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NeuroImage 30 (2006) 588 – 600

Dissociable networks for the expectancy and perception of emotional stimuli in the human brain

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Received 5 November 2004; revised 21 July 2005; accepted 24 September 2005
Available online 7 November 2005

William James posited that comparable brain regions were implicated in the anticipation and perception of a stimulus; however, dissociable networks (at least in part) may also underlie these processes. Recent functional neuroimaging studies have addressed this issue by comparing brain systems associated with the expectancy and perception of visual, tactile, nociceptive, and reward stimuli. In the present fMRI study, we addressed this issue in the domain of pictorial emotional stimuli (IAPS). Our paradigm involved the experimental conditions emotional expectancy, neutral expectancy, emotional picture perception, and neutral picture perception. Specifically, the emotional expectancy cue was uncertain in that it did not provide additional information regarding the positive or negative valence of the subsequent picture. Neutral expectancy and neutral picture perception served as control conditions, allowing the identification of expectancy and perception effects specific for emotion processing. To avoid contamination of the perception conditions by the preceding expectancy periods, 50% of the pictorial stimuli were presented without preceding expectancy cues. We found that the emotional expectancy cue specifically produced activation in the supracallosal anterior cingulate, cingulate motor area, and parieto-occipital sulcus. These regions were not significantly activated by emotional picture perception which recruited a different neuronal network, including the amygdala, insula, medial and lateral prefrontal cortex, cerebellum, and occipitotemporal areas. This dissociation may reflect a distinction between anticipatory and perceptive components of emotional stimulus processing.

Introduction

Immediate identification of motivationally relevant information and its translation into prompt action is critical for survival (Darwin, 1872). The expectancy (anticipation) of future events allows one to optimize the speed and accuracy of these processes (Ingvar, 1985). Expectancy may be regarded as preceding attention to an upcoming stimulus which is predicted by a contextual cue. Previously acquired knowledge in combination with current environmental information provides the basis for the generation of expectancy (Pavlov and Anrep, 1927). Expectancy can be observed in a variety of domains, including vision, somatosensation, reward, and emotion. *Emotional* expectancy concerns the anticipation of emotionally salient events. It prepares for focused affective and cognitive information processing and for early motor and autonomic reactions.

Functional neuroimaging has been used to study the neuronal correlates of various aspects in emotion processing (Phan et al., 2002). However, investigations directed at identifying brain regions associated with the expectancy of pictorial emotional stimuli have only recently begun (Ueda et al., 2003; Simmons et al., 2004). In contrast, expectancy-related processes have been investigated extensively in other domains. These include vision (Kastner et al., 1999; Shulman et al., 1999; Hopfinger et al., 2000), olfaction (Gottfried et al., 2002), touch sensation (Carlsson et al., 2000), viscerosensation (Phillips et al., 2003b), taste reward (O'Doherty et al., 2002), monetary reward (Breiter et al., 2001; Knutson et al., 2001; Kahn et al., 2002; Kirsch et al., 2003; Knutson et al., 2003; Tanaka et al., 2004), and pain (Reiman et al., 1989; Ploghaus et al., 2003; Singer et al., 2004).

Common to expectancy studies in all domains is the question of the relationship between expectancy- and perception-related activities in the human cortex. Two different

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doi:10.1016/j.neuroimage.2005.09.040

answers to this question may be considered. William James (1892) posed the theory that expectancy fundamentally depends on activation in the *same* networks that process the actual perception of a stimulus. Alternatively, one could propose that expectancy and perception largely involve *distinct* brain regions. Interestingly, imaging data have been reported in support of both hypotheses. In line with James' theory, largely overlapping networks were identified in the tactile and visual domains, where tactile expectancy produces activation in the primary and secondary somatosensory cortices (Carlsson et al., 2000), and the anticipation of moving objects activates the extrastriate visual area V5 (Shulman et al., 1999). In contrast, a considerable dissociation between networks has been observed in studies concerning reward (Knutson et al., 2001; O'Doherty et al., 2002; Knutson et al., 2003) and pain (Ploghaus et al., 2003). It would be reasonable to assume that the extent of overlap between expectancy and perception networks varies considerably depending on the domain studied and the paradigm employed. The present study tested the two abovementioned hypotheses in the domain of pictorial emotional stimuli.

The expectancy of pictorial emotional stimuli has been recently investigated using functional magnetic resonance imaging (fMRI) (Ueda et al., 2003; Simmons et al., 2004). These studies employed emotional expectancy cues that can be characterized as certain with regard to the valence of the emotional picture presented; the cues clearly predicted whether a positive or negative picture would follow. During positive expectancy, Ueda et al. (2003) observed signal increases in the left dorsolateral and medial prefrontal cortex and the cerebellum. Negative expectancy induced activation in the medial and lateral prefrontal cortex, amygdala, parahippocampal gyrus, perigenual anterior cingulate cortex (PAC), insula, and occipital regions (Ueda et al., 2003; Simmons et al., 2004). These findings suggest that there is a considerable overlap between networks involved in the expectancy and perception of emotional stimuli. However, a within-study comparison between expectancy and perception networks has not been carried out.

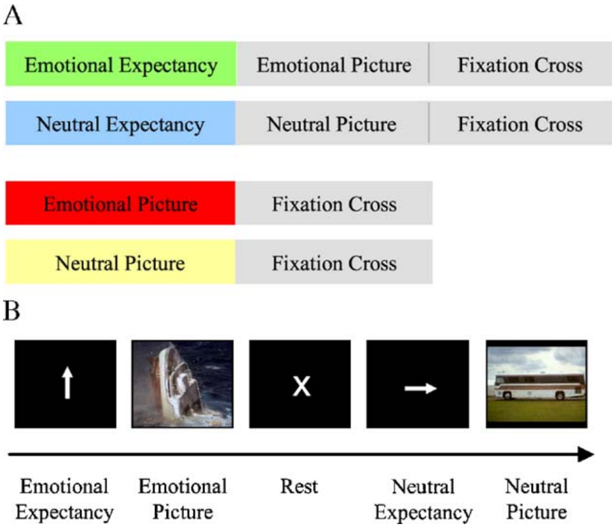

Fig. 1. fMRI paradigm. (A) Experimental conditions. Expectancy (emotional, neutral) and perception (emotional, neutral) conditions were distinguished. Emotional and neutral expectancy intervals (upright, horizontal arrow) preceded emotional and neutral picture perception, respectively. The upright arrow did not predict whether a positive or negative emotional picture would follow. (B) Example trials. The conditions 'emotional expectancy' (with subsequent emotional picture perception) and 'neutral expectancy' (with subsequent neutral picture perception) are illustrated. Stimuli are not drawn to scale.

This comparison is provided by the present study, which, in contrast to previous studies, employed valence-unspecific 'emotional' rather than 'positive' or 'negative' expectancy. The aim of our study was to examine the expectancy of emotional pictures in comparison to the perception of these stimuli. For this purpose, we searched for differences and commonalities between neuronal networks activated during the expectancy and perception of emotional pictures. Our paradigm used neutral expectancy and neutral picture perception as control conditions allowing the identification of anticipatory and perceptive components specific for emotion processing. The emotional expectancy cues employed in our paradigm (Fig. 1) were defined as uncertain in that they did not provide information as to whether a positive or negative emotional picture would follow. Our emotional expectancy condition may thus be considered an expectancy of a pictorial stimulus of uncertain emotional content. The employed expectancy condition differs from conventional Pavlovian conditioning in two regards. First, we informed our subjects in the study instruction about the association between the expectancy cues and subsequent pictorial stimuli. This was further practiced using additional test stimuli. Second and more importantly, in conventional conditioning, the cue is exclusively linked to *either* aversive *or* appetitive stimuli. In our study, by contrast, the emotional expectancy cue was followed in equal proportions by positive *and* negative stimuli. The emotional expectancy condition studied here can also be distinguished from reward anticipation. In reward paradigms, participants normally assume that the outcome of a trial depends on their task performance. In our study, by contrast, subjects were aware that they could not influence the valence of the presented stimuli. Finally, our paradigm differs from previous studies of pain expectancy. First, pain paradigms activate the nociceptive system which may interact with both the emotion and the expectancy network in a pain-specific way. Second, pain expectancy is exclusively directed at aversive stimuli, whereas emotional expectancy (as defined in our paradigm) equally refers to appetitive (positive) and aversive (negative) stimuli. In summary, reward and pain expectancy as well as conditioning paradigms certainly involve some emotional component; however, by using reward and pain stimuli, they involve an additional component specific for the respective paradigms. It seems plausible that this additional component could potentially activate a neuronal network of its own and interact with the emotion and expectancy networks in a domain-specific way. This means that conditioning, reward, and pain paradigms may activate both the emotion and the expectancy system differently from paradigms using classical emotion induction methods. It would therefore seem desirable to compare expectancy and perception also in relation to standardized and validated emotional stimuli (International Affective Picture System; Lang et al., 1999) that do not involve additional components of reward and pain. In doing so, we hypothesized that this approach may allow to further isolate the emotional component within the comparison between expectancy and perception networks. The main finding of our study is that uncertain emotional expectancy specifically activated the supracallosal anterior cingulate cortex, cingulate motor area, and parieto-occipital sulcus. This network was dissociable from the activations observed during emotional picture perception.

Materials and methods

Subjects

Seventeen healthy volunteers (age range: 21–37; 9 females) with no history of neurological or psychiatric illness (based on a physician's examination and interview) participated in this study after giving written informed consent. This study was approved by the institutional review board of the Beth Israel Deaconess Medical Center.

Experimental design

Standardized photographs taken from the International Affective Picture System (IAPS, Lang et al., 1999) were used as pictorial stimuli (Fig. 1). Pictures of this set are largely matched between valences with regard to color, luminance, complexity, and semantic content. Each picture presentation was followed by a rest period (8.5 s duration) that allowed subjects to emotionally recover from the picture. Prior to half of the photographs, attention-directing cues were presented (expectancy period, Fig. 1). An upwards-pointing arrow indicated that an emotional photograph would follow ('emotional expectancy'). A horizontal arrow signaled a neutral picture ('neutral expectancy'). The instruction for upwards-pointing arrows was to build up attention for subsequent emotional picture perception. During horizontal arrows, subjects had to build up attention for subsequent neutral picture perception. The other half of the photographs was not preceded by an arrow (Fig. 1). These trials without expectancy constituted the conditions 'emotional picture perception' and 'neutral picture perception.' The paradigm thus distinguished between expectancy and perception as well as between emotional and neutral conditions (Fig. 1). Neutral expectancy and neutral picture perception served as control conditions, allowing the identification of anticipatory and perceptive components specific for emotion processing. Each of the four condition types (emotional expectancy, neutral expectancy, emotional perception, and neutral perception) comprised of 64 trials presented over 8 runs. The conditions were pseudorandomized and counterbalanced within and across runs. The non-pictorial stimuli presented during these conditions (upright and horizontal arrows) were of equal shape, size, color, and luminance and were centered on a black background. The duration of both expectancy period and picture presentation was 5 s each. The relatively long duration of picture presentation was chosen to match the durations of expectancy and perception conditions. Furthermore, it was ascertained during behavioral pilot testing that several of the more complex pictures required longer processing times in order to be fully comprehended and appreciated (and thus induce the respective emotional responses). Similar durations were previously used in other studies (e.g., Schaefer et al., 2002).

Prior to the experiment, subjects were familiarized with the paradigm and completed a test run with 20 trials. The subjects were instructed to promptly press a button whenever they saw a photograph. This button press allowed the monitoring of the attentiveness of the subjects. The button response did not require a specific judgment because such cognitive demand could have interfered with emotional stimulus processing (Taylor et al., 2003). Due to technical difficulties, reaction times were not recorded in three subjects.

A day after the fMRI session, the paradigm was presented to the subjects again. This time, each picture was followed by a task period consisting of emotional valence and intensity rating as well as a surprise recognition test. Valence and intensity ratings were scored using a 9-point visual analogue scale, in which (1) meant 'very negative' or 'low intensity,' (5) meant 'neutral' or 'medium intensity,' and (9) meant 'very positive' or 'high intensity,' respectively. Although these post hoc ratings do not reflect the actual performance during scanning, it would seem reasonable to assume that subjects had similar experiences during the scanning and post hoc session. The valence ratings given by our subjects indicated that pictures classified as emotional and neutral in the paradigm were experienced as such. The average valence rating scores for the negative, neutral, and positive pictures employed were 1.81 (±0.54, SD), 5.14 (±0.30), and 7.26 (±0.73), respectively. Post hoc intensity ratings showed mean scores of 5.99 (±0.96) and 3.08 (±1.05) for emotional and neutral pictures, respectively. The recognition task tested for recognition of pictures presented during the fMRI session. We found mean hit rates of 0.74 (±0.00) and 0.63 (±0.00) and mean false alarm rates of 0.08 (±0.02) and 0.06 (±0.01) for emotional and neutral pictures, respectively. These relatively high recognition scores suggest that subjects had been attentive during the picture perception throughout the fMRI session.

fMRI data acquisition

MR images were acquired on a 3 T GE VH/1 (Milwaukee, WI, USA) whole-body scanner equipped with echo planar imaging (EPI) capabilities using the standard head coil for radio-frequency transmission and signal reception. A 3D T1-weighted structural image (1 mm^3 voxel size) was acquired for each subject for anatomical reference. For functional imaging, a gradient-echo EPI sequence was used with a repetition time (TR) of 3.016 s, an echo time (TE) of 20 ms, and a matrix of 64 × 64. Using a midsagittal scout image, a total of 36 contiguous axial slices were acquired parallel to the bicommissural plane covering the entire brain in less than 3 s (flip angle = 90°, FOV = 24 cm, 3 mm slices, skip 1 mm). A total of 196 T2*-weighted functional images were acquired per run. The first four acquisitions of each run were discarded due to T1 saturation effects. BOLD images were reconstructed to yield isotropic voxels, 4 mm on edge.

fMRI image analysis

Image processing and statistical analysis were performed using SPM99 (Wellcome Department of Imaging Neuroscience, London, UK). Each set of functional volumes was realigned to the first volume (Friston et al., 1995a), spatially normalized (Friston et al., 1995a) to a standard SPM99 template based upon the MNI reference brain (Evans et al., 1993), and finally smoothed using an 8-mm FWHM Gaussian kernel. The effect of global differences in scan intensity was removed by scaling each scan in proportion to its global intensity. Low-frequency drifts were removed using a temporal high-pass filter with a frequency of 1/200 Hz. High-frequency drifts were removed applying a low-pass filter convolving our data with the hemodynamic response function (HRF). Prior to statistical analysis, a whole-brain mask was created and was explicitly specified based on each subject's normalized inplane anatomical image. This was done to ensure that statistics are performed in all brain regions, including those where signals may be low in some subjects due to susceptibility artifacts (K. Christoff, http://www-psych.stanford.edu/~kalina/SPM99/Tools/glm_specmask.html).

Condition and subject effects were estimated using the general linear model approach (Friston et al., 1995b). We modeled six regressors of interest, convolved with the canonical hemodynamic response function (HRF) as implemented in SPM99 (Friston et al., 1998). Besides the four main experimental conditions (emotional and neutral expectancy; emotional and neutral picture perception without preceding expectancy; Fig. 1), we also modeled the emotional and neutral picture periods following the expectancy cues. Though not involved in the main contrasts of this study, these two conditions were modeled to reduce the possible confound of expectancy by subsequent picture-related BOLD responses. Since the paradigm did not distinguish between positive and negative valences during emotional expectancy, our analysis did not differentiate between positive and negative picture periods. In a first-level analysis, parameter estimates of stimulus-related activity were obtained at each voxel for each regressor and each subject (Friston et al., 1995b). Contrast images were constructed, whereby the size of a given effect at each voxel constitutes the image. For second-level random-effects analysis (Friston et al., 1999), these single-subject contrasts were entered into one-sample t tests across the 17 subjects. Foci were identified with a global height threshold of $P < 0.05$ FDR-corrected for multiple comparisons (false discovery rate, Genovese et al., 2002) and an extent threshold of $k = 5$ voxels.

Statistical parametric maps were first estimated for the two exploratory contrasts, 'expectancy > perception' and 'perception > expectancy.' The second step of the analysis was to identify brain regions activated during expectancy versus perception specifically in the emotional condition. The random-effects serial subtraction analysis '(emotional expectancy > neutral expectancy) > (emotional perception > neutral perception)' was calculated to identify brain areas specifically activated during expectancy in the emotional condition. To determine the contribution of each of the two constituents of the serial subtraction term, decomposition and masking analyses were carried out. To determine brain regions specifically activated during picture perception in the emotional condition, the contrast '(emotional perception > neutral perception) > (emotional expectancy > neutral expectancy)' was calculated. The third step of the analysis was to determine areas of activation common to both emotional expectancy and emotional picture perception. For this purpose, we performed a random-effects conjunction analysis between the contrasts 'emotional expectancy > neutral expectancy' and 'emotional perception > neutral perception' (Price and Friston, 1997).

It should be noted that the picture perception conditions ('emotional perception,' 'neutral perception') included only pictures without preceding expectancy period. Picture periods following expectancy were excluded from the main comparisons in order to avoid the additional effect of the expectancy-related activity. Reporting statistical parametric maps for contrasts involving the picture periods following expectancy would be beyond the scope of this paper. These will be reported separately.

To obtain the time course of activation in the supracallosal anterior cingulate cortex (peak voxel), we re-sampled the time series of the BOLD signals in 2-s time bins (cf. Sakai and Passingham, 2003). For this analysis, parameter estimates were contrasted between emotional and neutral trials *with* expectancy period. This contrast was chosen because it allowed subtracting the general expectancy effect, thus isolating the specific emotional expectancy effect. As a control, parameter estimates were contrasted between emotional and neutral trials *without* preceding expectancy period. This contrast, again, allowed subtracting the general perception effect, thus isolating the specific emotional perception effect. Time bins covered the time period from 8 s before to 10 s after the onset of a picture, regardless whether an expectancy period preceded the picture or not. The size of effect within each bin was averaged across trials for the 17 subjects, separately for each condition. The extracted contrasts of parameter estimates were smoothed by a kernel of 2 and plotted against time. For this analysis, data were not convolved with the canonical HRF.

To perform region of interest analyses based on an unbiased contrast, we used the contrast 'all conditions versus baseline.' For this baseline contrast, the resting condition was additionally modeled as a regressor. To avoid carry-over effects from the preceding picture period, the baseline condition was defined as the final 5 s of the fixation cross period following neutral pictures. The contrast 'all conditions versus baseline' was chosen because it allowed to identify signal increases associated with our paradigm, without favoring any condition. Based on this unbiased contrast, peak voxels were determined for four regions of interest, namely, the anterior cingulate (BA 24, BA 32), the dorsolateral prefrontal cortex (DLPFC; BA 46, BA 9), the amygdala, and the lateral occipital complex (LOC). We chose the anterior cingulate as region of interest because it has shown activation in various expectancy paradigms (Ploghaus et al., 1999; Carlsson et al., 2000; Kirsch et al., 2003; Porro et al., 2003; Ueda et al., 2003). The amygdala was included because it is commonly activated in emotion paradigms (Phan et al., 2002) and has also been implicated in aversive and appetitive conditioning (Buchel et al., 1998; LaBar et al., 1998; Buchel et al., 1999; Parkinson et al., 2000; Gottfried et al., 2002). The DLPFC was chosen because of its documented implication in both expectancy and emotion processing (Davidson and Irwin, 1999; Carlsson et al., 2000; Phillips et al., 2003a; Ueda et al., 2003; Simmons et al., 2004). Finally, LOC representing a high level perceptual brain area served as a control region. This region was chosen because its role in object recognition (fundamental in picture viewing) is well documented (Amedi et al., 2002). The group analysis for the above unbiased contrast produced peak voxels over smoothed volumes at [$x = -4$, $y = 4$, $z = 48$], [$x = 48$, $y = 4$, $z = 28$], [$x = 28$, $y = -4$, $z = -28$], and [$x = -48$, $y = -80$, $z = -16$] for the anterior cingulate, DLPFC, amygdala, and LOC, respectively. To characterize the pattern of activation in these peak voxels, contrasts of parameter estimates were determined by comparing each experimental condition separately to baseline. This analysis also included the picture conditions *with* preceding expectancy. The contrasts of parameter estimates were averaged for the 17 subjects, separately for each condition and each peak voxel.

Results

Behavioral performance

Participants were instructed to promptly press a button whenever they saw a photograph. No judgment was required for

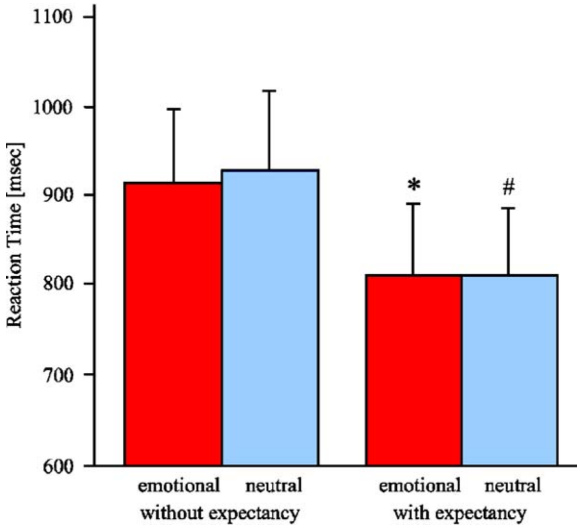

Fig. 2. Behavioral effect of expectancy. During fMRI, participants were instructed to promptly press a button whenever they saw a photograph. Mean reaction times are given for the different experimental conditions (see Fig. 1). Error bars show the standard error of the mean (SEM). *, # Indicate a significant difference from the respective condition without expectancy. *$P < 0.0005$, $t = 6.3$. #$P < 0.0005$, $t = 5.3$.

this response. Reaction times showed a significant effect of expectancy in the repeated-measures ANOVA ($F(1,13) = 41.6$, $P < 0.0005$) with faster responses in the conditions with expectancy (Fig. 2). Across subjects, the average difference between conditions with and without expectancy was 104 ms (±16.4 SEM) in emotional pictures and 116 ms (±13.9) in neutral pictures. No significant effect was observed for the factor emotion ($F(2,26) = 1.4$, $P = 0.24$) or for the interaction between expectancy and emotion ($F(2,26) = 1.9$, $P = 0.16$).

fMRI data

Expectancy versus perception

To compare expectancy with perception independent of emotion, neuronal activity during expectancy was contrasted with activity during perception (emotional and neutral conditions collapsed; $P < 0.05$ FDR-corrected). This contrast revealed signal increases in a broad neuronal network located in the midline of the brain, including the dorsomedial prefrontal cortex (BA 9, 10), pregenual and supracallosal anterior cingulate (BA 24, 32), cingulate motor area (BA 24), supplementary motor area (BA 6), posterior cingulate (BA 23, 29, 30, 31), precuneus, parieto-occipital sulcus (BA 7, 19, 31), and thalamus. In addition, the contrast showed differential activation in lateral parietal regions (angular and supramarginal gyrus, inferior parietal lobule; BA 39, 40), superior and middle temporal gyrus (BA 21, 22, 38), precentral gyrus (BA 6), and DLPFC (BA 9, 10). A very similar pattern of activation was identified by the contrast 'emotional expectancy > emotional perception'.

The reverse contrast ('perception > expectancy,' collapsed across conditions) revealed differential activation in the occipital and lingual gyri (BA 17, 18, 19), fusiform gyrus (BA 20, 37), inferior and middle temporal gyrus (BA 20, 37), insula, Broca's area (BA 44, 45), ventrolateral prefrontal cortex (BA 11, 47), cerebellum, amygdala, parahippocampal gyrus, uncus (BA 28, 34), and midbrain ($P < 0.05$ FDR-corrected). Again, very similar activations were observed when this contrast was separately performed for the emotional conditions ('emotional perception > emotional expectancy').

Expectancy of emotional pictures

To identify brain regions specifically activated during expectancy in the emotional condition, we performed the serial subtraction '(emotional expectancy > neutral expectancy) > (emotional perception > neutral perception).' This analysis revealed differential activation in the supracallosal anterior cingulate cortex (SAC), cingulate motor area (CMA), parieto-occipital sulcus, and superior and middle temporal gyrus ($P < 0.05$ FDR-corrected; Table 1).

It is important to note that this serial subtraction term may reveal activation mainly related to the contrast 'neutral perception > emotional perception' besides activation related to the contrast 'emotional expectancy > neutral expectancy.' To determine the contribution of each of the two constituents of the serial subtraction term, the term was decomposed in the next step. The contrast 'emotional expectancy > neutral expectancy' revealed activation in the SAC, CMA (including the supplementary and pre-supplementary motor area), and parieto-occipital sulcus ($P < 0.05$ FDR-corrected; Fig. 3A). The contrast 'neutral perception > emotional perception' showed activation in the left and right superior temporal gyrus ($P < 0.05$ FDR-corrected), indicating that interaction effects observed in this region are related to the perception rather than the expectancy conditions.

Finally, the serial subtraction term was exclusively masked with the contrast 'neutral perception > emotional perception' to isolate the activation specifically related to emotional expectancy. This procedure is more conservative than the above decomposition as it removes all voxels, which reach a significance level of $P < 0.05$ uncorrected in the mask contrast. The masking resulted in a single cluster of activation located in the SAC (Fig. 3B).

Perception of emotional pictures

To identify brain regions specifically activated during picture perception in the emotional condition, we performed the reverse serial subtraction, i.e., '(emotional perception > neutral perception) > (emotional expectancy > neutral expectancy).' This analysis revealed differential activation in the amygdala, insula, medial and lateral prefrontal cortex, putamen, midbrain, cerebel-

Table 1
(Emotional > neutral expectancy) > (emotional > neutral perception)

Region (Brodmann area)	Coordinates (MNI)			Peak t value	# of voxels
	x	y	z		
Supracallosal anterior cingulate (BA 24, BA 32)	−4	12	36	4.36	22
Cingulate motor area (BA 24)	−4	−8	44	4.85	13
Parieto-occipital sulcus (BA 7, 19, 31)	0	−76	36	4.98	17
Superior/middle temporal	52	−32	8	4.92	29
Gyrus (BA 21, 22)	−64	−12	−4	5.00	19

Peak voxel coordinates, $P < 0.05$ FDR-corrected.

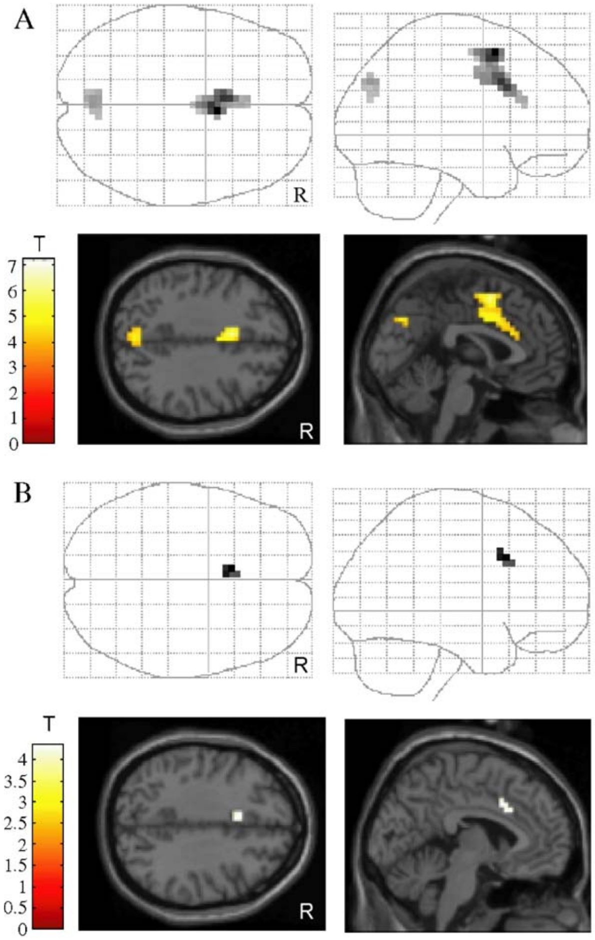

Fig. 3. (A) The contrast 'emotional expectancy > neutral expectancy,' presented in glass-brain projection and section (through $x = -4$, $y = 12$, $z = 36$) views. $P < 0.05$ FDR-corrected. (B) The contrast '(emotional expectancy > neutral expectancy) > (emotional perception > neutral perception)' exclusively masked with the contrast 'neutral perception > emotional perception'. The significance level was set at $P < 0.05$ FDR-corrected for the main contrast and at $P < 0.05$ uncorrected for the mask. Data are presented in glass-brain projection and section (through $x = -4$, $y = 12$, $z = 36$) views.

lum, and occipitotemporal visual regions ($P < 0.05$ FDR-corrected; Table 2). When the serial subtraction term was exclusively masked with 'neutral expectancy > emotional expectancy,' we observed a similar pattern of activation, however, with smaller clusters in the amygdala and absent effects in medial prefrontal cortex and midbrain.

Conjunction and dissociation between expectancy and perception of emotional pictures

While the above analyses served to identify differences between expectancy and perception networks, the next step was to determine a potential overlap between neuronal networks involved in the expectancy and perception of emotional stimuli. For this purpose, we carried out a conjunction analysis between the two constituents of the above serial subtraction, i.e., the contrasts 'emotional expectancy > neutral expectancy' and 'emotional perception > neutral perception.' The conjunction analysis revealed no overlapping voxels at $P < 0.05$ FDR-corrected. This dissociation of networks is illustrated in Fig. 4 which displays both contrasts with different color coding in one glass-brain ($P < 0.05$ FDR-corrected). When the threshold was exploratorily lowered to $P < 0.001$ uncorrected, the conjunction analysis revealed common activation in the right pre-supplemen-

Table 2
(Emotional > neutral perception) > (emotional > neutral expectancy)

Region (Brodmann area)	Coordinates (MNI)			Peak *t* value	# of voxels
	x	*y*	*z*		
Right amygdala	24	−4	−24	4.95	9
Left amygdala	−32	−4	−24	4.45	28
Right insula	40	4	16	5.2	9
Medial prefrontal cortex (BA 10)	−16	52	0	3.78	9
Left premotor cortex (BA 6)	−52	−4	28	4.16	22
Right Broca's area (BA 44, 45)	52	28	8	5.04	43
Left Broca's area (BA 44, 45)	−44	32	8	3.93	14
Right inferior/middle temporal and fusiform gyri (BA 20, 37)	52	−64	0	7.78	214
Left inferior/middle temporal and fusiform gyri (BA 20, 37)	−48	−60	−20	6.92	243
Right occipital and lingual gyri (BA 17, 18, 19)	8	−88	−8	7.61	527
Left occipital and lingual gyri (BA 17, 18, 19)	−12	−88	−8	7.47	385
Right cerebellum	24	−68	−20	6.37	203
Left cerebellum	−44	−48	−28	5.66	77
Left putamen	−20	−4	4	3.61	7
Right midbrain	20	−24	−4	4.17	8

Peak voxel coordinates, $P < 0.05$ FDR-corrected.

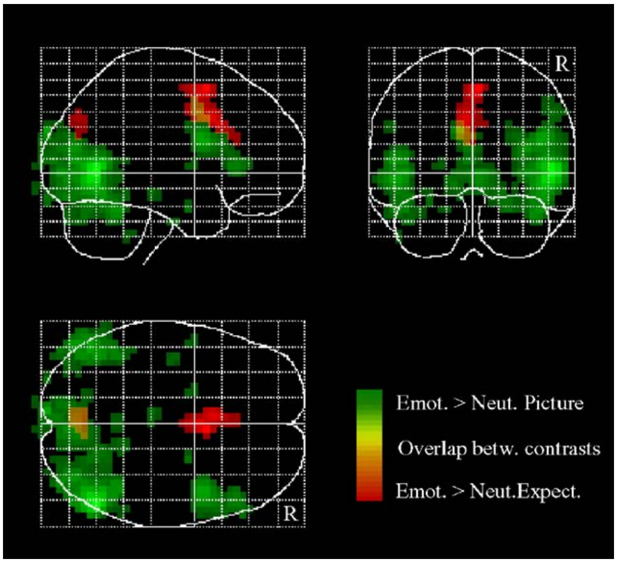

Fig. 4. Dissociation between networks activated during emotional expectancy and emotional picture perception. The contrasts 'emotional expectancy > neutral expectancy' (red) and 'emotional perception > neutral perception' (green), superimposed on one glass-brain. Yellow color code was used where contrasts appear overlapping in the respective projection view. Together, the three projection views reveal that the two contrasts involve distinct neuronal networks. $P < 0.05$ FDR-corrected.

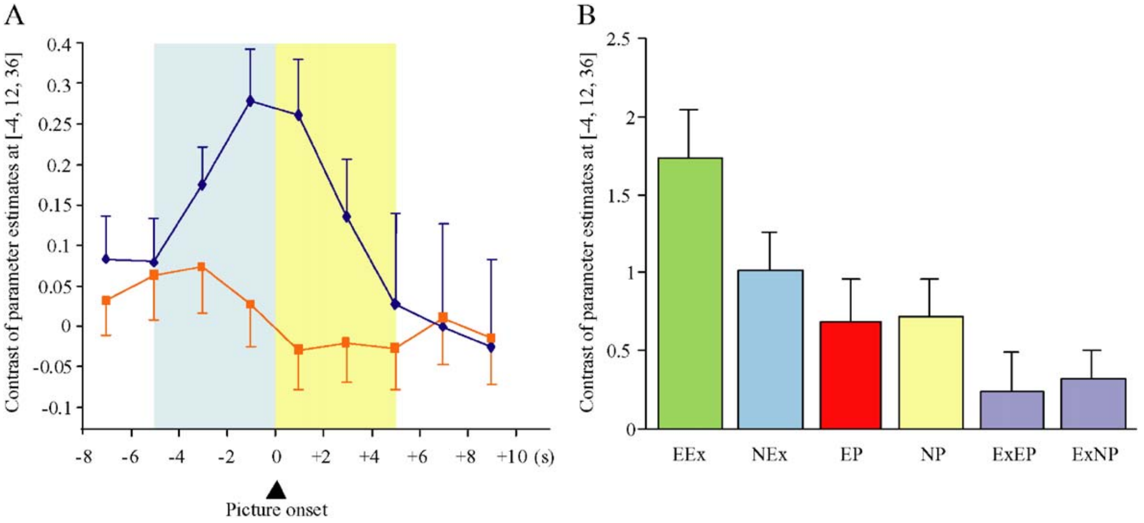

Fig. 5. Size of effect in the SAC. Values refer to the peak voxel over smoothed volumes identified in the group contrast '(emotional expectancy > neutral expectancy) > (emotional perception > neutral perception)' [$x = -4$, $y = 12$, $z = 36$]. (A) Size of effect over time. The blue line represents the contrast between emotional and neutral trials *with* expectancy. The orange line depicts the contrast between emotional and neutral trials *without* expectancy. Contrasts of parameter estimates were extracted from 2-s time bins. The yellow shaded area indicates the period of picture perception. This is preceded by the expectancy period (blue shaded area) in the conditions with expectancy. In the conditions without expectancy, the picture perception is preceded by the rest period. (B) Size of effect in the different experimental conditions. The bars represent the comparison between the different experimental conditions and baseline. The color coding for the different conditions is adapted from Fig. 1. Error bars show the standard error of the mean (SEM). EEx: emotional expectancy, NEx: neutral expectancy, EP: emotional picture perception without preceding expectancy, NP: neutral picture perception without preceding expectancy, ExEP: emotional picture perception with preceding expectancy, ExNP: neutral picture perception with preceding expectancy.

tary motor area ($x = 4$, $y = 12$, $z = 52$) and premotor cortex ($x = 48$, $y = 0$, $z = 44$).

The supracallosal anterior cingulate cortex

The above analyses have shown that the SAC is specifically activated during expectancy in the emotional condition. The group analysis revealed a peak voxel over smoothed volumes at [$x = -4$, $y = 12$, $z = 36$]. To determine the time course of activation in this SAC peak voxel, the time series of the BOLD signals was re-sampled in 2-s time bins (Fig. 5A). For this analysis, parameter estimates were contrasted between emotional and neutral trials *with* expectancy period (blue line). This contrast was chosen because it allowed subtracting the general expectancy effect and thus isolating the specific emotional expectancy effect. As a control, parameter estimates were contrasted between emotional and neutral trials *without* preceding expectancy period (orange line). The time course histogram demonstrates that the SAC activation related to emotional expectancy (blue line) largely occurred before the onset of the pictorial stimuli. Corresponding to the delay of the hemodynamic response, the peak of signal is observed 4–5 s after the onset of the expectancy period (blue shaded area). This signal decays during the subsequent presentation of emotional stimuli (yellow shaded area). No considerable signal changes are seen in the contrast 'emotional versus neutral trials *without* preceding expectancy' (orange line).

To further explore the activation pattern in the SAC, contrasts of parameter estimates were determined for each condition separately compared to baseline (Fig. 5B). Consistent with above findings, signal increases were largest during emotional expectancy. Neutral expectancy produced slightly larger signal increases than emotional and neutral picture perception. No considerable difference in signal intensity was observed between emotional and neutral picture perception. This lack of emotion effect also concerned the expected picture perception.

Region of interest analyses based on an unbiased contrast

The signal changes reported in Fig. 5 concern the SAC peak voxel identified by the serial subtraction contrast '(emotional expectancy > neutral expectancy) > (emotional perception > neutral perception).' In the last step, we explored the patterns of activation for four regions of interest independent of the above-studied main contrasts. For this purpose, peak voxels were determined for the anterior cingulate, dorsolateral prefrontal cortex (DLPFC), amygdala, and lateral occipital complex (LOC) based on the unbiased contrast 'all conditions versus baseline.' For each of these unbiased peak voxels, we determined contrasts of parameter estimates by comparing each condition separately to baseline (Fig. 6). Although the unbiased SAC peak voxel ($x = -4$, $y = 4$, $z = 48$) was located slightly more dorsally than the above-studied biased SAC peak voxel ($x = -4$, $y = 12$, $z = 36$), we found a similar pattern of activation. Also in the unbiased SAC peak voxel, emotional expectancy produced larger activation than neutral expectancy as well as emotional and neutral picture perception. Again, no considerable difference was observed between emotional and neutral picture perception, and this lack of emotion effect concerned both expected and unexpected picture perception. A different pattern of activation was observed in the DLPFC, amygdala, and LOC: in these regions, we did not find considerable activation during emotional expectancy compared to the other conditions. These regions consistently showed larger activation during emotional picture perception compared to neutral picture perception and to emotional expectancy. In addition, the amygdala

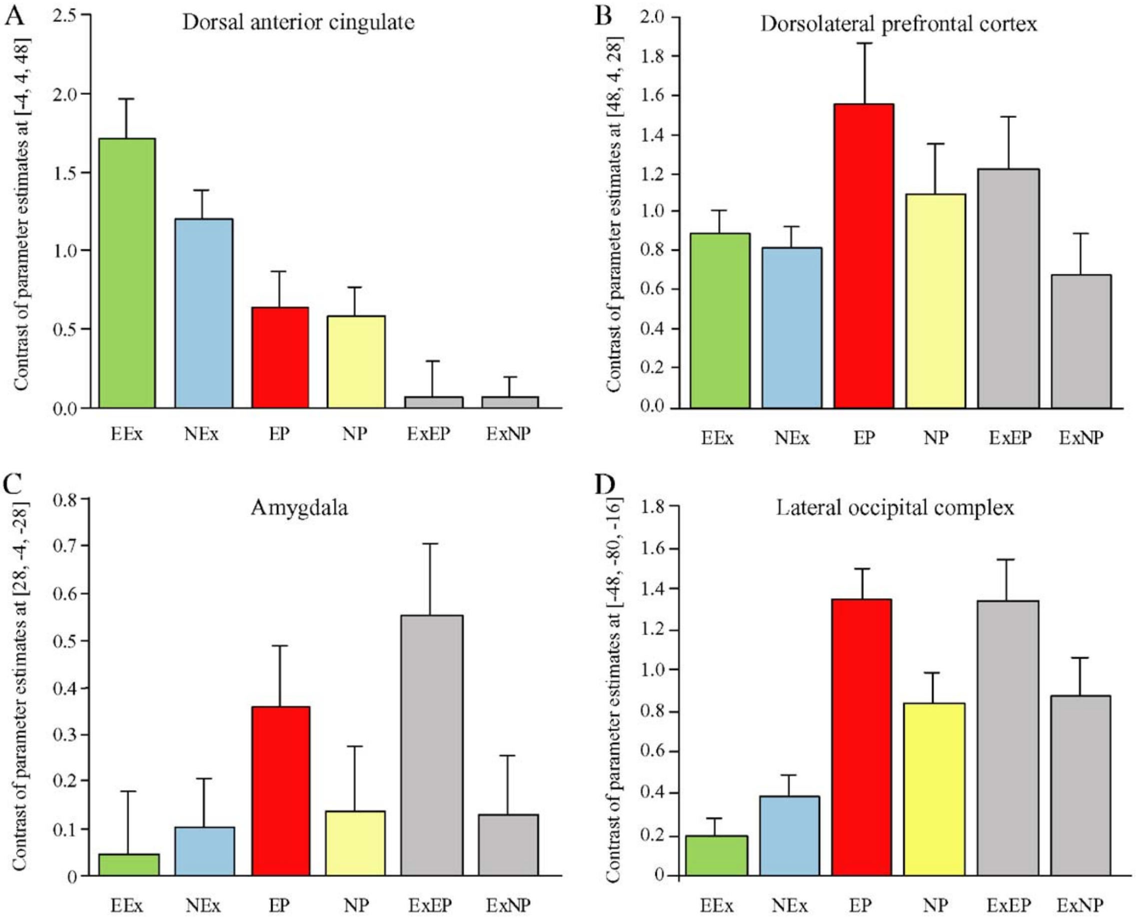

Fig. 6. Size of effect in four regions of interest: anterior cingulate (A), dorsolateral prefrontal cortex (B), amygdala (C), and lateral occipital complex (D). The bars represent the comparison between the different experimental conditions and baseline. Error bars show the standard error of the mean (SEM). The color coding for the different conditions is adapted from Fig. 1. Peak voxels were determined for each region of interest, based on the unbiased contrast 'all conditions versus baseline.' Right and left hemisphere showed comparable results (see Supplementary data). EEx: emotional expectancy, NEx: neutral expectancy, EP: emotional picture perception without preceding expectancy, NP: neutral picture perception without preceding expectancy, ExEP: emotional picture perception with preceding expectancy, ExNP: neutral picture perception with preceding expectancy.

showed larger activation during expected compared to non-expected emotional picture perception. This modulation of perception by expectancy was specific for the emotional condition and was not present in the SAC, DLPFC, and LOC.

Discussion

The present fMRI study examined the neural correlates of the expectancy of pictorial emotional stimuli in comparison to the perception of these stimuli. Neutral expectancy and neutral picture perception were used as control conditions in order to identify brain regions activated during expectancy versus perception specifically in the emotional condition. Our analyses revealed that the supracallosal anterior cingulate cortex (SAC), cingulate motor area (CMA), and parieto-occipital sulcus are specifically activated during expectancy in the emotional condition (*emotional expectancy network*). A different neuronal network was specifically associated with emotional picture perception. This *emotional perception network* involved a variety of brain regions previously reported in neuroimaging studies of emotion perception (Phan et al., 2002), including the amygdala, insula, medial and lateral prefrontal cortex, cerebellum, and occipitotemporal areas. Using conjunction analysis, we were not able to document a potential overlap between these two networks. Taken together, our findings suggest that separate networks are involved in the expectancy and perception of pictorial emotional stimuli.

Dissociation between the expectancy and perception of emotional stimuli

Our finding is in contrast to the hypothesis ventured by William James (1892) that largely the same brain regions were implicated in the anticipation and perception of a stimulus. Carlsson et al. (2000) have previously observed activation of the primary and secondary sensory cortex during both the expectancy and perception of tactile stimuli, lending some support to James' hypothesis. This anticipatory activation in sensory areas was interpreted as the result of tonic top–down regulation of neuronal activity. Our data suggest that such tonic pre-activation is less pronounced or even absent in the domain of emotional picture processing. Instead of anticipatory activation in the emotional perception network, we observed the involvement of a separate network during emotional expectancy. A similar dissociation has been observed in pain (Ploghaus et al., 1999) and reward (Knutson et al., 2001; O'Doherty et al., 2002; Knutson et al., 2003), although there are also indications for overlapping networks in reward (Breiter et al., 2001). O'Doherty et al. (2002) found activation in the ventral tegmental area, amygdala, and striatum during the expectancy of taste reward, whereas the insula and operculum were involved in reward consumption. Such dissociation seems to reflect the distinction between expectancy-related "wanting" and consumption-related "liking" in reward processing (Berridge, 1996). Similarly, our present finding of dissociable patterns of activation observed during different periods of our paradigm may reflect a distinction between anticipatory and perceptive components of emotional stimulus processing.

The expectancy of pictorial emotional stimuli has recently been studied using fMRI (Ueda et al., 2003; Simmons et al., 2004). These paradigms differed from ours in two aspects. First, they used valence-selective (certain) emotional expectancy, while we explored uncertain emotional expectancy. Second, they did not include a condition of 'emotional picture perception without preceding expectancy' so that a within-study comparison between emotional expectancy and perception networks could not be completed. Nonetheless, it appears that in these previous studies positive and negative expectancy produced signal increases in regions that are also activated during emotional stimulus perception in our study and elsewhere (Bush et al., 2000; Phan et al., 2002). These regions include the amygdala, insula, medial and lateral prefrontal cortex, cerebellum, and PAC. Thus, contrary to our findings, their data suggest that there is a considerable overlap between networks involved in emotional expectancy and perception. This discrepancy between study results might be related to differences between certain and uncertain emotional expectancy. This assumption is consistent with expectancy studies in other domains. For instance, findings for certain and uncertain *pain* expectancy are largely analogous to the results in emotional expectancy. Specifically, certain pain expectancy involves the PAC (Ploghaus et al., 1999, 2003), whereas uncertain pain expectancy is associated with activation in the SAC including the CMA (Hsieh et al., 1999; Porro et al., 2002; Jensen et al., 2003; Porro et al., 2003). Similarly, in the *reward* domain, Critchley et al. (2001) found that the expectancy of monetary reward produced larger activation in the SAC when higher outcome uncertainty was present. It seems that these findings are now extended to the domain of emotional picture processing. While certain emotional expectancy has previously been shown to produce activation in parts of the emotional perception network including the PAC, amygdala, insula, and lateral prefrontal cortex (Ueda et al., 2003; Simmons et al., 2004), the present study demonstrates that uncertain emotional expectancy involves brain regions (SAC, CMA, parieto-occipital sulcus) dissociable from the emotional perception network. However, it is acknowledged that the distinction between certain and uncertain emotional expectancy remains speculative as the within-study comparison between certain and uncertain expectancy of emotional pictures was not carried out.

The baseline comparisons shown in Fig. 6 revealed three different patterns of activation associated with our paradigm. First, the SAC showed differential activation during expectancy in the emotional condition (interaction between expectancy and emotion). Larger signal increases were observed during emotional expectancy compared to both neutral expectancy and emotional perception. No difference was found between emotional and neutral perception. Second, the DLPFC and LOC showed differential activation during picture perception in the emotional condition (interaction between perception and emotion). Larger signal increases were observed during emotional picture perception compared to both neutral picture perception and emotional expectancy; no difference was found between emotional and neutral expectancy. Third, the amygdala showed differential activation during emotional picture perception similar to the DLPFC and LOC. In addition, this region showed a specific effect of emotional expectancy on the period of picture perception. Larger signal increases were observed during emotional picture perception when it was preceded by emotional expectancy, while expectancy had no effect on neutral picture perception. The period of emotional expectancy itself was not associated with considerable signal changes in this region. Taken together, these findings illustrate that emotional expectancy and emotional picture perception produce activation in dissociable networks. In addition, these findings suggest that different brain regions are involved in the effect of emotional expectancy at distinct stages of emotional picture presentation. The SAC showed this effect during the expectancy period and the amygdala during the picture perception period, while the DLPFC and LOC were not affected by emotional expectancy.

In contrast to the present investigation, studies on aversive and appetitive conditioning have observed amygdalar activation related to conditioned stimuli (Buchel et al., 1998; LaBar et al., 1998; Buchel et al., 1999; Parkinson et al., 2000; Gottfried et al., 2002). It seems that this difference in findings is related to the difference in valence specificity between expectancy cues. In the mentioned conditioning studies, the cue was linked to *either* aversive *or* appetitive stimuli, whereas, in our study, the emotional expectancy cue is followed in equal proportions by both positive and negative stimuli. It might be speculated that the valence ambiguity of our expectancy cues might have prevented specific aversive or appetitive conditioning processes and related activation of the amygdala in our study.

A methodological challenge associated with expectancy studies is to disentangle cue- from target-related BOLD signals (Rees et al., 1997). Because of the temporal characteristics of the hemodynamic response, the regressors for 'expectancy' may be confounded by the subsequent picture periods. This confounder could be reduced by the inclusion of unpaired (Buchel et al., 1998) or misleading expectancy cues or the use of very irregular expectancy intervals (Chawla et al., 1999). These measures were not taken in our study for psychological reasons. Behavioral pilot tests indicated that the emotional expectancy cue would have become too 'arbitrary' and would not have sufficiently differed from the rest condition. This tendency to 'arbitrariness' of the emotional expectancy cue is related to two features of our paradigm: (1) we used uncertain emotional expectancy cues which by themselves introduce a considerable degree of uncertainty. (2) The fixation cross was followed by emotional pictures in 25% of the trials because our control condition consisted of pictures without preceding expectancy. While these two features were essential for our paradigm, we chose to omit unpaired, misleading, and irregular cues in order to not further lower the predictive value of the emotional expectancy cue. Given this situation, it must be acknowledged that decorrelation of expectancy- and picture-related BOLD responses can only be partially achieved in our study. This raises the possibility that the SAC activation observed in the serial subtraction contrast using 'emotional > neutral expectancy' as the first constituent could be related to the perception of expected emotional pictures rather than the emotional expectancy period per se. However, our results argue against this possibility. First, we found dissociable networks for the expectancy and perception of emotional stimuli. Rather than dissociable networks, one would have anticipated overlapping networks as a result of insufficient decorrelation. Second, the time course histogram (Fig. 5A) demonstrates that the SAC activation induced by emotional expectancy occurred *before* the onset of the subsequent picture presentation. Third, baseline comparisons showed a trend towards lower, rather than higher, signal intensities in the SAC during expected emotional pictures compared to unexpected emotional pictures and to expected neutral pictures (Figs. 5B and 6A). Taken together, our findings indicate that the SAC activation attributed to emotional expectancy was not critically confounded by the subsequent picture period.

Emotional expectancy and the supracallosal anterior cingulate cortex

In our paradigm, activation in the SAC (including CMA) was observed during expectancy specifically in the emotional condition. Based on lesion and functional neuroimaging studies, this region is considered a multi-integrative structure that is implicated in a variety of *affective*, *cognitive*, and *motor* processes related to adaptive behavior (Devinsky et al., 1995; Paus, 2001). Our findings contribute to this notion in that they highlight the anticipatory aspect in these processes.

Although the SAC is considered the 'cognitive division' of the anterior cingulate (Devinsky et al., 1995; Bush et al., 2000), several *affective* functions have also been proposed for this region. These functions relate to the processing of emotional attention (Lane et al., 2001; Vuilleumier et al., 2001), autonomic arousal (Fredrikson et al., 1998; Critchley et al., 2003), reward (Breiter et al., 1997; Bush et al., 2002), and pain (Rainville et al., 1997; Becerra et al., 2001; Rolls et al., 2003; Singer et al., 2004). Our data indicate that the processes mediated by the SAC are independent of the presence of emotional stimuli. In our study, mere expectancy of emotional pictures produced SAC activation. Even more, this response was clearly larger than the one related to the actual perception of emotional photographs. The latter did not differ from neutral picture perception and tended to produce smaller SAC activation than neutral expectancy. Taken together, these findings highlight the anticipatory character of SAC function. They suggest a role for the SAC in *preceding* emotional attention (e.g., emotional expectancy) rather than attentional processes requiring the actual presence of emotional stimuli.

Activation in the SAC (as well as the CMA and parieto-occipital sulcus) has previously been observed in paradigms used to study anticipatory anxiety (Chua et al., 1999), anticipatory arousal (Critchley et al., 2001), and the expectancy of reward (Kirsch et al., 2003) and pain (Hsieh et al., 1999; Porro et al., 2002; Jensen et al., 2003; Porro et al., 2003). Although these paradigms were not explicitly designed to study the expectancy of emotional stimuli, it seems plausible that they implicitly involved this aspect. In addition, these paradigms involved processes specifically related to reward and pain, which may interact with both the emotion and the expectancy network. Using standardized and validated stimuli from the IAPS, the present paradigm was designed to study emotional expectancy independent of reward and pain. In contrast to reward paradigms, subjects were aware that they could not influence the outcome of the trial. In contrast to pain paradigms, the nociceptive system was not activated, and the emotional expectancy cue did not distinguish between aversive and pleasant stimuli which might have prevented specific aversive conditioning processes (see above). In view of the present results, one might suggest that the SAC, CMA, and parieto-occipital sulcus are involved in emotional expectancy independent of reward and pain. Other brain regions activated during reward and pain expectancy may be related to non-emotional aspects of these paradigms; these regions include the ventral tegmental area, ventral striatum, and orbitofrontal cortex in reward expectancy (Breiter et al., 2001; Knutson et al., 2001; O'Doherty et al., 2002; Knutson et al., 2003) and the primary somatosensory cortex, medial prefrontal cortex, insula, and medial thalamus in pain expectancy (Ploghaus et al., 1999; Porro et al., 2002, 2003).

Figs. 5B and 6A show that signal increases in the SAC not only related to emotional expectancy, but also to neutral expectancy. This finding suggests that the arrows presented in the expectancy condition may also induce a nonspecific expectancy effect (attentional capture) in the SAC. Since the signal increase is greater during emotional compared to neutral expectancy, it might be concluded that both nonspecific attentional capture and specific emotional expectancy contribute to the activation observed during emotional expectancy.

It is also important to note that the observed SAC activation cannot simply be explained by a nonspecific arousal effect. A general arousal effect would be hypothesized to produce activation not only during emotional expectancy, but also during emotional picture perception. According to the normative data of the *IAPS* (Lang et al., 1999), the emotional pictures presented can be considered high arousing stimuli and the neutral pictures low arousing stimuli. Since the comparison 'emotional picture perception > neutral picture perception' did not produce differential SAC activation in our experiment (Figs. 4–6), we conclude that the SAC activation observed during emotional expectancy does not simply reflect general arousal. However, we cannot exclude a specific contribution of *anticipatory* arousal to the observed activation. One could argue for a distinction between *anticipatory* and *general* arousal and speculate that the SAC is specifically involved in the former.

The *cognitive* roles previously proposed for the SAC are related to Pavlovian conditioning (Buchel et al., 1998; LaBar et al., 1998) and the representation of conflict (Carter et al., 2000) and uncertainty (Critchley et al., 2001; Keri et al., 2004). The present study focused on emotional expectancy, which naturally involves elements of conditioning. Our paradigm, however, does not represent conventional Pavlovian conditioning (Pavlov and Anrep, 1927) because our subjects were familiarized with the association between the expectancy cues and subsequent pictorial stimuli prior to the experiment. Moreover, in conventional conditioning, the cue is linked to *either* aversive *or* appetitive stimuli. In our study, by contrast, the emotional expectancy cue was followed in equal proportions by positive *and* negative pictures. The emotional expectancy cue thus involved uncertainty with regard to the valence of the subsequent picture (positive or negative) which might have resulted in a conflict between approach and withdrawal. Our data therefore show that SAC involvement in conditioning or, more generally, in expectancy does not presuppose cues unequivocally associated with either aversive or appetitive stimuli.

Besides affective and cognitive processes, the SAC (especially its most caudal part, the CMA) has been implicated in the processing of *motor* response to behaviorally relevant stimuli. Because of its dense connections to primary and secondary motor regions, this region appears well suited to translate affective and cognitive information into action (Paus, 2001). It has been demonstrated that CMA activation does not reflect action performance per se but rather the anticipatory state in which one is ready to select an action in response to a motivationally salient stimuli (Woldorff et al., 1999). In our study, the CMA is activated during emotional expectancy compared to both neutral expectancy and emotional stimulus perception (Fig. 6). One might suggest that the expectancy of emotional pictures also implicates a state of preparedness for motor response (e.g., approach or withdrawal).

Besides the SAC and CMA, the parieto-occipital sulcus (which includes mesial parts of BA 7 and BA 19, extending into BA 31) was identified by the contrast '(emotional expectancy > neutral expectancy) > (emotional perception > neutral perception).' This finding is in accordance with previous studies showing activation in this region during the expectancy of pain (Buchel et al., 1998; Porro et al., 2003), tickling (Carlsson et al., 2000), monetary reward (Bjork et al., 2004), and emotional photographs (Ueda et al., 2003). The parieto-occipital sulcus can be considered the anterior part of the dorsal visual pathway, which projects from early visual areas to the posterior parietal cortex. Like the CMA, this dorsal stream is associated with processes related to action (Goodale and Milner, 1992; Goodale and Westwood, 2004). Specifically, this stream appears to mediate the required sensorimotor transformations for visually guided action. In our study, as well as in the other mentioned expectancy studies, the parieto-occipital sulcus is activated during the expectancy period, which does not involve visually guided action. However, we suggest that the expectancy of motivationally relevant stimuli might implicate a state of preparedness for action. This might produce anticipatory activation in the dorsal stream even in the absence of action-related visual stimulation. Such expectancy-related activation of specialized visual regions has extensively been studied for basic visual features such as color (Chawla et al., 1999), motion (Shulman et al., 1999), or spatial location (Kastner et al., 1999; Hopfinger et al., 2000).

Taken together, our findings point out the anticipatory character of SAC function. Based on the present results and previous studies, it might be suggested that this multi-integrative region is involved in emotional expectancy and its attendant state of preparedness for motor and autonomic response in situations of emotional salience.

Conclusions

Building on previous studies of visual, tactile, pain, and reward anticipation, we compared brain systems activated during the expectancy and perception of pictorial emotional stimuli. During the expectancy of emotional pictures, we observed activation in the supracallosal anterior cingulate, cingulate motor area, and parieto-occipital sulcus. This network of emotional expectancy was dissociable from regions specifically activated during emotional picture perception. We suggest that this dissociation reflects a distinction between anticipatory and perceptive components of emotional stimulus processing, as similarly proposed for pain and reward.

Acknowledgments

This work was supported by a grant within the Postdoc-Programme of the German Academic Exchange Service (DAAD, D/02/46858) to F.B., a Heisenberg grant from the German Research Foundation to G.N. (DFG, 304/4-1), a Human Frontier Science Program award to A.A., grant K24 RR018875 from the National Institutes of Health (NCRR) to A.P.-L., and the Harvard Thorndike General Clinical Research Center (NCRR MO1 RR01032).

Appendix A. Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.neuroimage.2005.09.040.

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