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Amygdala activation during masked presentation of emotional faces predicts conscious detection of threat-related faces

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Abstract

It has been argued that critical functions of the human amygdala are to modulate the moment-to-moment vigilance level and to enhance the processing and the consolidation of memories of emotionally arousing material. In this functional magnetic resonance study, pictures of human faces bearing fearful, angry, and happy expressions were presented to nine healthy volunteers using a backward masking procedure based on neutral facial expression. Activation of the left and right amygdala in response to the masked fearful faces (compared to neutral faces) was significantly correlated with the number of fearful faces detected. In addition, right but not left amygdala activation in response to the masked angry faces was significantly related to the number of angry faces detected. The present findings underscore the role of the amygdala in the detection and consolidation of memory for marginally perceptible threatening facial expression.

Keywords: Emotion recognition; Facial expression; Amygdala; Functional magnetic resonance imaging; Threat

1. Introduction

The amygdala is a brain structure located in the medial temporal lobe and known to be involved in the recognition of emotionally valenced stimuli (Adolphs, 2002; Rolls, 1999). Results from early functional neuroimaging studies indicate that the amygdala has a central role in the processing of threat-related facial expression, especially of fearful faces (Morris et al., 1996). Evidence was found that the amygdala responds to fearful faces even when processing them outside conscious awareness (Whalen et al., 1998; Williams, Morris, McGlone, Abbott, & Mattingley, 2004). These automatic processes are assumed to be mediated primarily through a short-latency pathway from the sensory thalamus to the amygdala (LeDoux, 1996). In a series of recent neuroimaging studies it was observed that the amygdala is also involved in the processing of happy, sad, and angry facial expression (Breiter et al., 1996; Wright, Martis, Shin, Fischer, & Rauch, 2002; Yang et al., 2002), even when the faces are presented below the level of conscious awareness (Killgore & Yurgelun-Todd, 2004; Nomura et al., 2004).

According to Whalen (1998) the amygdala should be considered an integral component of a constant vigilance system that is preferentially invoked during the perception of ambiguous stimuli of biological relevance such as facial emotions. Fearful faces provide information about the presence of threat but give little information about the source or location of that threat. Angry faces provide information about the source of the threat, but an angry face must not necessarily indicate an impending attack towards the observer. Happy facial expression normally indicates something positive but can, for example in case of an enemy, also signal that something negative is going to happen to the observer. Thus, to fully understand the biological relevance of facial emotions an observer needs additional context information. Data from animal research suggest

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that, immediately after the amygdala responds to a relevant stimulus, cortical neurons will demonstrate lower thresholds for the detection of subsequent sensory information (Kapp, Wilson, Pascoe, Supple, & Whalen, 1990). It has been therefore hypothesized that, in the presence of a masked emotion face, cortical thresholds for detecting sensory stimuli are lowered, and previously undetected stimuli would be noticed (Whalen, 1998). There is evidence that lesions of the human amygdala reduce the likelihood of marginally perceptible emotional stimuli reaching awareness (Anderson & Phelps, 2001). Nomura et al. (2004) observed a positive correlation of the activation of the amygdala in response to masked angry faces and judgment of anger (in rather neutral) target faces suggesting a subtle biasing or modulation function of the amygdala over the overt recognition process.

Converging findings of animal and human studies provide strong evidence that the amygdala is also critically involved in the acquisition and the retaining of memories of emotional experiences (see, e.g., Cahill, 2000; McGaugh, 2002, 2004, for reviews). Several functional brain imaging studies have shown that amygdala activity during encoding relates to long-term memory for emotionally arousing material but not to memory for emotionally neutral material (e.g., Cahill et al., 1996; Canli, Zhao, Brewer, Gabrieli, & Cahill, 2000; Hamann, Ely, Grafton, & Kilts, 1999). These studies support the "memory-modulation" hypothesis of amygdala function by showing a selective role for the amygdala in enhanced memory for emotional stimuli. Recently, Kilpatrick and Cahill (2003) using structural equation modeling of PET scans found evidence for an amygdala modulation of parahippocampal and ventrolateral prefrontal regions during emotionally influenced memory storage. Both of these brain regions are known to be involved in memory storage processes (e.g., Brewer, Zhao, Desmond, Glover, & Gabrieli, 1998; Wagner et al., 1998).

Backward masking procedures are used to investigate non-conscious automatic mechanisms of stimulus analysis. With these procedures, the conscious recognition of a target stimulus is blocked by an immediately following masking stimulus. The stimulus onset asynchrony (SOA) between target and mask appears to be the principal factor influencing recognition of masked facial emotion expressions (Esteves & Öhman, 1993). Conscious awareness of briefly shown emotional faces can be prevented by the use of neutral facial expressions as masking stimuli when SOAs are <40 ms (Esteves & Öhman, 1993).

In the present fMRI study we examined whether a high activation of the amygdala during the masked presentation of facial emotions is associated with a conscious detection of these facial expressions. It was hypothesized that the activation of the amygdala during the processing of marginally perceptible angry facial expression will correlate positively with the number of angry faces detected and the activation of the amygdala during the processing of marginally perceptible fearful facial expression will correlate positively with the number of fearful faces detected. It has been argued (Davis & Whalen, 2001) that the amygdala shows greater activation to a stimulus, the more ambiguous and threatening it is. Thus, provided that the amygdala is involved in the lowering of the perceptual threshold, fearful facial expressions can be expected to be detected more frequently than angry or happy facial expressions.

2. Method and procedure

Nine healthy right-handed volunteers (7 women and 2 men, mean age = 22.3 years, $SD = 2.1$) participated in this functional magnetic resonance study (fMRI) study. Handedness was defined by the Handedness Questionnaire (Raczkowski, Kalat, & Nebes, 1974). The subjects, all of whom were naive with regard to the hypotheses of the experiment, were told that they would see pictures of faces and that they should memorize them. They all gave written informed consent to the experiment, which was approved by the institutional ethics committee. All subjects had no history of psychiatric or neurological illness, were free of psychotropic medication, and had normal or corrected-to-normal vision. The DIA-X interview (Wittchen & Pfister, 1997), a standardized psychiatric screening interview, was administered to assess current and past psychiatric symptomatology.

Face stimuli consisted of fearful (F), angry (A), happy (H), and neutral (N) expressions of 10 individuals (Ekman & Friesen, 1976) which had undergone computer gray-scale normalization. Thus, 40 pictures were used in the fMRI experiment. All photographs were presented repeatedly.

Subjects were presented with alternating 30 s epochs of masked fearful, masked angry, masked happy, and neutral faces or a no-face control stimulus (a gray rectangle). Within epochs, masked stimuli were presented twice per second in a random sequence. Each trial had a duration of 500 ms. In masked face trials a fearful, angry, or happy expression was presented for 33 ms, followed immediately by a 467 ms neutral expression. In non-masked face trials neutral facial expression was shown for 500 ms. The no-face control stimulus was shown for 450 ms followed by a blank screen for 50 ms.

The order of the 30 s epochs containing facial stimuli was counterbalanced across subjects. There were four counterbalanced orders of presentation (Latin square design) [1. c (no-face control epoch), A, c, F, c, H, c, N, c, A, c, F, c, H, c, N; 2. c, F, c, N, c, A, c, H, c, F, c, N, c, A, c, H; 3. c, N, c, H, c, F, c, A, c, N, c, H, c, F, c, A; 4. c, H, c, A, c, N, c, F, c, H, c, A, c, N, c, F]. Thus, each face epoch was preceded by a no-face control epoch and was presented twice, so that the overall presentation time was 8 min.

In a first investigation face stimuli of Ekman and Friesen (1976) were presented to an independent sample (10 females and 10 males; age *M*, 28.4 years; *SD*, 8.4 years) with the task to identify the emotional quality of the masked faces. In this experiment masked faces were presented for 33 ms, followed immediately by a 333 ms neutral expression. The mean sensitivity index d' of study participants

was 0.49. That is, study participants performed at chance level (0.5) and were not able to consciously discriminate between emotional and neutral facial expressions.

Functional magnetic resonance study data were obtained while participants were lying supine in the MR scanner tunnel. Images were projected (Sharp XG-PC10XE projector) onto a screen at the rear of the scanner tunnel which could be viewed through a mirror (8 cm × 12 cm) mounted at the MR head coil. Image presentation was realized by means of the software package Experimental run time system (ERTS; Beringer, 1999). An intelligent pre-load algorithm is built into the runtime system managing the image switching process and allowing to realize each onset within one video refresh. The head position was stabilized by a vacuum head cushion.

T2* functional data were acquired at a 3 T scanner (Gyroscan Intera 3 T, Philips Medical Systems, Best, NL) using a single shot echoplanar sequence with parameters selected to minimize distortion in the region of central interest while retaining adequate S/N and T2* sensitivity according to suggestions made by Robinson, Windischberger, Rauscher, and Moser (2003). Volumes consisting of 25 axial slices were acquired (matrix 128^2, resolution 1.75 mm × 1.75 mm × 3.5 mm; TR = 3 s, TE = 30 ms, FA = 90°) 160 times in block design, 10 times per condition. Additionally, two anatomical datasets were acquired: T1 weighted inversion recovery and a high resolution T1 weighted 3 D sequence (isotropic pixel, 0.5 mm edge length) (Fig. 1). Functional imaging data were motion corrected, using a set of six rigid body transformations determined for each image, spatially normalized to standard MNI space (Montreal Neurological Institute) and smoothed (6 mm FWHM) using Statistical Parametric Mapping (SPM2, Wellcome Department of Cognitive Neurology, London, UK). Statistical analysis was performed by modeling the different conditions (angry, fearful, happy, neutral, and no-face) as variables within the context of the general linear model (modeled by a standard hemodynamic response function) on a voxel by voxel basis. Because of interindividual shape and location differences in the amygdala, coordinates of search regions for a small volume correction analysis were individually determined from normalized anatomical data (e.g., Convit et al., 1999). The following structures were defined as boundaries and only activation peaks within these boundaries were permitted for further analyses: the anterior hippocampus as identified on the sagittal plane was projected on the coronal view and marked as the *posterior* boundary. Since the most anterior slice of the amygdala is difficult to locate, the *anterior pole* of the amygdala was defined as the image in which its width was approx. 2.5 times the thickness of the adjacent entorhinal cortex located inferior. The hippocampal–amygdala-transitional area served as the *anterio-inferior* boundary, and a thin strip of parahippocampal white matter, the angular bundle, and was used to outline the *medial border*. Demarcation of the *superior-medial border* of the amygdala was done using the semilunar gyrus; the *superior-lateral* boundary was assigned by a thin stripe of white matter, which separates the amygdala from claustrum and nucleus caudatus. The temporal white matter and the extension of the temporal horn were used as the *inferior-lateral* and the hippocampus as the *inferior* boundary (Fig. 1).

These anatomical boundaries were used to make sure that all activation peaks were definitely located in the amygdala region. Manual tracings and analyses were done by an experienced neuroscientist (P.O.), who has implemented manual segmentation in different brain areas in a considerable number of imaging studies (Ohrmann et al., 2004, 2005; Pfleiderer et al., 2003, 2004; Michael, Erfurth, Ohrmann, Arolt, & Heindel, 2003a, 2003b, 2003c).

Checks were performed that the results were not influenced by motion artifact by rerunning the analyses using the estimated motion parameters as covariates of no interest in the design matrix and confirming that the results were unaffected.

The recognition task consisted of 40 black and white photographs of faces (neutral (mask) faces ($n = 10$), angry, fearful, and happy (prime) faces ($n = 4$, respectively), neutral distractor faces ($n = 10$), angry distractor faces ($n = 3$), fearful and happy distractor faces ($n = 2$, respectively), and a surprise expressing face). For each face, participants had to decide whether they had seen this facial expression during the fMRI experiment or not.

To investigate the activity of the amygdala in the processing of marginally perceptible facial emotion, the data obtained in response to masked emotion faces were subtracted from those obtained in response to neutral faces. For all subjects voxels of maximum activation ("peak voxels") elicited by emotion faces as compared to neutral faces were determined (see Table 1). The statistical threshold was set at $p < .05$ for all conditions.

According to the findings of previous fMRI studies the amygdala can habituate during repeated exposure to emotion faces (e.g., Breiter et al., 1996; Fischer et al., 2003). To examine whether habituation effects occurred in our data we calculated *t* scores for the voxels of maximum activation (see Table 1) and the two experimental blocks for each emotion (anger, fear, and joy) separately and compared them subsequently with paired samples *t* tests. Mean activation obtained in response to masked emotion faces for one block was subtracted from mean activation obtained in response to the no-face control condition (pooled no-face control epochs of blocks 1 and 2).

3. Results and discussion

The detection rate for emotion faces was low (4.4%). There were no significant differences in the detection of happy (*M*, 0.33; *SD*, 1.0), fearful (*M*, 0.33; *SD*, 0.7), and angry faces (*M*, 0.67; *SD*, 1.0) (Kruskal–Wallis test). None of the participants reported having seen an emotional distractor face (i.e., an emotion face not presented in the experiment).

Table 1
Voxels of maximum activation (peak voxels) elicited by (a) angry vs neutral, (b) fearful vs neutral and (c) happy vs neutral facial expression in the amygdala for the nine subjects

Subject	Side	(a) Angry		(b) Fearful		(c) Happy	
[sex]		*x*, *y*, *z*	*t* score	*x*, *y*, *z*	*t* score	*x*, *y*, *z*	*t* score
1 [female]	Left:	−16, −4, −28	3.03**	−16, −4, −26	3.66**	−18, −6, −28	0.92
	Right:	26, −10, −20	2.90*	26, −10, −20	2.30***	30, −2, −28	0.81
2 [male]	Left:	−24, −6, −26	2.35*	−30, −4, −26	2.61*	−30, −4, −20	1.95***
	Right:	24, −10, −26	4.31**	28, −4, −28	2.49*	10, −10, −24	1.16
3 [female]	Left:	−20, −4, −24	3.47**	−26, −8, −26	3.35**	−24, −8, −30	4.61**
	Right:	18, −6, −18	2.45*	16, −12, −20	1.72***	18, −6, −18	3.20**
4 [female]	Left:	−16, −4, −18	4.59**	−28, −8, −20	5.07**	−22, −4, −22	3.45**
	Right:	24, −8, −16	3.26**	26, −2, −22	3.57**	24, 0, −24	2.60*
5 [male]	Left:	−14, −6, −16	1.35	−22, −10, −16	1.50	−18, −6, −20	2.31***
	Right:	20, −8, −14	1.21	20, −6, −16	2.39*	26, 0, −16	1.35
6 [female]	Left:	−26, −12, −18	4.64**	−24, −12, −20	4.17**	−18, −4, −20	2.90*
	Right:	22, −12, −18	4.32**	28, −12, −18	4.20**	22, −12, −20	3.97**
7 [female]	Left:	−28, −4, −20	3.09**	−22, −8, −16	2.49*	−22, −10, −24	2.87*
	Right:	24, −10, −16	3.12**	16, −12, −16	2.80*	16, −12, −16	3.79**
8 [female]	Left:	−18, −4, −18	4.32**	−18, −4, −18	3.70**	−18, −4, −18	4.44**
	Right:	16, −4, −18	2.59*	14, −2, −20	3.26**	18, −2, −18	3.07**
9 [female]	Left:	−32, −12, −18	1.87***	−30, −10, −30	2.71*	−16, −4, −24	3.14**
	Right:	28, −12, −16	2.19***	18, −10, −22	1.79***	28, −4, −16	3.47**

* $p < .01$.
** $p < .001$ (p values small volume corrected).
*** $p < .05$.

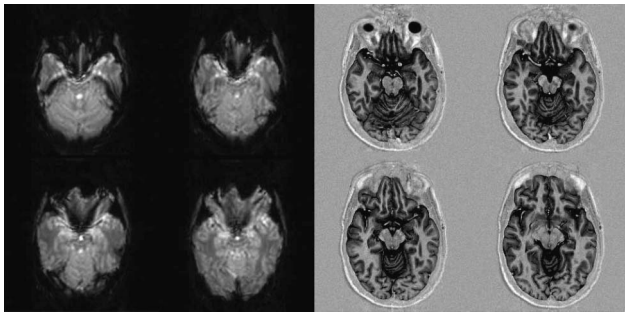

Fig. 1. Four axial echoplanar images for a single subject (left) without any preprocessing steps and corresponding anatomical slices (right) (Inversion recovery, 512 × 512 matrix, identical slice thickness).

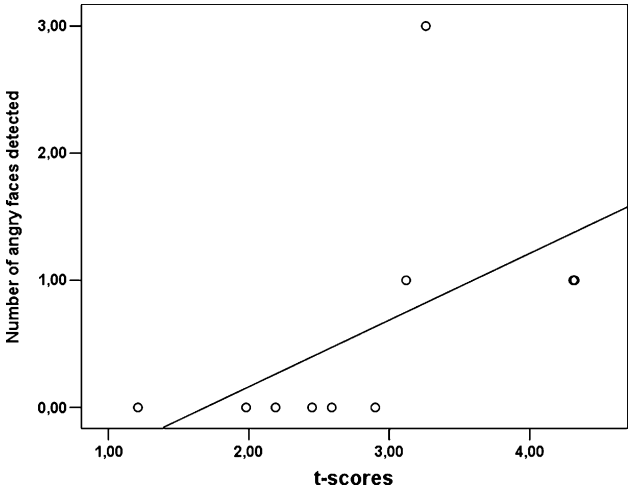

Fig. 2. Scatterplot of right amygdala activity (t score as measure) in response to masked angry faces and number of angry faces detected.

Bilateral amygdala activation in response to the masked fearful faces compared to neutral faces (t values) was significantly correlated with the number of fearful faces detected (Spearman's correlation coefficient $rs = .71$ and .73, $p < .05$). Furthermore, right but not left amygdala activation in response to the masked angry faces was significantly correlated with the number of angry faces detected ($r = .82$, $p < .01$ vs $r = .48$; $p = .19$) (see also Fig. 2). Amygdala activation during the masked presentation of happy faces was not associated with the detection of happy faces ($r = -.14$ (right amygdala), $r = .27$ (left amygdala)). A correlation analysis based on the data from female subjects ($n = 7$) only yielded the same pattern of results: bilateral amygdala activation in response to the masked fearful faces was correlated with the number of detected fearful faces (Spearman's correlation coefficient $rs = .76$ and .80, $p < .05$). Right but not left amygdala activation in response to the masked angry faces was significantly correlated with the number of detected angry faces ($r = .84$, $p < .05$ vs $r = .60$; $p = .16$). Amygdala activation during the masked presentation of happy faces was not significantly correlated with the detection of happy faces. According to results from Mann–Whitney U tests males did not differ significantly from females either regarding amygdala activation (t scores) or number of detected faces ($ps > .10$). However, statistical power to detect differences between sexes was low in the present study due to small sample size. Results of the habituation analysis indicated no significant activation differences between blocks (block 1 and block 2) for the emotion conditions ($ps > .10$).

The present results indicate an association between amygdala activation and the detection of masked threat-related facial expression and thus confirm our main hypothesis. High amygdala activation facilitated the visual processing of inputs of fearful and angry faces and made these threat-indicating or directly threatening stimuli more available for conscious information processing. Our preliminary findings are consistent with results from neuroimaging studies showing that the degree of activity in the amygdala during encoding of emotional visual stimuli is predictive of subsequent recall (e.g., Cahill et al., 1996; Hamann et al., 1999). According to our results there is no association between amygdala activation and detection of masked happy expression. This correlational pattern could indicate that the amygdala is more involved in supporting and enhancing perceptual vigilance and subsequent memory for negative, threatening facial expression compared to positive facial expression. Our data are consistent with the "memory-modulation" hypothesis of amygdala function by showing a regulating role for the amygdala in the process of perception and short-term memory for (marginally perceptible) threat stimuli.

Recently, human brain imaging evidence has begun to reveal a gender-related hemispheric lateralization of amygdala function with respect to memory for emotional material, at least as regards negatively valenced material (Cahill et al., 2001, Cahill, Uncapher, Kilpatrick, Alkire, & Turner, 2004; Canli, Desmond, Zhao, & Gabrieli, 2002). It was found that in men activity of the right hemisphere amygdala was related to long-term incidental memory for arousing material, whereas in women activity of the left hemisphere amygdala was related to memory for arousing material. The results of the present study support only in part the hemispheric lateralization hypothesis of amygdala function: in our female subjects memory for fearful faces was correlated with left and right amygdala activation and memory for angry faces was only related to right amygdala activation. Our results for fearful faces are more in line with the notion that bilateral amygdala activity during memory encoding is involved in episodic recognition memory for emotion stimuli (Cahill et al., 1996; Hamann et al., 1999). Future investigations are needed to further clarify the question whether there are sex-related lateralization differences in amygdala function with respect to memory for facial emotion.

Contrary to our hypothesis, we found no evidence that detection rates for fearful faces, i.e., highly ambiguous and threatening social stimuli, were higher than those for angry or happy faces. The overall detection rate in our experiment was low. This was to be expected, since various studies using a similar experimental protocol had reported that very brief SOAs <40 ms were found to block conscious recognition of emotion faces (Esteves & Öhman, 1993; Whalen et al., 1998). However, our results indicate that at least some people are able to detect masked emotion faces—in case of fearful or angry faces, these persons were characterized by high amygdala activation during face presentation.

According to Whalen (1998) the amygdala is involved in increasing vigilance for emotion stimuli either by lowering neuronal thresholds in sensory systems, probably via activation of cholinergic neurons in the basal forebrain (i.e., the substantia innominata), and/or by activation of cholinergic, dopaminergic, serotonergic, and noradrenergic neurons in the brainstem that have widespread influences on the thalamic and subthalamic sensory and motor transmission (Davis & Whalen, 2001). Interestingly, neural responses in several brain regions relevant to visual information processing (e.g., inferior occipital gyri, middle temporal gyrus, and fusiform gyrus) were found to be better predicted by amygdala activity during the processing of fearful faces compared to happy faces, indicating a category-specific connectivity (Morris et al., 1998). Memory for marginally perceptible threatening faces may also result from modulatory influences from the amygdala on memory storage processes occurring on other brain regions such as the parahippocampal gyrus and the ventrolateral prefrontal cortex.

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