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The 'when' and 'where' of perceiving signals of threat versus non-threat

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We tested the proposal that signals of potential threat are given precedence over positive and neutral signals, reflected in earlier and more pronounced changes in neural activity. The temporal sequence ('when') and source localization ('where') of event-related potentials (ERPs) elicited by fearful and happy facial expressions, compared to neutral control expressions, were examined for 219 healthy subjects. We scored ERPs over occipito-temporal sites (N80, 50–120 ms; P120, 80–180 ms; N170, 120–220 ms; P230, 180–290 ms; N250, 230–350 ms) and their polarity-reversed counterparts over medial sites (P80, 40–120 ms; N120, 80–150 ms; VPP, 120–220 ms; N200, 150–280 ms; P300, 280–450 ms). In addition to scoring peak amplitude and latency, the anatomical sources of activity were determined using low resolution brain electromagnetic tomography (LORETA). Fearful faces were distinguished by persistent increases in positivity, associated with a dynamical shift from temporo-frontal (first 120 ms) to more distributed cortical sources (120–220 ms) and back (220–450 ms). By contrast, expressions of happiness produced a discrete enhancement of negativity, later in the time course (230–350 ms) and localized to the fusiform region of the temporal cortex. In common, fear and happiness modulated the face-related N170, and produced generally greater right hemisphere activity. These findings support the proposal that fear signals are given precedence in the neural processing systems, such that processing of positive signals may be suppressed until vigilance for potential danger is completed. While fear may be processed via parallel pathways (one initiated prior to structural encoding), neural systems supporting positively valenced input may be more localized and rely on structural encoding.

Keywords: Event-related potentials ERPs; LORETA source localization; Amygdala; Medial prefrontal; Emotion; Fear; Happiness

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Introduction

Emotional expressions provide universal signals of emotional state and communicate biologically salient events in our environment (Ekman et al., 1972). Fundamental dimensions of positive and negative emotion have been elucidated across psychophysical, psychophysiological and animal neuroscience techniques (Levenson et al., 1990; Rolls, 1999; Sokolov and Boucsein, 2000). In terms of action tendencies, these dimensions may correspond to the motivational systems for approach and avoidance, respectively (Lang et al., 1998). In this regard, the human organism has evolved to give precedence to signals of potential danger, associated with the need to avoid harm. Signals of danger will engage the neural mechanisms for initial sensory input, and positive signals will be processed only once safety is assured, allowing approach tendencies to proceed (Williams, in press). In this study, we focused on salient facial expressions of negative and positive emotion, fear and happiness, as innate signals of potential danger versus safety and pleasure, respectively (Blair, 2003; Ekman et al., 1972).

A number of studies have investigated whether responses to negatively valenced stimuli are enhanced relative to positive or neutral stimuli, reflecting a 'negativity bias' (Smith et al., 2003). Behavioral studies have observed faster detection times for threat-related versus positive stimuli (Hansen and Hansen, 1988; Öhman et al., 2001). Event-related potentials (ERPs) provide a high temporal resolution measure of neural activity, and are particularly well suited to investigation of the temporal sequence of emotion processing. In ERP studies, negatively valenced picture stimuli have been found to elicit comparatively larger ERPs, consistent with a negativity bias (Ito et al., 1998; Smith et al., 2003). ERPs, as well as magnetoencephalograph (MEG) recording, have also been applied in the study of facial expressions of emotion. Facial expression stimuli allow for a more specific focus on signals of potential threat, as opposed to a generally negative valence.

Relative to neutral, fearful faces have been shown to elicit larger and faster responses within 150 ms post-stimulus (Taylor et al., 2004; Williams et al., 2004a). Enhanced early positivity (P120) over fronto-central sites has also been associated with a reduction in its negative-going concomitant (N120) (Eimer and Holmes, 2002). Early ERP differentiation of fear signals has been most apparent under implicit conditions, when the task does not focus attention on the stimulus content (e.g., Pizzagalli et al., 1999; Williams et al., 2004a). It has been suggested that early appraisal of potential danger may occur via a direct visual pathway, which proceeds prior to structural encoding of the stimuli in primary thalamo-cortical pathways (Liddell et al., 2005; Williams et al., in press). By contrast, when subjects pay explicit attention to the stimulus content, or induce a corresponding mood, a common ERP modulation within 100 ms is observed for fear and happy, as well as other negative emotions (Eger et al., 2003; Esslen et al., 2004). Attention to fearful expressions has also been associated with a later onset of amygdala modulation (Krolak-Salmon et al., 2004), suggesting that under these conditions, a direct pathway for processing fear-specific stimuli may be inhibited.

Fearful faces have also been found to elicit a distributed and sustained positivity beyond 250 ms post-stimulus (Eimer and Holmes, 2002), consistent with ongoing elaboration and context processing within cortical pathways. Studies focusing on general emotion modulation have also revealed an enhancement of late positivity, compatible with the period of the P300 (Campanella et al., 2002; Lang et al., 1990; Orozco and Ehlers, 1998), while others have reported an enhancement of later slow wave activity (448–616 ms; Vanderploeg et al., 1987). These later enhancements in positivity have been observed for variable inter-stimulus intervals (Naumann et al., 1992), suggesting they cannot be explained by a simple anticipatory effect.

The perceptual analysis of facial features has been associated with a specific ERP, the N170, which peaks 150–200 ms post-stimulus and is prominent over occipito-temporal sites (Halgren et al., 2000; Jeffreys, 1989; Bentin et al., 1996). The fronto-central concomitant of the N170 is the vertex positive potential (VPP). According to the conventional account of face processing, structural encoding of features precedes expression analysis (Streit et al., 2000). Consistent with this account, it has been reported that the N170 is enhanced by attention but not by emotional facial expression (Holmes et al., 2003). However, neurons selective for distinct facial expressions have been identified in the superior temporal cortex (Hasselmo et al., 1989), and other studies report a general enhancement of the N170 by emotional expressions relative to neutral for the N170 (Ashley et al., 2004).

The VPP of the N170/VPP complex has been found to show a specific enhancement in response to fearful faces (Ashley et al., 2004), suggesting that signals of potential danger may continue to be given precedence during structural encoding. An enhancement of negativity has also been observed later in the temporal sequence, around 240 ms post-stimulus, interpreted as an index of emotional expression encoding (Streit et al., 2000). This activity may correspond to the N250 implicated in the global rather than local processing of visual input (Han et al., 2000). Expressions of happiness, on the other hand, have been associated with a specific increase in right temporal negativity in the period of the N250, relative to both neutral and other visual stimuli (Carretié and Iglesias, 1995).

These ERP findings shed light on the dynamic sequence of facial emotion processing, thought to involve the interaction of distributed neural systems, engaged at various points in time (Adolphs, 2002). Within the first 120 ms post-stimulus, coarse perceptual discrimination of visual signals of emotion may be achieved via direct feedforward pathways. Finer-grained perceptual analysis occurring around 170 ms post-stimulus may be subserved by slower cortical pathways operating in parallel, which may be reciprocally modulated by salient signals of emotion. Conceptual knowledge of the stimulus and context processing occurs during sustained attention to emotional signals around 250 ms post-stimulus and beyond, and involve reactivation of these parallel pathways (Adolphs, 2002).

The right hemisphere has been emphasized in emotion processing across the time course (Adolphs, 2002). Convergent depth recording and neuroimaging evidence points to the preferential involvement of right sided activity within the first 200 ms of stimulus processing (Halgren et al., 1995; Kawasaki et al., 2001; Pizzagalli et al., 1999, 2002; Streit et al., 2000). Similarly, cortical regions associated with sustained attention to emotion signals have also shown a preferential right-sided engagement (Adolphs et al., 2000, 2001; Anderson et al., 2000; Kawasaki et al., 2001; Marinkovic et al., 2000). However, lateralized effects may vary with the temporal dynamics of responses to individual emotions. For fear, transient versus sustained processing of fear-related signals has been found to engage relatively greater right versus left amygdala activity, respectively (Liu et al., 1999; Phillips et al., 2001; Williams et al., 2004b; Wright et al., 2001).

To date, the spatio-temporal profile of neural activity involved in the implicit perception of facial emotions signaling fear and happiness has not been identified. We examined both the temporal sequence ('when') and source localization ('where') of ERPs elicited by fearful and happy expressions, relative to neutral control faces. To minimize the effects of sampling variation, we drew on a large and standardized sample of over 200 healthy subjects. It was expected that fearful faces would be distinguished from happiness by early-onset activity, commencing prior to structural encoding (within 120 ms) and persisting throughout the time course. By contrast, we expected expressions of happiness to be characterized by later-onset negativity, commencing after structural encoding (beyond 170 ms) and following a comparatively short time course. Both expressions of fear and happiness were expected to enhance the N170, reflecting modulation of encoding for face stimuli.

Method

Subjects

The participant pool comprised a total of 219 healthy individuals (mean age = 34.94; SD = 12.42 years), with an even distribution of sexes (112 males, 107 females), recruited in collaboration with the Brain Resource International Database (http://www.brainresource.com; Gordon, 2003; 2005). Subjects were screened using stringent and standardized exclusion criteria: history of mental illness, brain injury, neurological disorder or other serious medical condition, and history of substance abuse. Participants provided written informed consent in accordance with national health and medical research council guidelines.

Behavioral task

Face stimuli displaying neutral and evoked expressions of fear and happiness were selected from a standardized set of facial emotion stimuli (Gur et al., 2002), on the basis that they had been rated as the most accurate representations of each respective emotion. Stimuli were equated in terms of size, gray scale parameters and central alignment of the face within the image (with eyes as the midpoint reference). During ERP recording, expressions of fear, happiness and neutral were presented in blocks containing eight stimuli each, randomized within the block. There were four repeat blocks for each expression, making a total of 32 stimuli per expression. Stimuli were presented for 500 ms, with an inter-stimulus interval of 700 ms, such that the total stimulus onset asynchrony was 1200 ms. To ensure subjects maintained vigilance for the task, they were instructed to attend to the faces in preparation for post-testing briefings. Participants were able to consistently recognize the expression with well above-chance accuracy (fear 83.6%; happy 98.9%; neutral, 76.8%) in post-scan assessments, indicating that any differential effects in ERPs were unlikely to be due to visual processing difficulties. However, there was a significant difference in recognition accuracy for these expressions ($F(2,210) = 16.64$, $P < 0.0001$), which planned contrasts showed was due to lower accuracy for fear relative to neutral ($P = 0.001$), but higher accuracy for happy relative to neutral ($P < 0.0001$) and to fear ($P = 0.003$). These differences were taken into account in the interpretation of image analyses.

ERP data acquisition

Participants were asked to refrain from smoking and caffeine for 2 h prior testing. They were seated in a sound and light attenuated room, with temperature controlled at 24°C. Data were acquired continuously at 500 Hz with skin resistance of <5 kOhms from 26 electrode sites, using a Quikcap and NuAmps system according to the international 10–10 electrode system. An additional 4 channels were used to record EOG for detection of any eye movement artifacts, and data were recorded relative to the virtual ground. Data were then referenced offline to linked mastoids, and eye movement correction was undertaken offline using the Gratton et al. (1983) procedure.

ERP data reduction and analysis

Individual single-trial ERP epochs were filtered with a low-pass Tukey (cosine taper) filter function that attenuated frequencies above 25 Hz. Single-trials were then averaged to form ERP waveforms for each condition (fear, happiness and neutral) across each site. The use of a large subject sample meant that highly consistent components and their topography could be readily identified. Following inspection of the waveforms across all 26 sites for each of the 219 subjects, components implicated in face processing were found to be particularly prominent at temporal (left, T5; right T6), visual occipital (left, O1; right O2) and medial (Fz, Cz) sites. Superimposition of waveforms across all subjects at each site, and across all sites, showed that the N170 component was particularly prominent at the occipito-temporal sites (T5, T6, O1, O2), and the polarity reversed concomitant of this component, the VPP, was most pronounced at medial fronto-central sites (Fz, Cz), consistent with previous ERP evidence for the topography of components elicited by face stimuli (Ashley et al., 2004; Bentin et al., 1996; Jeffreys, 1989). Due to the polarity reversal of the N170/VPP complex, these components were less prominent at the sites occurring between fronto-central and occipito-temporal regions. At these sites where the N170/VPP complex was prominent, we also observed components occurring both prior to and after this complex, which followed the same pattern of polarity reversal.

The following components were identified as the largest peak within the respective latency windows across medial and occipito-temporal sites of interest: *temporal* (T5, T6) P120 (80–180 ms post-stimulus), N170 (120–220 ms), P230 (180–290 ms) and N250 (230–350 ms); *occipital* (O1, O2) N80 (50–120 ms), P120 (80–180 ms), N170 (120–220 ms), P230 (180–290 ms) and N250 (230–350 ms). The corresponding *medial* (Fz, Cz) components were the P80 (40–120 ms; concomitant of the N80), N120 (80–150 ms; concomitant of the P120), VPP (120–220 ms; concomitant of the N170), N200 (150–280 ms; concomitant of the P230) and P300 (280–450 ms; concomitant of the N250). Each component was quantified in terms of peak amplitude (positivity or negativity) and latency of the peak. Outliers were defined as values beyond 2.5 standard deviations from the mean, and formed only 1.5% of data. These values were excluded and replaced with age-appropriate (within 1 year) group means.

Repeated measures multivariate analyses of variance (MANOVAs) were used to analyze the amplitude for each component, with emotion (fear, happy versus neutral) and site as within-subjects factors. Planned contrasts were used to examine main effects for emotion at a significance level of $P < 0.05$. Given the inclusion of multiple factors, interaction effects for emotion by occipito-temporal laterality were examined at a corrected level of $P < 0.008$.

Source localization

Neuronal activity was localized using the LORETA inverse solution method (Pascual-Marqui, 1999). This procedure computes the three dimensional distribution of the electrically active neuronal generators in the brain as a current density value (A/m2) at each voxel. The linear LORETA solution relies on a criterion of contiguity, that the activity at any given voxel in cortical gray matter must be as similar as possible to the average activity of neighboring voxels. This criterion draws on electrophysiological evidence for the highly synchronized activity of neighboring neurons, necessary for generating the EEG (Pascual-Marqui et al., 2002). Simulation experiments have also demonstrated accurate localization based on this property (Menendez et al., 2001; Pascual-Marqui, 1999; Pascual-Marqui et al., 2002; Phillips et al., 2002).

We used LORETA with a three-shell spherical head model registered to the neuroanatomical atlas of Talairach and Tournoux (1988). Electrode coordinates were calculated by cross-registration of spherical and realistic head geometry following Towle et al. (1993). Computations were restricted to cortical gray matter and subcortical hippocampi and amygdala. We note that the ventricles are not included in LORETA solution space. Only voxels in which the probability of being gray matter was at least 0.33 (maximum 1.00), and for which this probability also exceeded that of a) being white matter and b) being cerebrospinal fluid were labeled as gray matter. A spatial resolution of 7 mm was used, producing a three-dimensional LORETA image of 2394 voxels in total for each scalp potential distribution map. This LORETA method has been validated for face processing areas, as well as localization to other

cortical regions (Pascual-Marqui et al., 2002). We used this method to identify significant source clusters, at the threshold of $P < 0.01$ (corrected for multiple comparisons according to the contiguity of voxels criterion), for the epochs in which ERP components showed emotion effects.

Results

Fig. 1 shows the ERP waveforms recorded over medial fronto-central (Fz, Cz), temporal (T5, T6) and occipital (O1, O2) sites for fear and happy relative to neutral, superimposed on a schematic brain to represent these recording sites. These waveforms showed high inter-subject consistency across the 219 subjects.

Fear relative to happiness and neutral: Peak amplitude and latency

MANOVA results are first reported for significant effects involving emotion, which planned contrasts showed were due to fear relative to happiness and/or neutral, for each region of interest. Over the medial fronto-central region, fear was characterized by significant enhancements in positivity for P80, VPP and P300, together with a discrete reduction in negativity for N200.

Over the medial fronto-central region, peak amplitude for the P80 (40–120 ms) showed a significant main effect for emotion ($F(2,436) = 3.35$, $P < 0.05$). This effect was due to *greater positivity* for fear relative to happy ($t(218) = 2.45$, $P < 0.05$) (Fig. 1, Table 1).

There was also significant main effect for emotion for the medial VPP (120–220 ms) amplitude ($F(2,436) = 18.74$, $P < 0.001$), due to greater *positivity* to fear relative to both neutral ($t(218) = 5.15$, $P < 0.001$) and happy ($t(218) = 5.20$, $P < 0.001$) (Fig. 1; Table 1).

For the medial P300 (280–450 ms) a further significant effect for emotion was observed ($F(2,436) = 15.14$, $P < 0.001$), due to greater *positivity* to fear relative to both neutral ($t(218) = 5.35$, $P < 0.001$) and happy ($t(218) = 3.46$, $P < 0.01$) (Fig. 1, Table 1).

By contrast, for the medial N200 (150–280 ms), the significant main effect for emotion ($F(2,436) = 3.66$, $P < 0.05$) was due to *reduced negativity* for fear relative to neutral ($t(218) = 2.61$, $P < 0.05$), feasibly due to the preceding enhancement of the VPP (Fig. 1, Table 1).

The spatio-temporal distribution of the relatively enhanced P80, VPP and P300 amplitude, and reduced N200 amplitude, for fear is illustrated in Fig. 2.

There were no significant effects for latency associated with fear relative to happiness or neutral.

Happiness relative to fear and neutral: Peak amplitude and latency

Perception of happiness was associated with distinctive effects over the temporal region, for N250 *negativity*.

A significant main effect for emotion for the N250 (230–350 ms) over the temporal sites ($F(2,436) = 14.46$, $P < 0.001$) was due to greater peak *negativity* for happy expressions compared to both neutral ($t(218) = 5.10$, $P < 0.001$) and fear ($t(218) = 4.20$, $P < 0.001$). A similar pattern was revealed for N250 over the occipital region. The main effect for emotion ($F(2,436) = 11.27$, $P < 0.001$) was again due to *greater negativity* for happy compared to neutral ($t(218) = 3.37$, $P < 0.01$) and fear ($t(218) = 4.63$, $P < 0.001$).

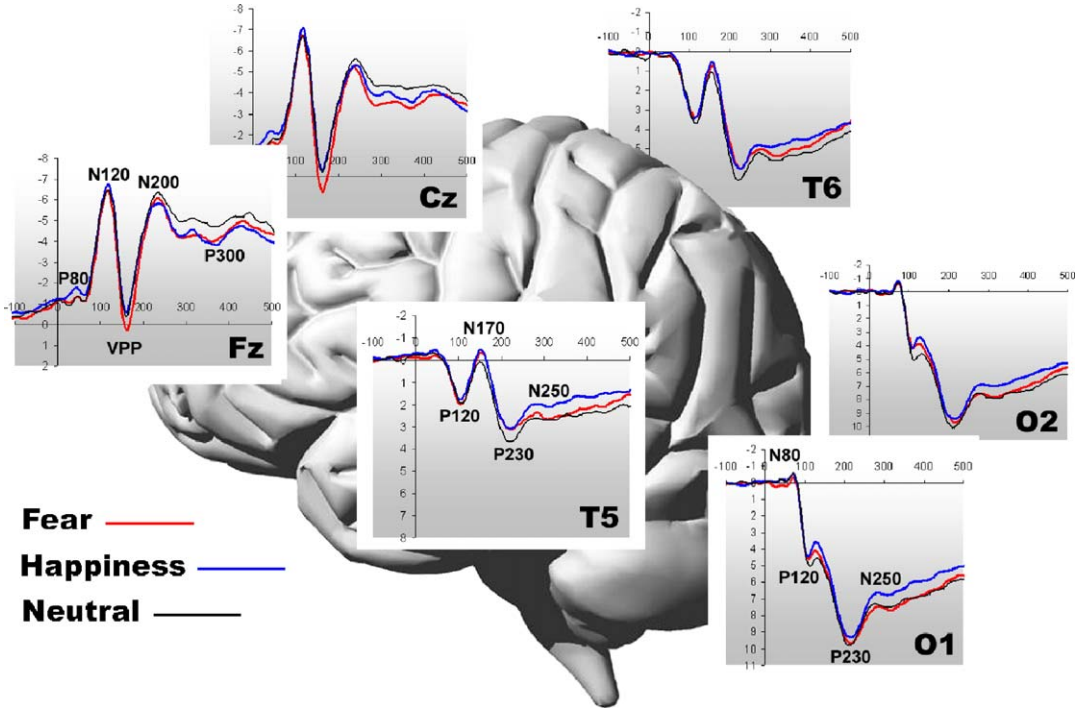

Fig. 1. ERP waveforms elicited in response to fear, happy and neutral face stimuli, recorded over medial fronto-central (Fz and Cz), temporal (T5 and T6) and occipital (O1 and O2) sites. Sites indicated by odd numbers are located in the left side of each region, and those indicated by even numbers in the right side. The waveforms are superimposed on a schematic brain to represent the spatial distribution of the sites over fronto-central, temporal and occipital regions.

Table 1
Summary of the time course of significant ERP effects specific to fear and happiness, in common for emotion (fear and happiness) relative to neutral, and for the impact of fear on laterality

	40–120 ms	120–220 ms	150–280 ms	230–350 ms	280–450 ms
Fear (F)					
Increased Positivity	Positivity P80	Positivity VPP			Positivity P300
Medial fronto-central region					
Reduced negativity			Negativity N200		
Medial fronto-central region					
Happiness (H)					
Increased negativity				Negativity N250	
Temporo-Occipital regions					
Slowed negativity				⟶ N250	
Temporal region					
Emotion (F and H)					
Increased negativity		Negativity N170			
Temporo-Occipital regions					
Reduced positivity	Positivity P120		Positivity P230		
Temporo (P120)-Occipital (P230) regions					
Laterality (F)					
Increased right-sided	Positivity P120	Negativity N170			
Occipital region					

There was a corresponding main effect for peak N250 latency over the temporal region [$F(2,436) = 6.50$, $P < 0.001$], due to generally *slower* latency (by 6.1 ms on average) for happy compared to fear ($t(218) = 3.51$, $P < 0.01$).

Common effects for fear and happiness relative to neutral: Peak amplitude and latency

Perception of fear and happiness also produced some common effects due to general emotion modulation, observed over temporo-occipital sites.

For the N170, significant effects for emotion over temporal ($F(2,436) = 11.12$, $P < 0.001$) and occipital ($F(2,436) = 13.14$, $P < 0.001$) regions, were due to significantly *enhanced negativity* for both fear and happy relative to neutral (Fear: temporal $t(218) = 2.84$, $P < 0.01$ and occipital ($t(218) = 3.21$, $P < 0.01$; Happiness: temporal $t(218) = 4.60$, $P < 0.001$ and occipital ($t(218) = 5.05$, $P < 0.01$).

By contrast, emotion was associated with *reduced positivity* for both fear and happiness over temporo-occipital regions within the first 250 ms post-stimulus. For the occipital P120, the significant emotion effect ($F(2,436) = 8.74$, $P < 0.001$) was reflected in reduced positivity for fear ($t(218) = 2.92$, $P < 0.01$) and happy ($t(218) = 3.94$, $P < 0.001$) relative to neutral. A similar pattern was revealed for the temporal P230, for which the significant emotion effect ($F(2,436) = 9.59$, $P < 0.001$) was due to reduced positivity

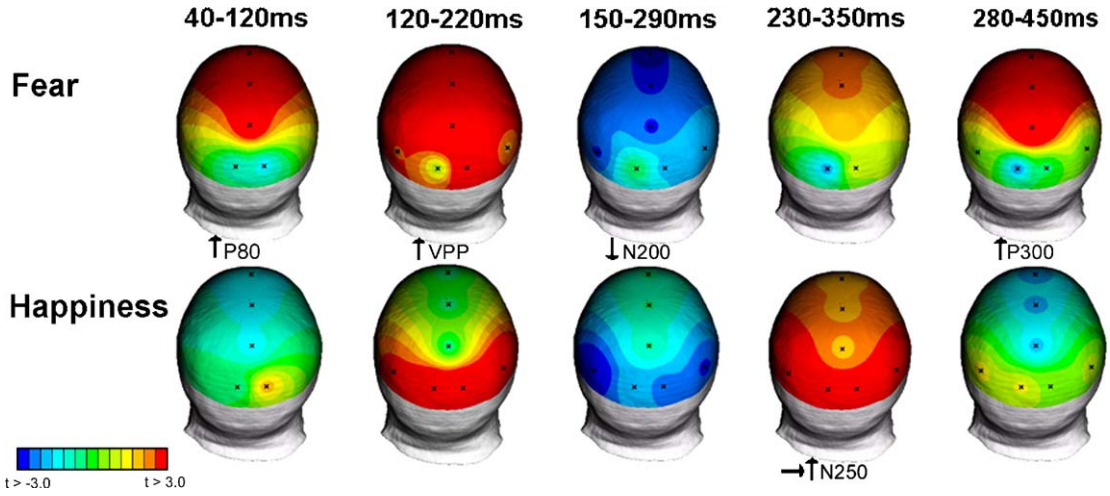

Fig. 2. Topographical maps illustrate the spatio-temporal distribution of neural activity in response to fear and happy relative to neutral face stimuli. The time course of activity in which peak ERP components were identified is shown in the top row. Each statistical parameter headmap shows the distribution of activity over medial fronto-central (Fz, Cz), temporal (T5, T6) and occipital (O1, O2) recording sites. Each headmap shows this viewed from the back of the head. Regions colored red indicate an increase in activity across midline, temporal or occipital regions, regions colored blue indicate a reduction in activity and green indicates no significant difference.

for both fear ($t(218) = 2.82$, $P < 0.01$) and happiness ($t(218) = 4.17$, $P < 0.001$) relative to neutral.

There were no common effects of fear and happiness relative to neutral on peak latency.

Effects of emotion on laterality: Peak amplitude and latency

Emotion effects on laterality were revealed for the P120 ($F(2,436) = 7.45$, $P < 0.001$) and N170 ($F(2,436) = 6.39$, $P < 0.01$), over the occipital region. Emotion by laterality interactions were due to the fact that fear elicited a greater enhancement in activity relative to neutral over the right than left occipital region, for the P120 ($t(218) = 3.61$, $P < 0.001$) and subsequent N170 ($t(218) = 3.32$, $P < 0.008$) components (Figs. 1E, F). Happiness did not show a significant impact on laterality.

There were no interactions between emotion and laterality for latency.

Fear: LORETA source localization

The increases in positivity throughout the time course in response to fear (relative to happiness and neutral) were associated with sources in the temporal, frontal, occipital and parietal cortices, as summarized in Table 2, and depicted in Fig. 3. The comparative reduction in negativity for fear occurring around 230–350 ms post-stimulus was associated with sources in the parietal cortex in particular (Table 2; Fig. 3).

In the early latency period of 40–120 ms post-stimulus, the enhanced positivity for fear was localized to five significant clusters, within the temporal and frontal regions (Table 2; Fig. 3). The subsequent period (120–220 ms post-stimulus) of enhanced positivity for fearful faces was associated with a more distributed pattern of activity over temporal, frontal, occipital and parietal regions, localized to four supra-threshold clusters (Table 2; Fig. 3). The strongest sources (at $P < 0.0001$) were apparent in the medial prefrontal region, consistent with the topography of the VPP elicited in this period. The later period (280–450 ms) of enhanced positivity for fear was again associated with sources in temporal and frontal regions, as well as in the occipital cortex (Table 2; Fig. 3). The temporal and frontal sources suggested a re-emergence of the activity observed during the initial 40–120 ms period.

In contrast to the pattern of sources for periods of enhanced positivity, the attenuation of negativity over the period 150–280 ms post-stimulus for fear was associated with a far more localized source in the parietal cortex. (Table 2; Fig. 3).

Happiness: LORETA source localization

The period of increased negativity for happiness (occurring 230–350 ms post-stimulus, corresponding to the N250) was

Table 2
The regions and associated Brodmann Area (BA) and Talairach coordinates for the localization of activity over 40 to 450 ms post-stimulus (coordinates are for the central location of each supra-threshold regional cluster)

	40–120 ms	120–220 ms	150–280 ms	230–350 ms	280–450 ms
Fear: enhanced positivity					
Temporal cortex					
Right	25, −10, −16 18, −24, −16				18, −12, −16
Bilateral, BA20	35, −31, −16 −45, −45, −20	46, −32, −20			31, −29, −16
Right, BA22/42	59, −11, 8	60, −18, 8			
Frontal cortex					
Bilateral, BA23/24	4, −24, 40 −3, −24, 40	4, 22, 36 −3, −21, 36			
Bilateral, BA6/24/32	4, −24, 50	4, −14, 50 −4, −12, 50, 18, 48, −6 −14, 50, −6			10, 48, 8 −11, 50, 8
Right, BA46					50, 42, 15
Occipital cortex					
Bilateral, BA18/19		25,−53,64 −17, −53, 64 4, −81, 15 −3, −81, 15			10, −78, 29 −8, −78, 29
Parietal cortex					
Bilateral, BA7/40		46, −46, 43 −31, −60, 57			
Fear: reduced negativity					
Parietal cortex					
Left, BA40			−50, −45, 22		
Happiness: enhanced negativity					
Temporal cortex					
Bilateral, BA20				35, −35, −20 −38, −35, −20	

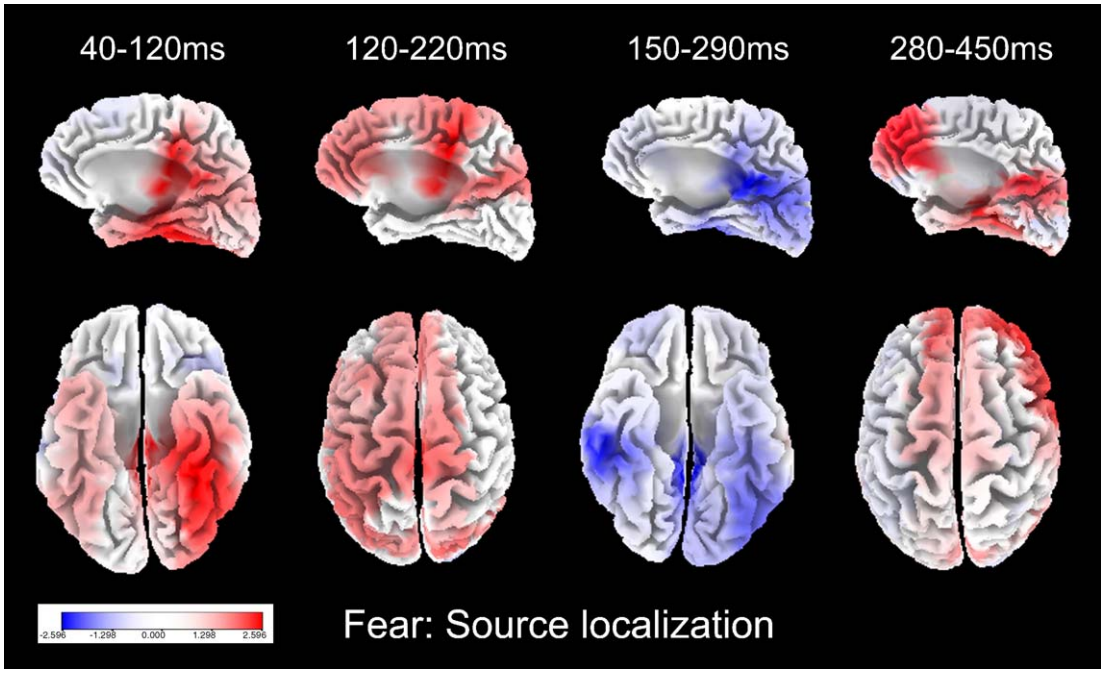

Fig. 3. LORETA-based statistical nonparametric maps (SnPM) depicting the localization of sources for the contrast of fear relative to happiness. Sources are depicted for the increased positivity over the periods 40–120 ms (P80), 120–220 (VPP) and 280–450 ms (P300) post-stimulus, and for the reduced negativity during 150–290 ms (N200) post-stimulus. The results of the source localization are displayed on the 'fiducial cortical surface' (boundary midway through cortical thickness), presented in both right hemisphere sagittal view (top row) and as viewed from the bottom (40–120 ms and 150–290 ms) or top (120–220 ms and 280–450 ms) of the cortex (bottom row). Significant increases in activity are shown in red, and significant reductions in blue, at the corrected threshold of $P < 0.01$. The legend shows the associated scale of t values.

associated with a comparatively localized source within the temporal cortex. The two super-threshold clusters suggested sources in an area corresponding to the bilateral fusiform gyri (Table 2; Fig. 4), although precise neuroanatomical localization is of course precluded by the LORETA technique.

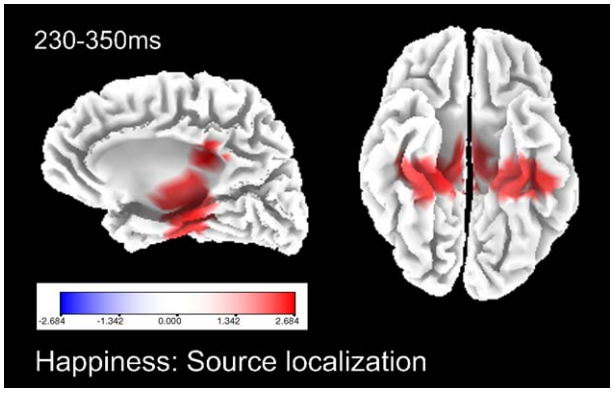

Fig. 4. LORETA-based statistical nonparametric maps (SnPM) depicting the source localization for the contrast of happiness relative to neutral, for the period 230–350 ms (N250) post-stimulus. Sources are depicted for the increased negativity for happiness over this period. The results of the source localization are displayed on the 'fiducial cortical surface' (boundary midway through cortical thickness), presented in both right hemisphere sagittal view (left) and as viewed from the bottom of the cortex (right). Significant increases in activity are shown in red, and significant reductions in blue (no reductions were observed), at the corrected threshold of $P < 0.01$. The legend shows the associated scale of t values.

Discussion

Signals of threat versus non-threat were distinguished by the profile of *when* neural activity was elicited, and *where* the sources of this activity were identified in the brain. Fearful faces were distinguished by early positivity (within 120 ms post-stimulus, associated with temporal and frontal sources). Positivity persisted over the time course, associated with a dynamical shift to distributed cortical sources (120–220 ms) and back to more localized temporal and frontal sources (220–450 ms). By contrast, expressions of happiness elicited discrete enhancement of negativity over temporal sites, within a later time frame (230–350 ms post-stimulus), with localized sources in an area consistent with the fusiform region of the temporal cortex. In common, signals of fear and happiness both modulated the face-related N170 and positive components occurring over the occipital–temporal regions. While these differences reflected relatively subtle changes in activity to emotional stimuli, the use of a large subject group and the consistency of ERP components across individual subjects provided the power to detect these differences.

Our observation that positivity was enhanced for fear, but not happiness, early in the time course is consistent with the view that signals of potential threat are given precedence in neural processing streams (Williams, in press). This early enhancement was sourced to temporal and frontal regions, consistent with evidence that these regions are part of a mechanism for early automatic alerting to potential threat (Liddell et al., 2004, 2005; Williams et al., in press). Source localization studies have also revealed prefrontal responses to other signals of potential danger within 150 ms post-stimulus (Carretié et al., 2005).

Enhanced positivity to fear was not only found to start early, but persisted throughout the processing sequence, such that the face-related VPP (120–220 ms post-stimulus) and subsequent P300 (280–450 ms post-stimulus) were increased. This pattern of enhancement suggests that appraisal of fear may commence early and prior to detailed perceptual processing and encoding, and that elaboration of fear-related input may be largely separable from these processes (Streit et al., 2000). Initial appraisal of fear may be enhanced by more detailed encoding during the 120–220 ms post-stimulus period, as reflected in enhanced VPP positivity. The persistence of enhanced positivity to fear during 280 to 450 ms (P300) suggests that signals of potential danger also serve to enhance ongoing stimulus elaboration and context evaluation. The sources of this persistent positivity suggested the involvement of distributed and interacting networks, which may be reactivated throughout the sequence of fear processing.

The most diffuse cortical sources were observed during the 120–220 ms period of the VPP, and the presence of occipito-parietal as well as fronto-temporal sources suggested that the visual encoding of face stimuli thought to occur during this period is enhanced by fear-related valence. Indeed, neuroimaging studies have revealed a reciprocal modulation between visual association areas and regions elicited preferentially by fear-related stimuli (Hariri et al., 2003). The re-emergence of sources in the temporal and frontal sources during 280–450 ms post-stimulus provides further support for the interaction of distributed networks over the time course of fear processing. Ongoing interactions within fronto-temporal networks may provide feedback necessary to bind information about facial expressions and their context (Halgren et al., 1995). The fronto-central scalp distribution of P300 enhancements observed during 280–450 ms post-stimulus, compared to the typical parietal distribution in cognitive tasks, may reflect the elaboration of the emotional content of incoming signals in particular (Sokolov and Boucsein, 2000). While P300 enhancement has been observed for positive as well as negative expressions (e.g., Campanella et al., 2002), the sensitivity to reveal small fear-specific increases in this study may be due to the use of a larger subject sample.

It is possible that the enhanced positivity for fear reflects a contribution from subcortical (e.g., amygdala) modulation of cortical activity, as suggested in previous localization research into fearful face stimuli (Esslen et al., 2004). Such modulation would necessarily be indirect, given that closed-field subcortical structures such as the amygdala do not themselves generate scalp-recorded ERPs. However, this proposal accords with functional magnetic resonance imaging (fMRI) evidence for reciprocal modulation between the amygdala and distributed visual and medial prefrontal cortices (Das et al., 2005; Hariri et al., 2003). The presence of early as well as later increases in activation for fear in this study is also consistent with evidence that amygdala modulation may involve activation of parallel neural systems for emotion perception, one operating rapidly and implicitly, the other more slowly and explicitly (Liddell et al., 2005; Morris et al., 1999; Williams et al., in press). Nonetheless, complementary techniques, such as depth-recording and the integration of ERPs with fMRI, are required to verify the role of limbic modulation in response to fear stimuli.

In contrast to fear, signals of happiness were distinguished by an increase in negativity and a slowing of response during a single time period, 230–350 ms post-stimulus (N250). This change was apparent over occipito-temporal regions, and localized to clusters in a temporal region corresponding to the fusiform area. In scalp-recorded ERP studies, the N250 has also been associated with the progression from global to more local processing of stimuli (Han et al., 2000). Thus, an enhancement of occipito-temporal negativity around 250 ms for expressions of happiness may reflect the preferential reliance on more controlled local processing of facial features, following the structural encoding of the face around 170 ms post-stimulus. A reliance on later processing may account for the relative ease with which signals of happiness are recognized (Kirita and Endo, 1995). The potential impact of stimulus recognition is considered further in the following section.

It is notable that, while fear elicited persistent increases in positivity and distributed sources, the increase in negativity for happiness was constrained to a discrete post-stimulus period of 230–350 ms and more localized sources. These distinctive profiles not only support the precedence of fear, but suggest that mechanisms for seeking positive stimulation may be suppressed until vigilance for potential danger is complete and safety assured, or fear signals acted upon. However, alternative explanations should also be considered. In light of the observation that expressions of fear were less readily recognized, but happy more easily, than neutral expressions during the post-scan behavioral ratings, one possibility is that the relatively greater difficulty in fear recognition required more effort and therefore more positivity throughout the time course, while the more localized increase in negativity for happiness reflected the relative ease of recognition. Yet, counter to this possibility is our finding that increases in positivity for fear occurred prior to the period of structural encoding required for recognition. Moreover, recognition for changes in expression has been associated with the N170 ERP component in particular (Guillaume and Tiberghien, 2001), which in this study did not distinguish emotional valence, as detailed further in the following section.

In common, both fearful and happy expressions served to enhance the encoding of face stimuli, as indexed by the N170. Both positive and negative emotion have previously been found to modulate the N170 (Campanella et al., 2002; Izmailov et al., 2001), although null reports do exist (e.g., Eimer and Holmes, 2002). These negative findings might reflect a comparative lack of power due to smaller sample sizes. We have previously found that body responses to emotion stimuli are elicited within a similar time period to the N170 (Williams et al., 2004a), which might account for a broader modulation of this component by emotion. This suggestion would also accord with the view that the positive components are sensitive to threat-related valence, while the N170 may be modulated by the more general effects of emotional arousal. Emotion also generally elicited more prominent right-sided activity throughout the processing sequence, consistent with the role of the right hemisphere is appraising face and emotion stimuli (Adolphs, 2002).

A common reduction in responses to both fear and happiness was also revealed for the occipital P120 and temporal P230 relative to neutral. The ERP waveforms suggest that the P120 reduction in particular might be due to the incipient onset of the N170, while variation in the P230 might similarly reflect the offset of the N170 (Fig. 1). Alternatively, it is possible the common decrease in P230 reflects the neural synchrony required to make the transition from one phase of face stimulus processing to the next (Rodriguez et al., 1999).

Taken together, the findings suggest that neural activity is more sensitive to expressions of fear than happiness, consistent with the

view that potential signals of danger will gain precedence in the processing sequence. The spatio-temporal profile of responses suggests that appraisal of potential threat commences prior to and unfolds largely independently from structural encoding of these signals. Early positivity within 120 ms of stimulus onset may reflect an initial sweep of feedforward processing, serving an early alerting function. The persistence of responses to potential threat may reflect feedback within interacting fear pathways over longer time scales, supporting the elaboration and context evaluation of fear stimuli. By contrast, responses to positively valenced stimuli may not proceed until appraisal for potential threat is complete. An opposing neural mechanism of this kind might account for the enhancements in negativity rather than positivity, and the later onset of these enhancements. Future research is warranted to determine whether the spatio-temporal profile of responses to fear is distinct from that elicited by other signals of danger, such as anger and disgust. The use of subliminal stimuli might also further elucidate the automatic manner in which neural precedence may be given to signals of potential danger.

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