disengaging from an invalid fearful face to reorient toward a task-relevant target on the opposite side involves motivational processes in ventromedial frontal cortex and/or executive control processes in anterior ACC that may become activated within the same time-range to resolve any competition between reflexive emotional signals and goal-driven attentional set.

Collectively, our electrical and hemodynamic brain-imaging results highlight the complexity of the spatio-temporal dynamics underlying the prioritization of attention resources to threat. These data converge with other evidence suggesting that some emotional influences originating from phylogenetically ancient systems in "limbic" brain regions can act in parallel with top-down influences traditionally associated with selective attention or executive functions of fronto-parietal cortical areas (LeDoux, 1996; Ohman and Mineka, 2001; Vuilleumier, 2005). In this perspective, emotion is not separated from cognition (Zajonc, 1980) but plays a fundamental role in regulating brain functions involved in perception, attention and adaptive behaviors.

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