

Segregating intra-amygdalar responses to dynamic facial emotion with cytoarchitectonic maximum probability maps

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ABSTRACT

Multiple lines of evidence converge on the human amygdala as a core moderator of facial emotion perception. The major subregions of the human amygdala have been anatomically delineated, but the individual contribution of these subregions to facial emotion perception is unclear. Here we combined functional MRI (fMRI) with cytoarchitectonically defined maximum probabilistic maps to investigate the response characteristics of amygdala subregions in 14 subjects presented with dynamic animations of angry and happy relative to neutral facial expressions. We localized facial emotion-related signal changes in the basolateral and superficial (cortical) subregions of the left amygdala, with most robust responses observed to happy faces. Moreover, we demonstrate a differential neural response to happy faces in ventromedial prefrontal cortex, which is consistent with a hypothesized role of this brain region in positive valence processing. Furthermore, angry and happy faces both evoked temporopolar responses. Our findings extend current models of facial emotion perception in humans by suggesting an intrinsic functional differentiation within the amygdala related to the extraction of value from facial expressions.

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1. Introduction

A pancultural means of signaling emotion in humans is through facial expressions (Darwin, 1872; Ekman, 1993). Perceiving facial emotion is critical for social interaction and engages a distributed neural network (Haxby et al., 2002) centered around the amygdala (Adolphs and Spezio, 2006). Human amygdala responses to facial emotion have been demonstrated at a neuronal (Fried et al., 1997, 2002) and systems level (Vuilleumier and Pourtois, 2007), occurring as early as 200 ms post-stimulus (Krolak-Salmon et al., 2004; Palermo and Rhodes, 2007). Larger activations of the human amygdala to fearful than to happy faces, together with fear recognition (Adolphs et al., 1994, 1995; Hurlemann et al., 2007) and social judgment (Adolphs et al., 1998) deficits in patients with selective bilateral amygdala lesion, have led to proposals that the amygdala is preferentially engaged by socio-emotional signals of impending physical threat and danger (Zald, 2003; Phelps, 2006).

Current concepts of the amygdala's role in facial emotion perception are substantially influenced by findings in nonhuman primates (Rolls, 2007). Single-cell recording research has demonstrated that the monkey amygdala contains face-selective neurons, and that activity of these neurons is higher for threatening faces than for appeasing faces (Gothard et al., 2007). This is consistent with larger signals to threatening than to appeasing faces in functional magnetic resonance imaging (fMRI) studies of the monkey amygdala (Hoffman et al., 2007). As monkeys never see static faces, recent studies used movieclips of dynamic facial emotion to stimulate the amygdala (Kuraoka and Nakamura, 2007). fMRI studies in humans have demonstrated larger amygdala responses to dynamic relative to static facial emotion (LaBar et al., 2003; Sato et al., 2004; but see Kilts et al., 2003), reflecting the eminent ecological relevance of rapid nonverbal communication of dynamic changes in subjective emotional states (Kamachi et al., 2001; van der Gaag et al., 2007). Moreover, fMRI evidence indicates that computer-generated static displays of human facial emotion engage the amygdala in a manner equivalent to natural stimuli, yet have the advantage of being highly manipulable and controllable (Moser et al., 2007). This suggests a fundamental role of the amygdala in extracting socio-emotional value from a face, independent of its genuine biological or virtual nature.

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The amygdala is not a homogeneous structure. Based on differences in connectivity, cyto-, myelo-, and chemoarchitecture, the amygdala can be differentiated into a basolateral, superficial, and centromedial subregion (Amunts et al., 2005). While fMRI studies in monkeys emphasize the role of the basolateral amygdala in facial emotion perception (Hoffman et al., 2007), the individual contribution of amygdala subregions to this function in humans is unclear. The principle aim of the present fMRI study was to test 14 healthy volunteers on a face perception task involving virtual animations of angry, happy, and neutral facial expressions in order to examine the intrinsic functional differentiation within the amygdala related to the perception of dynamic facial emotion. The rationale was to use maximum probabilistic anatomical maps of the basolateral, superficial, and centromedial amygdala based on histological analysis of ten human post-mortem brains (Amunts et al., 2005; Eickhoff et al., 2005, 2006) for analysis of blood oxygenation level dependent (BOLD) contrast sensitive high-resolution MR images acquired on a 3T scanner.

2. Methods

2.1. Subjects

The present study was approved by the local ethics committee of the Medical Faculty of the University of Bonn and is in accordance with the latest revision of the 1964 Declaration of Helsinki. Informed written consent was obtained from 14 right-handed volunteers (7 male, 7 female; age range 21–31 years; mean age 25.4 ± 2.4 years, normal or corrected-to-normal vision, recruited by local advertisement). All volunteers had never been on psychoactive medication and were free from current of past neurological or psychiatric disorder as assessed by an experienced clinician.

2.2. Stimulus design and presentation

We generated homogeneous dynamic facial animations displaying emotional and neutral expressions using the software package Poser 5 (Curious Labs, Inc., Santa Cruz, CA, USA) (see also Moser et al., 2007). Virtual modeling of human faces holds several methodological advantages because it allows a higher level of standardization and experimental control. Face proportions, surface textures, movements, and the intensity of facial emotion can be systematically varied. Furthermore, large numbers of stimuli can be created under equal lighting conditions, viewing angles and focus lengths.

In our stimulus set, faces were presented in frontal view with the gaze focused on the observer. Settings for luminance and contrast were fixed. Animations were presented against a deep black background. Male and female faces varied in hair color, hair style, eye color, facial contour, shape of nose, eye brows and skin texture. In a standardized manner, dynamic angry, happy, and neutral facial expressions were created by morphing nose, eyes, tongue, eye brows, mouth, wrinkles, lips and the overall mien. Consistent with previous studies (LaBar et al., 2003), stimuli were presented at a rate of 30 frames/s for a total duration of 45 frames/1.5 s. Dynamic changes in happy and angry facial expressions occurred between key frames 5 and 35 after stimulus onset. Facial emotion peaked at key frame 35 and remained stable for the final 0.33 s. Movements in neutral facial expressions involved a brief downward movement of the lips, eye brows and eye lids. Maximum changes were reached at key frame 25, after which the expression returned to the initial display. Stimuli are exemplified online (Supplementary Video 1). The stimulus set comprised a total of 90 computer-generated animations (30 happy, angry, and neutral, half female) that were

rated, together with stimuli taken from a widely used series of natural static faces (Ekman and Friesen, 1976), in an independent behavioral validation study by 12 judges (6 male, 6 female; age range 22–30 years; mean age 25.3 ± 2.8 years) on a 9-point scale according to their perceived valence, arousal and distinctiveness (i.e., “how pleasant/intense/distinct is the emotion?”, Lang et al., 1997). Subjective ratings were analyzed using repeated-measures analyses of variance (ANOVAs) followed by Bonferroni-corrected pair-wise comparisons.

Before fMRI scanning, subjects were instructed that they would be exposed to hostile (aggressive), happy (smiling), and neutral animations of human faces. During fMRI scanning, subjects were required to perform a dichotomic gender judgment task. Push-button response times were analyzed using a repeated-measures ANOVA. Stimuli were presented for 1.5 s in a fixed-random slow event-related design. The inter-trial interval consisting of a black background with a white fixation cross varied between 13.2 and 20.9 s in order to allow the hemodynamic response of the amygdala to return to baseline levels (LaBar et al., 2003). Stimulus delivery and response recording was carried out using Presentation 11 (Neurobehavioral Systems, Inc., Albany, CA, USA).

2.3. fMRI acquisition

MR images were acquired on a Siemens Magnetom Tim Trio 3.0T System (Siemens Medical Solutions, Erlangen, Germany). Sequence parameters were: T2*-weighted echoplanar images (EPI) with BOLD contrast, echo time (TE) = 33 ms, repetition time (TR) = 2200 ms, flip angle = 90°, slice thickness 2.0 mm, interslice gap 1.0 mm, FoV = 256 mm, matrix size 128 × 128, voxel size = 2.0 mm × 2.0 mm × 3.0 mm; 29 axial slices were oriented along the anterior–posterior commissure line. The fMRI time series consisted of 700 volumes.

Randomly selected images from our EPI sequence and images depicting the mean standard deviation of the signal amplitude across the fMRI session are provided in our supplementary material section (Supplementary Figs. 1 and 2). The EPI images demonstrate the high quality of our MR protocol. Furthermore, signal variance in the amygdala is almost the same as in cortical regions, suggesting no significant signal drop-out in the amygdala.

2.4. fMRI data analysis

All fMRI analyses were carried out using MATLAB 7.0.1 (The MathWorks, Inc., Natick, MA, USA) and Statistical Parametric Mapping 5 (SPM5, Wellcome Trust Centre for Neuroimaging, London, UK, <http://www.fil.ion.ucl.ac.uk/spm>). For each subject, the EPI images were slice-time corrected and spatially realigned to the first image in the series to correct for head movements. The EPI images were then normalized to the Montreal Neurological Institute (MNI) template implemented in SPM5 (re-sampled to 2 mm × 2 mm × 2 mm voxels). Most fMRI studies of human amygdala responses used smoothing kernels between 8 and 12 mm full-width-half-maximum (FWHM) (Zald, 2003). We used a Gaussian kernel of 8 mm FWHM to improve the signal-to-noise ratio and the sensitivity to detect an activation given it exists (Hopfinger et al., 2000; Smith, 2001; Brett et al., 2007; see also Ball et al., 2007). In addition, we conducted a separate confirmatory ROI analysis using a 4-mm FWHM kernel to test the reliability of the localization of activated voxels within amygdala subregions.

Within each subject, the task-related neural activity for each condition (i.e., angry, happy and neutral) was modeled with a box-car function convolved with the canonical hemodynamic response function and its temporal derivative as implemented in SPM5. A high-pass filter was applied eliminating signal drifts

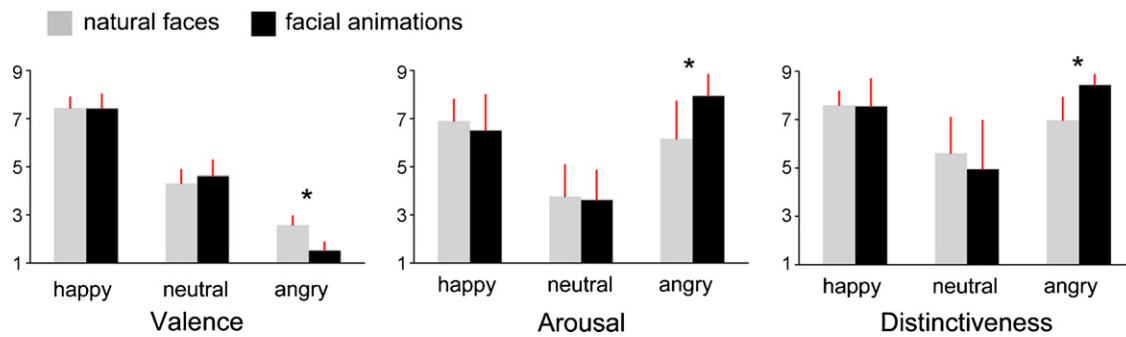


Fig. 1. Mean ratings of arousal, valence and distinctiveness (1: low; 9: high) obtained for angry, happy, and neutral computer-animated faces compared to natural static faces taken from the Ekman and Friesen series (Ekman and Friesen, 1976). Error bars indicate the standard deviation (S.D.).

slower than 128 s. Statistical parametric maps were derived by applying linear contrasts to the parameter estimates for the three conditions (happy, angry and neutral), resulting in a t -statistic for every voxel. For group statistics, baseline contrasts for the three conditions calculated on the single subject level were used within a general linear model random effects analysis in order to attain pair-wise t -statistics for the events of interest [i.e., (happy + angry) > neutral, neutral > (happy + angry), happy > neutral, angry > neutral, happy > angry and angry > happy].

For a hypothesis-driven analysis of the amygdala, a region of interest (ROI) consisting of the amygdala bilaterally was defined using cytoarchitectonic maximum probability maps derived from histological analysis of 10 human post-mortem brains (Amunts et al., 2005) as provided by the SPM Anatomy toolbox (Version 1.4, http://www.fz-juelich.de/inb/inb-3//spm_anatomy_toolbox; Eickhoff et al., 2005, 2006). These maps enclose the basolateral amygdaloid group (lateral, basolateral, basomedial and paralaminar nuclei), the centromedial amygdaloid group (central and medial nuclei), and the superficial amygdaloid group (anterior amygdaloid area, ventral and posterior cortical nuclei) (Amunts et al., 2005; for visualization see Ball et al., 2007) and define the most likely cytoarchitectonic area at each voxel of the reference space (Eickhoff et al., 2005, 2006). Thus, maximum probability maps allow for the non-overlapping anatomical localization of activated voxel clusters and provide a high degree of sensitivity compared to other methods of ROI definition (Eickhoff et al., 2006). Significant activations are reported at a threshold of $p < 0.05$, family-wise error corrected, and an extent threshold of $k > 3$ voxels. For every cluster, the relative contribution of voxels located within specific amygdala subregions is quantified (%). In our confirmatory ROI analysis based on 4-mm smoothed functional data, we used a significance threshold of $p < 0.001$.

In order to investigate which other brain regions might be differentially active during the processing of emotional stimuli, we additionally conducted a whole brain analysis. Here, activations are reported at a significance threshold of $p < 0.001$ (uncorrected) and an extent threshold of $k > 3$ voxels. The anatomical localization of significant activations was assessed by reference to the MNI standard stereotactic space which approximates the Talairach space (Talairach and Tournoux, 1988).

3. Results

3.1. Behavioral validation study

The fMRI stimulus set comprised a total of 90 computer-generated animations that were rated, together with static face stimuli taken from the Ekman and Friesen series (Ekman and Friesen, 1976), by 12 independent judges on a 9-point

scale according to their perceived valence, arousal and distinctiveness. A repeated-measures ANOVA for stimulus type (i.e., natural face and computer animations) and emotional category (i.e., happy, angry and neutral) computed on valence and arousal ratings revealed main stimulus type (valence, $F_{(1,11)} = 6.660$, $p = 0.026$; arousal, $F_{(1,11)} = 11.028$, $p = 0.007$), emotional category (valence, $F_{(2,22)} = 451.619$, $p < 0.001$; arousal, $F_{(2,22)} = 62.953$, $p < 0.001$), and stimulus type \times emotional category interaction (valence, $F_{(2,22)} = 15.326$, $p < 0.001$; arousal, $F_{(2,22)} = 12.143$, $p < 0.001$) effects (Fig. 1). All face stimuli were rated according to their presumed valence (i.e., happy > neutral > angry; all $p < 0.001$, Bonferroni corrected for multiple comparisons). Happy and angry faces were rated as more arousing than neutral stimuli (both $p < 0.001$), whereas angry faces were judged to be more arousing than happy faces ($p = 0.040$). Only ratings of angry faces differed between stimulus sets: computer-animated angry faces scored lower in valence and higher in arousal than the natural angry faces (both $p < 0.001$). A repeated-measures ANOVA conducted on distinctiveness ratings revealed a main effect of emotional category ($F_{(2,22)} = 21.494$, $p < 0.001$) as well as an interaction between stimulus type and emotional category ($F_{(2,22)} = 13.203$, $p < 0.001$) (Fig. 1). Happy and angry faces were rated as more distinct than neutral faces (both $p \leq 0.002$), and computer-animated angry faces were judged to be more distinct than natural angry faces ($p < 0.001$).

3.2. Reaction time measures

The gender judgment response times (mean \pm S.D.) measured during fMRI scanning were as follows: happy faces, 1.20 (0.18) s; neutral faces, 1.11 (0.15) s; angry faces, 1.16 (0.18) s. A repeated-measures ANOVA revealed a main effect of emotional category ($F_{(2,26)} = 7.719$, $p = 0.002$). Bonferroni-adjusted pair-wise comparisons demonstrated faster responses to neutral versus happy facial expressions ($p = 0.003$), and a trend toward faster responses to neutral versus angry facial expressions, whereas there was no difference in response times between happy and angry facial expressions ($p > 0.05$).

3.3. fMRI results

ROI analysis for the amygdala as a whole. The emotional (i.e., happy and angry) > neutral contrast revealed activation of two clusters in the left amygdala (Fig. 2): 83.0% of the larger cluster containing 22 voxels was assigned to the superficial amygdala; 13.6% of this cluster was assigned to the basolateral amygdala; 87.5% of the second cluster containing five voxels was allocated to the basolateral amygdala. The reverse contrast (i.e., neutral > emotional) yielded no significant results. The ROI analysis for happy compared

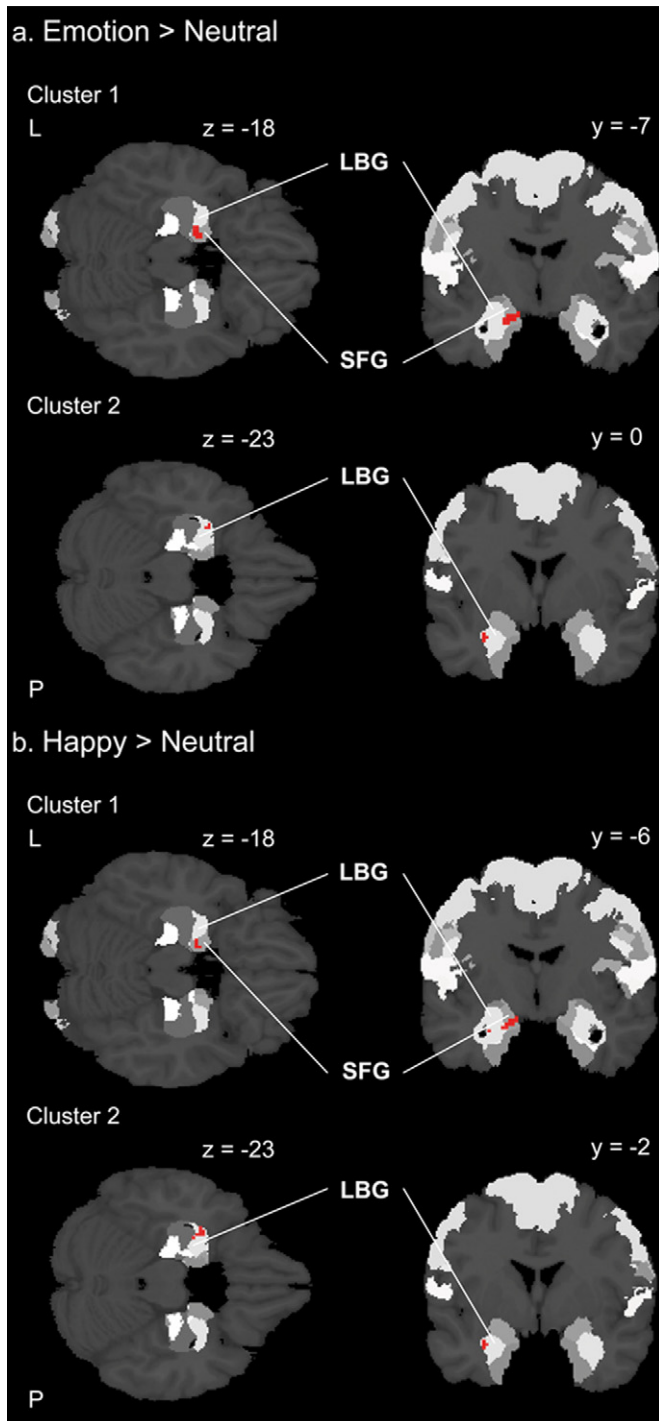


Fig. 2. Region of interest (ROI) analysis. Presented are axial and coronal sections through the cytoarchitectonic maximum probability maps showing differential amygdala activations as revealed by the contrasts: (a) emotion > neutral and (b) happy > neutral. Abbreviations: L, left; LBG, basolateral group; P, posterior; SFG, superficial group.

to neutral stimuli showed similar results as the emotional > neutral contrast: 82.1% of a larger cluster (14 voxels) was assigned to the superficial amygdala, whereas 8.0% was assigned to the basolateral amygdala; 93.3% of a smaller cluster (13 voxels) covered the basolateral amygdala (Fig. 2). The ROI analysis for angry relative to neutral stimuli as well as additional contrasts between happy and angry stimuli revealed no significant amygdala responses. Fig. 3

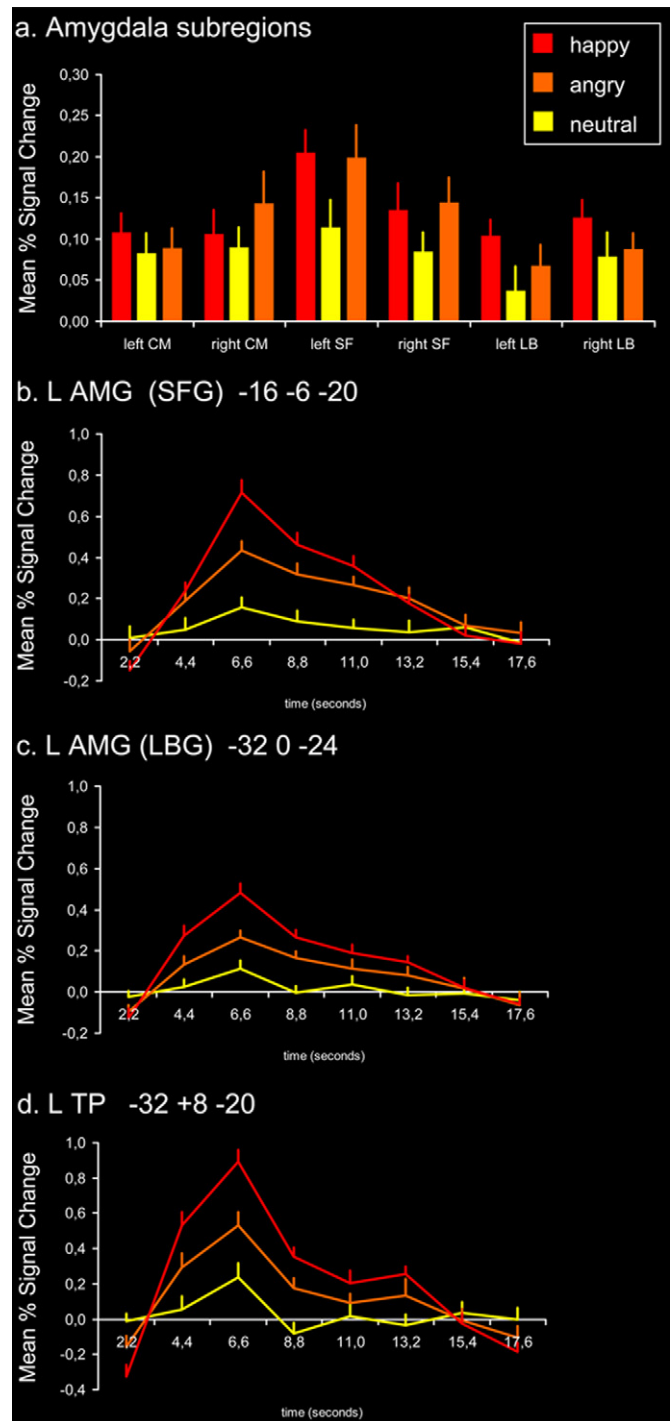


Fig. 3. Region of interest (ROI) analysis. (a) Mean BOLD percent signal changes for voxels with 90–100% assignment probability to amygdala subregions. (b–d) Signal time courses for a voxel showing maximum activation in the contrast emotion > neutral. Abbreviations: AMG, amygdala; TP, temporal pole; CM, centromedial; SF, superficial; LB, basolateral. Error bars indicate the standard error of the mean (S.E.M.).

depicts the mean BOLD percent signal changes within different amygdala subregions.

As detailed in Section 2.4, we performed an additional confirmatory ROI analysis with 4-mm smoothed functional data. The emotional > neutral contrast revealed one cluster of five voxels located within the left superficial amygdala. The happy > neutral contrast yielded two clusters: a larger cluster (eight voxels) was

Table 1

List of brain regions showing a significant activation in response to dynamic animations of emotional (happy and angry) faces relative to neutral faces

Contrast	Region	Side	MNI-coordinates			k	Z
			X	Y	Z		
Emotional > neutral	Medial orbital gyrus	R	12	50	-8	7	3.30
	Temporal pole	L	-32	8	-20	170	4.29
	Insula	L	-28	16	-14		3.21
	Insula	R	36	10	4	12	3.39
	Amygdala	R	16	-2	-22	26	3.37
	Amygdala	L	-16	-6	-20	43	3.82
	Middle cingulate gyrus	L	-10	-18	34	5	3.26
	Fusiform gyrus	L	-24	-32	-20	9	3.45
	Inferior temporal gyrus	R	48	-62	-8	42	3.84
	Middle occipital gyrus	L	-28	-86	10	12	3.42
Happy > neutral	Lateral orbital gyrus	R	34	54	-4	7	3.64
	Medial orbital gyrus	R	6	36	-14	359	4.02
	Straight gyrus	R	2	18	-20		3.77
	Straight gyrus	L	-8	22	-14		3.69
	Anterior cingulate gyrus	R	16	34	26	18	3.37
	Anterior cingulate gyrus	L	-10	32	8	30	4.01
	temporal pole	R	40	14	-42	50	3.73
	Temporal pole	L	-32	8	-20	150	4.06
	Amygdala	L	-32	0	-24		4.12
	Hippocampal formation	L	-26	-8	-26		3.30
	Amygdala	R	16	-2	-22	7	3.22
	Amygdala	L	-16	-6	-20	37	3.63
	Parahippocampal gyrus	L	-24	-32	-18	39	3.92
	Fusiform gyrus	L	-34	-36	-18	5	3.27
	Fusiform gyrus	R	36	-42	-10	28	3.57
	Inferior temporal gyrus	R	48	-62	-8	36	3.85
	Middle occipital gyrus	L	-28	-86	10	8	3.37
Angry > neutral	Temporal pole	L	-34	10	-18	58	3.88
	Insula	R	36	10	4	10	3.40
	Amygdala	L	-16	-6	-18	4	3.24

Significance threshold: $p < 0.001$, uncorrected.

allocated to the left superficial amygdala; 68.8% of a second cluster (two voxels) was assigned to the left basolateral amygdala. The angry > neutral contrast revealed a small cluster of two voxels and was allocated to the left amygdala. The ROI analysis of the happy > angry contrast yielded two clusters within the left amygdala: 91.7% of a larger cluster (six voxels) and 62.5% of a second cluster (two voxels) were assigned to the left basolateral amygdala (Supplementary Fig. 3). No other contrasts produced significant results.

Whole brain analysis. The emotional > neutral contrast demonstrated activations in left middle occipital gyrus, left fusiform gyrus, right inferior temporal gyrus, amygdala (bilaterally), left temporal pole, insula (bilaterally), left middle cingulate gyrus, and more rostral regions including the right medial orbital gyrus (Table 1

and Figs. 3 and 4). A separate analysis for happy versus neutral stimuli showed similar activation patterns. In addition, activations in left hippocampal formation, right temporal pole, right fusiform gyrus, right lateral orbital gyrus, anterior cingulate gyrus (bilaterally) and straight gyrus (bilaterally) were found (Table 1 and Figs. 3 and 4). Angry relative to neutral stimuli activated left temporal pole, left amygdala and right insula (Table 1 and Figs. 3 and 4). The angry > happy contrast revealed no suprathreshold voxels, whereas the happy > angry contrast yielded activations in hippocampal formation (bilaterally), right temporal pole and right caudate nucleus as well as in several prefrontal regions including the lateral orbital gyri (bilaterally), medial frontal gyri (bilaterally), left straight gyrus, and anterior cingulate gyrus (bilaterally) (Table 2 and Fig. 4).

Table 2

List of brain regions showing a significant activation in response to dynamic animations of happy faces compared to angry faces

Contrast	Region	Side	MNI-coordinates			k	Z
			X	Y	Z		
Happy > angry	Medial frontal gyrus	R	8	52	0	4	3.24
	Lateral orbital gyrus	R	34	54	-4	568	4.90
	Anterior cingulate gyrus	R	14	34	2		4.16
	Anterior cingulate gyrus	L	-10	30	8	366	4.69
	Lateral orbital gyrus	L	-34	50	-2		3.98
	Medial frontal gyrus	L	-16	52	12		3.92
	Caudate head	L	-8	14	-10	74	4.08
	Straight gyrus	L	-12	28	-14		3.54
	Temporal pole	R	52	12	-22	4	3.18
	Hippocampal formation	R	36	-28	-14	16	3.58
	Hippocampal formation	L	-14	-40	10	4	3.22
Angry > happy	No suprathreshold clusters						

Significance threshold: $p < 0.001$, uncorrected.

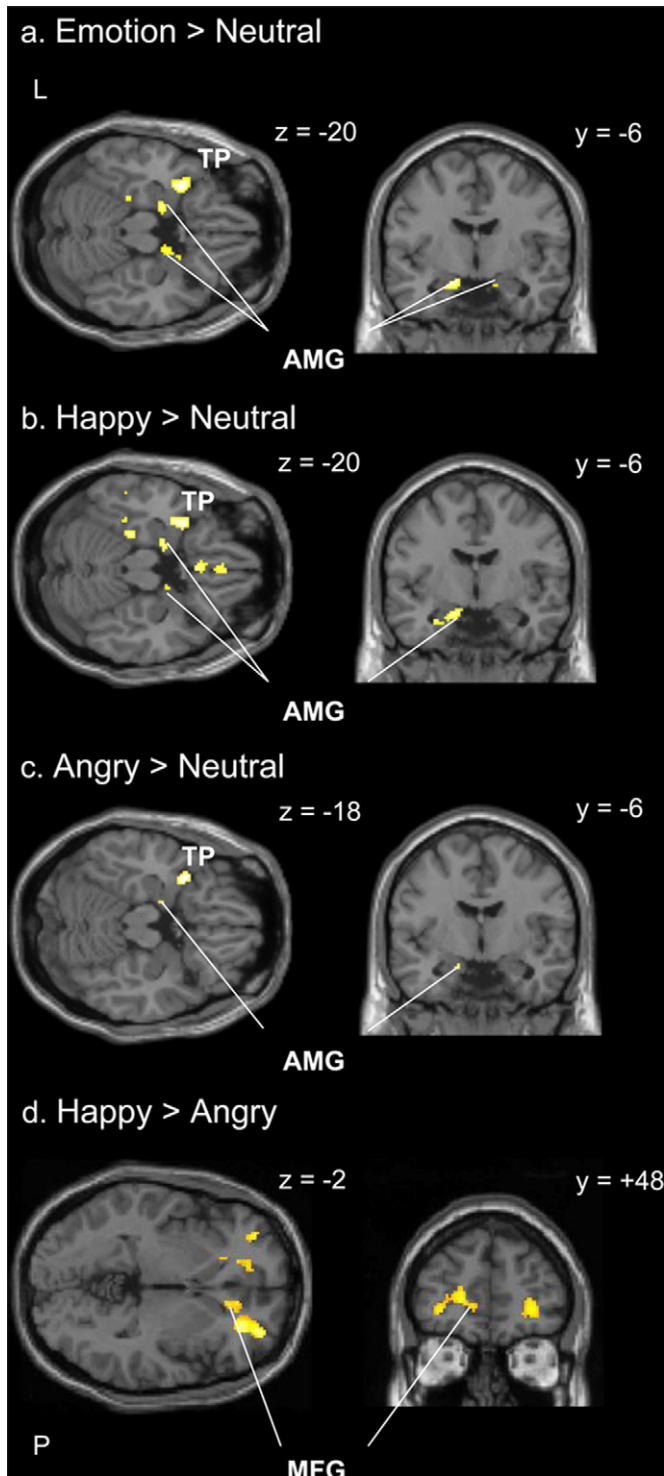


Fig. 4. Whole brain analysis. (a–d) Whole brain analysis. Differential activity as revealed by the contrasts (a) emotion > neutral, (b) happy > neutral and (c) happy > angry, superimposed on coronal and sagittal sections of a single subject brain template provided by SPM5. Abbreviations: L, left; MFG, medial frontal gyrus; P, posterior; R, right.

4. Discussion

Consistent with our experimental rationale, dynamic animations of facial emotion elicited robust differential amygdala responses. As determined by cytoarchitectonic maximum probabilistic maps, these responses were primarily located in the basolateral and superficial (cortical) subregions of the left amygdala. This pattern was present in 8- and 4-mm smoothed functional data and is compatible with current concepts of the functional architecture of the mammalian amygdala (McDonald, 1998, 2003; LeDoux, 2007).

In accord with evidence from single-cell recording (Gothard et al., 2007) and fMRI (Hoffman et al., 2007) research in monkeys, we localized activation to dynamic facial emotion within the basolateral amygdala. This subregion receives the majority of cortical and subcortical input to the amygdala and plays an essential role in attaching emotional value to incoming information, as evidenced by conditioning experiments in monkeys (Paton et al., 2006) and rodents (Amorapanth et al., 2000; Repa et al., 2001; Anglada-Figueroa and Quirk, 2005). We localized the most robust responses to dynamic facial emotion in the superficial (cortical) amygdala, suggesting a key role of this specific subregion in the perceptual encoding of facial emotion. While the basolateral and superficial (cortical) amygdala have both been identified as important sites of plasticity in conditioning experiments, the centromedial amygdala coordinates – via efferent projections to hypothalamus and brainstem areas – behavioral, endocrine and autonomic changes that together form an integrated conditioned response (Gonzalez-Lima and Scheich, 1986; Anglada-Figueroa and Quirk, 2005; Phelps and LeDoux, 2005; LeDoux, 2007). Although our data indicate that the perceptual encoding of dynamic facial emotion engages the centromedial amygdala, responses to emotional and neutral stimuli did not significantly differ from each other, perhaps due to a lack of conditioned value.

Beside empirical support for an equal engagement of the amygdala in the perception of appetitive and aversive facial emotion (e.g., Winston et al., 2003; van der Gaag et al., 2007), there is substantial evidence from studies in monkeys (Gothard et al., 2007) and humans (e.g., Morris et al., 1996) for a neural response bias of the amygdala toward facial signals of impending physical threat and danger (Zald, 2003; Phelps, 2006). As the emotional basis of aggressive threat in monkeys is assumed to be homologous with human anger (Blanchard et al., 1984; Lawrence et al., 2007), one might predict that the basolateral amygdala would be particularly sensitive to facial expressions of anger. In the present study, angry faces scored high in arousal and low in valence ratings, however, we observed no robust differential response to angry faces in the basolateral amygdala, most likely due to significant variation in perceived threat across subjects. It thus appears from our findings that in contrast to natural angry faces, their virtual counterparts fail to effectively engage the amygdala. We speculate that the obvious absence of real physical danger and threat in virtual stimuli might reduce amygdala responsiveness to these stimuli. This interpretation is compatible with findings that amygdala responses are modulated by contextual information (Phelps, 2006) and reflect the extent to which a social encounter makes one feel guarded or safe (Haxby et al., 2002). However, we also note that the presence of amygdala responses to natural angry faces in controls (e.g., Whalen et al., 2001; Adams et al., 2003; LaBar et al., 2003; Strauss et al., 2005; Lawrence et al., 2007; but see Blair et al., 1999) as well as the absence of such responses in patients with selective bilateral amygdala damage (e.g., Sato et al., 2002; Graham et al., 2007; but see Adolphs et al., 1999; Siebert et al., 2005; Hurlmann et al., 2007) have inconsistently been reported in the literature.

In view of accumulating evidence for differential effects of gender on socio-emotional processing (Hamann, 2005; Cahill, 2006), we carried out a separate analysis with subjects' gender as a second factor. However, this analysis yielded no significant results, most probably due to the small sample size in the present study ($n = 14$).

Extending our analyses to the whole brain, we detected robust temporopolar activation to both angry and happy face stimuli, a finding consistent with previous fMRI studies using emotional face stimuli (e.g., Phillips et al., 1998; Blair et al., 1999; Tsukiura et al., 2003; Kim et al., 2005). Classic lesion studies in monkeys (e.g., Klüver and Bucy, 1937) and humans (Damasio et al., 1990; Gorno-Tempini et al., 2004) provide converging evidence for engagement of the temporal pole in the production as well as recognition of facial expressions (Olson et al., 2007). In addition, an ability to infer emotional states, desires, intentions, and beliefs of others (theory of mind, ToM) involves the temporal pole (Olson et al., 2007). Findings of overlapping activations for ToM and empathy tasks in the temporal pole have led to proposals that this region contributes to inferences about the mental state of others (Frith and Frith, 2003).

By calculating a happy versus angry contrast, we isolated a differential neural response to positive valence in the ventromedial prefrontal cortex. This result is in line with a functional parcellation of the prefrontal cortex along the emotional dimensions of arousal and valence, with the ventromedial subregion specifically coding positive valence (Dolcos et al., 2004). The emotion versus neutral contrast revealed robust activations of face-processing regions within occipito-temporal cortices including the occipital gyrus and the fusiform gyrus (Kanwisher et al., 1997; Haxby et al., 2002), perhaps reflective of distant modulatory influences of the amygdala (Amaral and Price, 1984; Vuilleumier et al., 2004).

In conclusion, the present fMRI study – although limited by the use of virtual stimuli – extends current models of human facial emotion perception by suggesting an internal amygdala organization related to the extraction of value from facial expressions. Thus, our findings add to emerging evidence (Ball et al., 2007) that the combined use of fMRI and probabilistic anatomical maps is feasible to shed new light on the functional architecture of the human amygdala by specifying the response properties of its constituent subregions.

Conflict of interest

None.

Acknowledgments

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jneumeth.2008.04.004.

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