Task Instructions Modulate Neural Responses to Fearful Facial Expressions

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Background: *The amygdala, hippocampus, ventral, and dorsal prefrontal cortices have been demonstrated to be involved in the response to fearful facial expressions. Little is known, however, about the effect of task instructions upon the intensity of responses within these regions to fear-inducing stimuli.*

Methods: *Using functional magnetic resonance imaging, we examined neural responses to alternating, 30-sec blocks of fearful and neutral expressions in nine right-handed male volunteers during three different 5-min conditions: 1) passive viewing; 2) performance of a gender-decision task, with no explicit judgment of facial emotion; 3) performance of an emotionality judgment task — an explicitly emotional task.*

Results: *There was a significant effect of task upon activation within the left hippocampus and the left inferior occipital gyrus, and upon the magnitude of response within the left hippocampus, with maximal activation in these regions occurring during passive viewing, and minimal during performance of the explicit task. Performance of the gender-decision and explicit tasks, but not passive viewing, was also associated with activation within ventral frontal cortex.*

Conclusions: *Neural responses to fearful facial expressions are modulated by task instructions.* Biol Psychiatry 2003; 53:226–232 © 2003 Society of Biological Psychiatry

Key Words: Amygdala, hippocampus, fear, fMRI, task instructions

Introduction

Lesion and functional neuroimaging studies have demonstrated the roles of different brain regions in the perception of certain basic emotions. Many of these studies have employed as stimuli facial expressions from the series of Ekman and Friesen (1976), in which subjects view different identities displaying facial expressions of fear, disgust, anger, sadness, happiness, and surprise, in addition to a neutral expression. Using these stimuli, it has been demonstrated in human subjects that the amygdala is of particular importance for the perception of fearful facial expressions (Adolphs et al 1994; Breiter et al 1996; Calder et al 1996; Morris et al 1996; Phillips et al 1997), and may modulate the visual cortical response to these stimuli (Morris et al 1998). Other neural regions also demonstrated to be involved in the response to fearful expressions are the hippocampus and amygdalohippocampal junction (Critchley et al 2000; Phillips et al 1998), and ventral and dorsolateral prefrontal cortices (Hariri et al 2000; Sprengelmeyer et al 1998).

A range of tasks has been employed in previous studies investigating neural responses to fearful facial expressions. In the majority of functional neuroimaging studies either no task (Breiter et al 1996; Buchel et al 1998) or an indirect or implicit task of emotion judgment has been performed (e.g., a judgment of gender rather than the emotion displayed by the face, to allow subjects to attend to facial expressions without becoming aware of the nature of the study) (Morris et al 1996; Phillips et al 1997; Phillips et al 1998); however, if the task involves generation of emotional meaning or interpretation, or the representation of the subjective emotional response, previous studies point to activation of bilateral medial/middle prefrontal cortex (Brodmann area [BA] 9) and dorsal anterior cingulate gyrus (BA 24/32) (Lane et al 1997; Partiot et al 1995; Teasdale et al 1999).

In more recent studies, neural responses to a range of different positive and negative, but not specifically fearful, facial expressions have been compared during performance of explicit facial expression labeling and other more indirect or implicit tasks of emotion processing (Nakamura et al 1999; Narumoto et al 2000). These studies have demonstrated in response to positive and negative facial expressions, increased blood flow (Nakamura et al 1999), and activation (Narumoto et al 2000) of right dorsolateral and ventral frontal cortices during performance of explicit, emotion labeling tasks compared with more implicit tasks. In another study, neural responses to facial expressions of fear and anger were examined during performance of

different tasks (Hariri et al 2000). Here, subjects matched a target facial expression of anger or fear either with one of two other facial expressions, or with one of two emotion labels. Performance of the matching task was associated with significantly greater activation in bilateral amygdalae than performance of the labeling task, while performance of the labeling task was associated with significantly greater activation of the right dorsolateral prefrontal cortex (BA 44 and 45) than performance of the matching task; however, the designs of these three studies did not permit direct examination of the effect of type of task upon neural responses to a specific series of facial expressions because of the employment of different types of facial expression or different combinations of facial expression and word labels during performance of the implicit and explicit tasks.

The effect of task type during presentation of a single series of positive and negative facial, but not fearful, facial expressions has been examined in two previous studies (Critchley et al 2000; Gorno-Tempini et al 2001). In the first, subjects viewed alternating blocks of mixed happy and angry compared with neutral facial expressions. Here, performance of an implicit (gender-decision) emotion-processing task was associated with greater activation in the amygdalohippocampal junction than during performance of an explicit, emotion-labeling task. The design of this study did not permit a distinction between neural responses to happy and angry facial expressions, however, because of the contrast between two different facial expressions (happy and angry) versus one facial expression (neutral) in both experiments. In the second study, subjects viewed neutral, happy or disgusted facial expressions, and performed either a gender-decision task or an explicit, emotion-recognition task. Performance of the explicit task was associated with significantly greater activation within the right middle and dorsolateral prefrontal cortices.

To our knowledge, there has been no examination of the effect of performance of different types of task upon neural responses to presentation of an identical series of fearful facial expressions. We report here a study in which the sequence of stimuli was identical in each of three experimental conditions and only the task performed in each of the conditions was varied. We examined neural responses to a single series of fearful and neutral expressions during three different conditions: 1) passive viewing without task performance; 2) performance of a gender-decision task, which did not involve explicit judgment of facial emotion; 3) performance of an emotionality judgment task — an explicit emotion-processing task. Findings from previous studies allowed us to predict that, compared with passive viewing and performance of the gender-decision task, performance of the explicit task would be associated with a reduction of the

amygdalar and hippocampal responses to fearful faces, and that this reduction would be associated with greater right dorsolateral and/or ventral frontal cortical activation (although we were unable to predict the specific location of frontal activation).

Methods and Materials

Stimuli and Procedure

Nine right-handed healthy male subjects without previous history of psychiatric or physical illness, head injury, psychotropic medication use, or substance abuse (mean age, 29, range 21–42 years; mean number of years of education, 18, range 16–22) participated in three 5-min experimental conditions. The study was approved by the Ethical Committee (Research) of the Institute of Psychiatry. Written, informed consent was obtained from each subject after the details of the procedure had been explained. Eight identities displaying facial expressions of fear or mild happiness from a standard series (Ekman and Friesen 1976), manipulated with computer software to depict different intensities of the facial expression (Calder et al 1997), were employed. Expressions depicting mild happiness (25%) were used as neutral stimuli, as in previous studies (Morris et al 1996; Phillips et al 1998). In each 5-min experiment, subjects viewed the same series of alternating, 30-sec blocks of fearful and neutral facial expressions. Each facial expression was presented for 3 sec, with an interstimulus interval of 0.75 sec. During each experiment, subjects performed one of three tasks.

1) No task (*passive viewing*): subjects were requested to attend to stimuli presented on the screen, and were told that they would be asked questions regarding the stimuli after the scanning session.

2) A *gender-decision* task in which emotion processing was only an implicit feature: subjects were asked to decide upon the gender of the face and press the corresponding one of two buttons with the right thumb.

3) An *explicit emotion processing* task: subjects were asked to decide whether the face presented was more or less emotional than the previous expression, and again pressed the corresponding one of two buttons with the right thumb.

All subjects were able to correctly identify the gender and the intensity of emotion displayed by each face. The order of presentation of the three conditions and the order of the blocks (fear or neutral first) were counterbalanced across subjects. After scanning, all subjects were requested to identify examples of the emotional facial expressions employed, choosing one out of a total of seven different expressions (neutral, fear, disgust, happy, sad, angry, sad).

Image Acquisition

Gradient echo echoplanar images were acquired on a GE Signa 1.5T Neurovascular system (General Electric, Milwaukee WI, USA) at the Maudsley Hospital, London. One hundred T2*-weighted images depicting BOLD contrast (Ogawa et al 1990) were acquired over 5 min (for each task) at each of 14 near-axial noncontiguous 5-mm thick planes parallel to the intercommissural (AC-PC) line: TE 40 msec, TR 3 sec, in-plane resolution 5 mm, interslice gap 0.5 mm. This EPI dataset provided complete

coverage of the temporal lobes (including hippocampus and amygdala) and almost complete coverage of frontal, occipital, and parietal lobes (Simmons et al 1999).

Image Analysis

Following motion correction (Bullmore et al 1999a), periodic change in T2*-weighted signal intensity at the (fundamental) experimentally determined frequency of alternation between A and B conditions ($=1/60$ Hz in all three experimental conditions) was estimated by an iterated least squares fit of a sinusoidal regression model to the fMRI time series observed at each voxel (Bullmore et al 1996). This model included sine and cosine waves at the fundamental AB frequency of the experimental input function, parameterized by coefficients (γ, δ). The power of periodic response to the input function was estimated by ($\gamma^2 + \delta^2$), and this fundamental power divided by its SE yielded a standardized test statistic, the fundamental power quotient (FPQ), at each voxel. Parametric maps representing FPQ observed at each intracerebral voxel were constructed. To sample the distribution of FPQ under the null hypothesis that observed values of FPQ were not determined by experimental design (with few assumptions), the 99 images observed in each anatomical plane were randomly permuted and FPQ was estimated exactly as above in each permuted time series. This process was repeated 10 times, resulting in 10 permuted parametric maps of FPQ at each plane for each subject.

Observed and randomized FPQ maps were transformed into the standard space of Talairach and Tournoux (1988), and smoothed by a 2D Gaussian filter with full width half maximum $= 11$ mm. A generic brain activation map (GBAM) (reconstituted voxel size: $3 \times 3 \times 5.5$ mm^3) was produced for each experimental condition by testing the median observed FPQ at each intracerebral voxel in standard space (Talairach and Tournoux 1988) against a critical value of the permutation distribution for median FPQ ascertained from the permuted FPQ maps (Brammer et al 1997), such that the probability threshold for activation at each voxel was $p \leq .004$.

Comparison of Generic Brain Activation Maps

To estimate between-condition differences in mean power of functional activation, we fitted an analysis of covariance model at each intracerebral voxel of the standardized power maps after their co-registration in standard (Talairach) space. We used a nonparametric mode of inference on spatially informed test statistics to identify brain regions which showed significant difference in mean power of response between conditions; for full details of this method and its validation, see Bullmore et al (1999b). Briefly, fitting an analysis of covariance (ANCOVA) model at each intracerebral voxel generated a map of the estimated coefficient of the factor coding experimental condition; this coefficient, divided by its SE, was our standardized voxel test statistic b. Equivalent analysis after repeated randomization of the vector coding group generated a distribution under the null-hypothesis of no between condition difference. The critical value at Prob(b) $= .05$ ($CV_{.05}$) was calculated and the voxel test statistic map was thresholded such that if $|b| > CV_{.05}$,

the value was set to b-$CV_{.05}$. Otherwise, it was set to zero. This procedure generated a set of suprathreshold voxel clusters in three dimensions, each of which can be described in terms of its mass, or the sum of suprathreshold voxel statistics it comprises. The mass of each cluster was tested against a null distribution ascertained by similar thresholding of the voxel test statistic after randomization.

The rationale for this nonparametric mode of inference is that test statistics for image analysis which incorporate spatial information, such as 3D cluster mass, are generally more powerful than other possible test statistics, such as b, which are informed only by data at a single voxel. Besides greater sensitivity to between-condition differences in brain function that are located over a spatial neighborhood of voxels, another advantage of cluster-level inference compared with voxel-level testing is that it substantially mitigates the multiple comparisons problem. The search volume or number of clusters to be tested is typically 1–2 orders of magnitude less than the number of voxels, meaning that satisfactory type 1 error control can be obtained without such severe risk of type 2 error.

BETWEEN-CONDITION COMPARISON OF THE AMYGDALAR AND HIPPOCAMPAL RESPONSES. We predicted a significant reduction in the amygdalar and hippocampal responses during performance of the explicit compared with the other tasks, and therefore compared the mean power of amygdalar and hippocampal responses across the three experimental tasks. We used the peak FPQ in index voxels defining the amygdalar and hippocampal regions as an accurate measurement of the power of the response in these regions during performance of each task. The power of response was averaged over each index voxel and its eight nearest neighbors in two dimensions (total cortical volume $= 0.57$ cm^3 for each region). Statistical comparisons for responses within these regions were made for the three conditions using repeated measures ANCOVA and post hoc matched-pairs t tests.

Results

Facial Expression Recognition Accuracy

Mean accuracy of recognition of the fearful facial expressions was 84.7% (range: 37.5%–100%).

Generic Brain Activation Maps

PASSIVE VIEWING. Major regions activated more by fearful than neutral facial expressions included the left amygdala, left hippocampus, the left putamen, bilateral cerebellum, and left lingual gyrus (Table 1 and Figure 1).

GENDER-DECISION TASK. Major regions activated more by fearful than neutral faces included visual processing regions (the right fusiform and superior temporal gyrus), the left posterior cingulate gyrus, the right hippocampus, and the right ventral frontal gyrus (Table 2 and Figure 1).

Table 1. Major Activated Regions During Passive Viewing

Approximate BA	Side	x^a	y^a	z^a	FPQ	No. of Voxels
Fear > Neutral						
Lingual Gyrus (18)[b]	L	−25	−73	−7	1.7	47
Hippocampus[b]	L	−17	−23	−7	1.7	40
Cerebellum	R/L	0	−56	−13	1.7	11
Amygdala	L	−21	−7	−13	1.4	8
Putamen	L	−25	0	−2	1.5	6
Fusiform Gyrus (21)	R	47	−10	−24	1.4	6
Neutral > Fear						
Posterior Cingulate Gyrus (30)	L	−7	−52	9	1.8	12
Insula	L	−36	0	−2	1.5	10
Superior Temporal Gyrus (22)	L	−50	−10	4	1.5	9
Hippocampus	R	36	−13	−13	1.5	8
Anterior Cingulate Gyrus (25)	R	4	7	−7	1.4	6
Lingual Gyrus (18)	R	7	−69	−2	1.4	6
Cerebellum	L	−4	−63	−13	1.4	6

BA, Brodmann area; FPQ, fundamental power quotient.
[a]The cluster with the largest number of voxels within each region is reported. Talairach co-ordinates refer to the voxel with the maximum FPQ in each cluster. All voxels were identified by a one-tailed test of the null hypothesis that median FPQ is not determined by experimental design. The threshold for activation was $p < .004$.
[b]These regions were activated to a significantly greater extent during passive viewing compared with performance of the explicit task.

EXPLICIT TASK. Major regions activated more by fearful than neutral faces included the left ventral frontal gyrus and cerebellum, but not the amygdala or hippocampus (Table 3 and Figure 1).
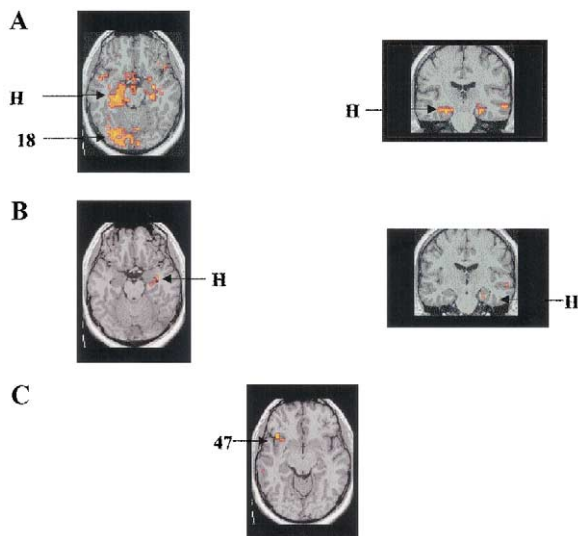

Figure 1. Generic brain activations superimposed upon a spoiled gradient echo (SPGR) structural template are demonstrated within the left hippocampus (H) and left lingual gyrus (Brodmann area [BA] 18) in transverse ($z = -7$) and coronal ($y = -23$) brain slices during (**A**) passive viewing and within the right hippocampus (H) at transverse ($z = -13$), and coronal ($y = -17$) brain slices in (**B**) performance of the gender-decision task. Generic brain activation is demonstrated within the left ventral frontal cortex (BA 47) in a transverse ($z = -7$) brain slice during (**C**) performance of the explicit task.

In all three conditions, there were regions activated more by neutral than fearful facial expressions. During passive viewing, these included visual processing regions (the left lingual and superior temporal gyri), the left posterior cingulate gyrus, the right hippocampus, the left insula and the right ventral anterior cingulate gyrus (Table 1). During the gender-decision task, they included bilateral cerebellum, and the right insula (Table 2). During the explicit task, they included the left insula and putamen (Table 3). We have previously reported maximal nonstationarity (i.e., variability) of the right, but not the left, amygdalar response to neutral faces presented in alternating blocks with fearful facial expressions (Phillips et al 2001). In view of the lack of consensus regarding the interpretation of activation during presentation of neutral stimuli in previous studies examining neural correlates of emotion processing (Phillips et al 2001), however, we offer no further interpretation of these findings.

Comparison of Generic Brain Activation Maps

There was a significant effect of task ($p = .05$; number of false-positive clusters of activation < 1) upon neural responses to presentation of fearful and neutral facial expressions in two three-dimensional clusters of activation centered within the left hippocampus and the left inferior occipital gyrus (and including the left lingual gyrus; BA 18). Further analysis revealed that this effect was due to significantly greater activation in these regions ($p = .05$; number of false-positive clusters of activation < 1) during passive viewing compared with performance of the explicit task (Table 1). No other regions were activated to a significantly greater extent during performance of the other tasks.

Table 2. Major Activated Regions During Performance of the Gender Decision Task

Approximate BA	Side	x^a	y^a	z^a	FPQ	No. of Voxels
Fear > Neutral						
Posterior Cingulate Gyrus (30)	L	−17	−52	9	1.6	22
Superior Temporal Gyrus (38)	R	32	−60	−18	1.5	13
Fusiform Gyrus (37)	R	21	−50	−7	1.7	10
Ventral Frontal Gyrus (47)	R	47	23	−7	1.6	7
Hippocampus	R	28	−46	−2	1.4	6
		25	−17	−13	1.5	4
Thalamus	R/L	0	−13	4	1.4	5
Neutral > Fear						
Cerebellum	R	32	−60	−18	1.5	13
	L	−28	−52	−18	1.5	5
Insula	R	36	−7	4	1.5	8
Superior Temporal Gyrus (22)	R	57	−17	4	1.4	5

BA, Brodmann area; FPQ, fundamental power quotient.

[a]The cluster with the largest number of voxels within each region is reported. Talairach co-ordinates refer to the voxel with the maximum FPQ in each cluster. All voxels were identified by a one-tailed test of the null hypothesis that median FPQ is not determined by experimental design. The threshold for activation was $p < .004$.

Between-Condition Comparison of Amygdalar and Hippocampal Responses

Index voxels for the amygdala and hippocampus were defined by the Talairach co-ordinates of the peak FPQ observed in the left amygdala and left hippocampus during passive viewing: (x = −21; y = −7; z = −13 and x = −17; y = −23; z = −7), and the right hippocampus during performance of the gender-decision task (x = 25; y = −17; z = −13). There was a significant effect of condition upon peak FPQ within the left hippocampus ($F = 4.84$; df 2,16; $p = .02$). The greatest peak FPQ in this region occurred during passive viewing, and the smallest during performance of the explicit task (matched pairs t tests: passive viewing vs. explicit task: $t = 2.68$; df 8; $p = .03$; passive viewing vs. gender-decision task: $t = 2.72$; df 8; $p = .03$). There was no significant effect of condition upon peak FPQ within the right hippocampus or left amygdala ($p > 0.1$).

Discussion

Our findings indicate that different types of tasks affect the neural response to presentation of alternating blocks of fearful and neutral facial expressions. Specifically, we observed significantly increased activation within the left hippocampus and left inferior occipital gyrus during passive viewing compared with performance of the gender-decision task or the explicit emotionality judgment task. The increased hippocampal activity during passive viewing of fearful facial stimuli may reflect the role of the hippocampus in anxiety, including the perception of novel, fear-inducing stimuli (Gray 1982), in addition to its roles in episodic memory (Aggleton and Brown 1999) and spatial cognition (O'Keefe and Nadel 1978). The model proposed by Gray (Gray 1982; Gray and McNaughton 2000) attributes to the hippocampus a single computational function, flexibly allocated to different classes of problem depending upon momentary environmental demands. In the light of this model, our results suggest that hippocampal involvement in passive viewing of fearful facial expressions is overshadowed when demands upon cognitive functioning increase.

Consistent with this interpretation, we also demonstrated a significant effect of task upon a measure of the power of regional activation, the peak FPQ, within the left

Table 3. Major Activated Regions During Performance of the Explicit Task

Approximate BA	Side	x^a	y^a	z^a	FPQ	No. of Voxels
Fear > Neutral						
Ventral Frontal Gyrus (47)	L	−32	7	−7	1.5	8
		−32	26	−7	1.5	4
Lingual Gyrus (18)	L	−11	−43	−2	1.5	6
Cerebellum	L	−17	−46	−7	1.5	6
Neutral > Fear						
Insula	L	−32	4	4	1.8	7
Putamen	L	−28	−20	4	1.6	7

BA, Brodmann area; FPQ, fundamental power quotient

[a]The cluster with the largest number of voxels within each region is reported. Talairach co-ordinates refer to the voxel with the maximum FPQ in each cluster. All voxels were identified by a one-tailed test of the null hypothesis that median FPQ is not determined by experimental design. The threshold for activation was $p < .004$.

hippocampus. The greatest peak FPQ in this region occurred during passive viewing, and the smallest during performance of the explicit emotion-processing task. This finding supports previous reports of decreased activation within the amygdala (Hariri et al 2000) and the amygdalohippocampal region (Critchley et al 2000) during performance of explicit, emotion-labeling tasks, compared with other more implicit emotion-processing tasks.

We demonstrated activation within the amygdala during the passive viewing task, but not during performance of the gender-decision task. Previous studies have reported amygdala activation to fearful faces during passive viewing (Breiter et al 1996; Buchel et al 1998) and performance of a gender-decision task (Morris et al 1996; Phillips et al 1997; Phillips et al 1998). Our finding of an absence of amygdalar activation to the fearful faces during performance of the gender-decision task is therefore surprising, although this has been previously reported (Sprengelmeyer et al 1998). This unpredicted finding may have resulted from susceptibility-induced magnetic field inhomogeneities in the amygdalar region and the relatively large voxel size in the images obtained in this study, both of which can lead to signal loss in the amygdala. The employment of high-resolution fMRI and small image voxel size in future studies examining neural responses to fearful stimuli may provide solutions to this problem (Merboldt et al 2001).

Activation of the right dorsolateral prefrontal cortex (BA 44 and 45) during performance of explicit, emotion-labeling tasks (Hariri et al 2000; Nakamura et al 1999) has been reported previously. The negative correlation between percentage signal change in the dorsolateral prefrontal cortex and the amygdala demonstrated by Hariri et al (Hariri et al 2000) was interpreted as demonstrating a role for this region in the modulation of the amygdalar response to emotional facial expressions. We did not observe activation within the right dorsolateral prefrontal cortex during performance of the explicit emotion-processing task. This may be due to the fact that the explicit task in our study involved a decision about the intensity of emotion displayed by each face rather than an overt, emotion labeling task per se.

A region of the left ventral frontal cortex (BA 47) was activated during performance of the explicit emotion-processing task, and a similar, right -sided region during performance of the implicit emotion-processing task. Activation of right BA 47 has been reported during the performance of emotional facial expression delayed matching-to-sample tasks compared with face delayed matching-to-sample tasks (Nakamura et al 1999). This region has also been reported as being activated in response to fearful, sad, and angry facial expressions during the performance of a gender-decision task (Blair et

al 1999; Sprengelmeyer et al 1998), and during recall-generated, but not film-generated, emotions (Reiman et al 1997). Related ventral frontal regions, the orbitofrontal cortex, and the ventromedial frontal cortex have been associated, respectively, with the representation of the emotionally salient states of reward and punishment (O'Doherty et al 2001; Rolls 2000), and decision-making tasks requiring the manipulation of emotionally salient information (Bechara et al 1998).

Our finding of ventral frontal cortical activation during the gender-decision and explicit emotion-processing tasks, but not the passive-viewing task, may therefore reflect the increased requirement for manipulation and representation of emotionally salient information during performance of the former two tasks compared with the latter. It should also be noted, however, that the explicit task involved working memory, in that the subject was required to compare successive facial stimuli. This factor may have played an additional role in determining our pattern of results.

The inferior occipital gyrus (BA 18) was activated significantly more during passive viewing than the other tasks. In a previous study, a positive modulatory effect of the amygdala upon the visual cortical response to fearful facial expressions has been postulated (Morris et al 1998). The absence of an amygdalar response during performance of the explicit emotion processing task may, therefore, have resulted in reduced modulation of visual regions.

In summary, our findings demonstrate that the extent of activation within neural regions previously demonstrated to be involved in the response to fearful facial expressions, the amygdala, hippocampus, and ventral frontal cortex may be modulated by the performance of different types of task. In particular, our findings demonstrate that performance of an explicit, emotion-labeling task is associated with a significant reduction in the hippocampal response to these stimuli.

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