NeuroImage

www.elsevier.com/locate/ynimg
NeuroImage 27 (2005) 26 – 36

The neural bases of amusement and sadness: A comparison of block contrast and subject-specific emotion intensity regression approaches

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Received 21 June 2004; revised 14 March 2005; accepted 17 March 2005
Available online 10 May 2005

Neuroimaging studies have made substantial progress in elucidating the neural bases of emotion. However, few studies to date have directly addressed the subject-specific, time-varying nature of emotional responding. In the present study, we employed functional magnetic resonance imaging to examine the neural bases of two common emotions–amusement and sadness–using both (a) a stimulus-based block contrast approach and (b) a subject-specific regression analysis using continuous ratings of emotional intensity. Thirteen women viewed a set of nine 2-min amusing, sad, or neutral film clips two times. During the first viewing, participants watched the film stimuli. During the second viewing, they made continuous ratings of the intensity of their own amusement and sadness during the first film viewing. For sad films, both block contrast and subject-specific regression approaches resulted in activations in medial prefrontal cortex, inferior frontal gyrus, superior temporal gyrus, precuneus, lingual gyrus, amygdala, and thalamus. For amusing films, the subject-specific regression analysis demonstrated significant activations not detected by the block contrast in medial, inferior frontal gyrus, dorsolateral prefrontal cortex, posterior cingulate, temporal lobes, hippocampus, thalamus, and caudate. These results suggest a relationship between emotion-specific temporal dynamics and the sensitivity of different data analytic methods for identifying emotion-related neural responses. These findings shed light on the neural bases of amusement and sadness, and highlight the value of using emotional film stimuli and subject-specific continuous emotion ratings to characterize the dynamic, time-varying components of emotional responses.

Keywords: Neural bases; Amusement; Sadness; Emotion

Introduction

One of the primary goals of affective neuroscience is to delineate the neural bases of emotional responding (Davidson, 2003; LeDoux, 2000). However, two related features of emotion make this a particularly difficult goal to achieve. The first is that unlike other affective phenomena such as moods, emotions are relatively short-lived responses that involve rapidly varying changes across multiple response systems (Davidson, 2002; Gross, 2001; Levenson, 1994). The second feature of emotion that makes an elucidation of neural bases difficult is that emotions typically arise via an ongoing process of interpretation of the environment (Scherer, 2000). This leads to substantial differences among individuals as their emotions unfold over time even when these individuals are in ostensibly the "same" emotion-eliciting situation.

In the present study, we address these challenges with the aim of (1) comparing a stimulus-based block contrast approach with a subject-specific regression approach that utilizes continuous subjective ratings of emotional responding in the context of powerfully emotion-evocative films, and (2) clarifying the neural bases of two important emotions, namely amusement and sadness. Our focus on amusement and sadness was dictated by the accumulating evidence that positive and negative emotions differ substantially in their neural bases (Davidson and Irwin, 1999; Phan et al., 2002; Wager et al., 2003), and by the growing recognition of the general importance of both negative and positive emotions in adaptive functioning (Davidson, 2002; Larsen et al., 2003).

To date, the predominant experimental designs and data analytic approaches employed in PET and fMRI studies of emotion have consisted of either contrasts of average signal between two conditions in a block design experiment or of averaging across trials of a similar type in an event-related design experiment (Phan et al., 2003, 2004a,b). While the block contrast

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doi:10.1016/j.neuroimage.2005.03.018

approach is associated with robust signal magnitude, this approach blurs signal variation during the time course of a block and precludes an analysis of dynamic changes in emotion experience-related neural activity within and across blocks. Furthermore, for a fixed MR scanning time, the number of time points acquired during the experiment must be divided across the different block conditions.

Another important limitation of studies to date is that they have not assessed the subjective impact of the emotion induction as it varies over time for each individual participant. Although several studies have used online discrete emotion ratings from participants during MR scanning (e.g., Phan et al., 2004a,b) or post hoc summary ratings post-MR scanning as a measure of individual participant experience (e.g., Taylor et al., 2003), no studies have used within MR scanner subject-specific continuous emotion ratings as a predictor of BOLD response. This is problematic because even when discrete emotion ratings are measured during MR scanning, they are likely to be confounded with response demand biases that manifest as a tendency to endorse particular multiple-choice categories more often than others (Elfenbein et al., 2002).

To address these limitations, the current study employs a subject-specific regression model based on continuous measurement of emotion intensity using a potentiometer rating device with a continuous rating scale. Previous behavioral studies have demonstrated that reliable and valid continuous ratings of emotional experience may be obtained for emotion film viewing (Mauss et al., in press) and conflict conversations in dyads (Levenson and Gottman, 1985). The use of a methodology utilizing a continuous self-rating has been shown to reduce such response demand biases and related potential confounds such as memory deficits and availability heuristics (Craske and Tsao, 1999). Thus, continuous measurement of the impact of experimental stimuli on ongoing emotion experience may be associated with enhanced reliability estimates of emotion intensity. Continuous online measurement may provide a more robust index of whether participants actually achieved and maintained a meaningful level of emotion intensity during emotionally-evocative stimuli. Currently, in the field of emotion research, despite the promise of autonomic physiological measures to differentiate positive vs. negative emotions (e.g., Larsen et al., 2003), self-report continues to serve as the most reliable index of emotional responding (e.g., Barrett, 2004).

We expected that use of a subject-specific regressor (e.g., discrete or continuous subjective ratings) of the BOLD signal time series would provide a temporally refined index of the relationship between self-reported experience and neural activity. This led us to hypothesize that subject-specific amusement and sadness intensity ratings measured continuously during amusing and sad film clips would serve as a more robust predictor of the BOLD signal compared to conventional block contrast analyses in emotion-related brain regions. In particular, based on the view that subject-specific emotion ratings would serve as a more temporally refined regressor of BOLD response, compared to the more static block contrast approach, we expected to find brain activation patterns more closely associated with shifts in ongoing emotion experience in emotion-related areas. Based on a converging consensus from several recent meta-analyses of neuroimaging studies of emotion (Baas et al., 2004; Maddock, 1999; Phan et al., 2002, 2004a,b; Wager et al., 2003), we expected that both data analytic approaches would result in activations in emotion-related brain regions including limbic (amygdala, anterior cingulate cortex, hippocampus) and paralimbic (medial PFC, insula, retrosplenial gyrus, anterior temporal pole, thalamus) areas for both sad and amusing films.

Methods

Participants

Thirteen female volunteers (mean age = 19.7 ± 1.0 years, range 18–21 years) were recruited from the Stanford University community. All participants were right-handed, had normal visual acuity, and were screened for history of any psychiatric or medical illness. We choose to enroll only women to control for systematic gender biases in emotion experience which include greater levels of affective reactivity to positive and negative emotion films in women compared to men (Kring and Gordon, 1998). Participants were paid $20 per hour for their participation and gave informed consent in accordance with guidelines set forth by the Stanford Medical Human Subjects Committee.

Film stimuli

Studies have found that emotion-eliciting films are effective means of eliciting specific target emotions (Gross and Levenson, 1995; Hagemann et al., 1999). Compared to presentation of static emotional slides, emotion-generative film clips provide a dynamically unfolding context within which emotions may be produced (1) for a more prolonged duration, (2) in a more dynamic time-varying manner, and (3) with greater intensity (Gross and Levenson, 1995).

In the present study, participants viewed a series of nine 2-min color film clips, as shown in Fig. 1. Two amusing and two sad film clips were drawn from prior studies (Gross and Levenson, 1995). These included two amusing film clips of comedic routines performed by Robin Williams and Bill Cosby, and two sad film clips from the Champ and Stepmom. The amusing film clips entailed a single actor conducting a comedic routine. The sad film clips both displayed an adult and a child in a very sad interaction. We carefully selected five non-emotional film clips that were matched to the emotion film clips in terms of duration, number of actors, and social interaction. The neutral film clips consisted of two clips with a single actor (demonstrating cooking skills and interior designing) and three clips with two actors (demonstrating home repair and sewing). Two counterbalanced versions of each series of nine film clips were created to control for the potential confound of order of the amusing and sad film clips. No order effects were observed.

Procedure

Immediately before entering the MR scanner, participants indicated how they felt using a standard set of emotions, including amusement and sadness (Gross and Levenson, 1995). Inside the MR scanner, participants first viewed the series of sad, amusing, and neutral film clips in a single 18-min run with the explicit instruction to respond naturally to the film content. This was immediately followed by a second viewing of the same stimuli prior to which each participant was instructed on the use of an MR-compatible rating dial and asked to provide continuous retro-

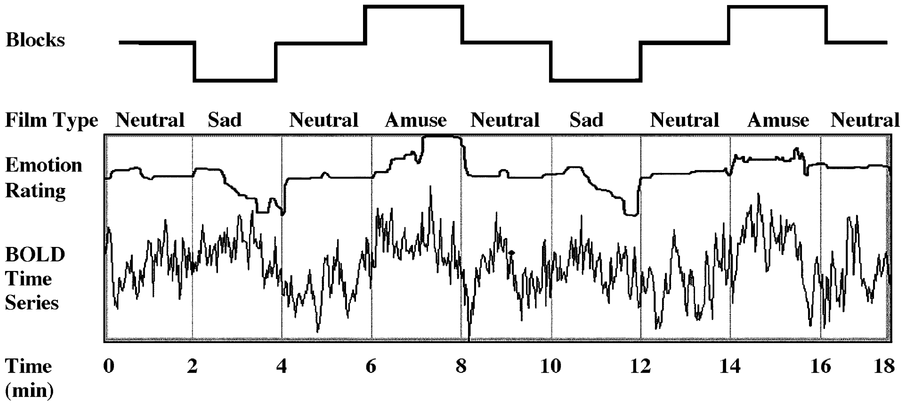


Fig. 1. Experimental design. Two-minute blocks of neutral, sad, and amusing film clips with an example of continuous dynamic emotion ratings and BOLD signal time series for the contrast of Emotion > Neutral Films in left inferior frontal gyrus BA 45 (−55 19 1) from a single participant.

spective emotion intensity ratings of emotion experienced during the initial viewing.

Continuous emotion ratings were acquired on a continuous scale using the rating dial held in the right hand while lying supine inside the MR scanner. The rating dial consisted of a knob mounted on a potentiometer whose output voltage was continuously recorded during the scan with a data logger (AD Instruments, Inc.) at 40 Hz. Participants viewed a small bar graph meter connected to the potentiometer and mounted on one side of the projection screen.

The retrospective emotion rating obtained during the second viewing of the film stimuli was used as an estimate of the emotion experienced during the initial viewing. We employed retrospective emotion ratings as a proxy for concurrent ratings of emotion experience during initial film viewing to avoid contaminating emotional responding with an additional rating task. To evaluate the validity of this retrospective emotion rating procedure, we collected emotion rating data for the same film stimulus set from a separate sample of 14 females (matched on age, gender, education, handedness to the original sample of 13 females). These 14 women provided concurrent ratings using the same rating dial as well as retrospective ratings. We found a very high degree of concurrence between online (first viewing) and retrospective (second viewing) emotion ratings for amusing ($r = 0.90$, $P < 0.001$), sad ($r = 0.98$, $P < 0.001$), and neutral ($r = 0.88$, $P < 0.001$) film clips. The correlation of retrospective emotion ratings for the original 13 females and the additional 14 females was 0.95; there was no significant difference between these groups.

Image acquisition

Imaging was performed on a General Electric 3-T Signa magnet with a T2*-weighted gradient echo spiral in/out pulse sequence using blood oxygenation level-dependent (BOLD) contrast (Glover and Lai, 2001) and using a custom-built quadrature "dome" elliptical bird cage head coil. Head movement was minimized using a bite bar formed with the subject's dental impression. Functional images (560 volumes per functional run) were obtained from 25 sequential axial slices using the following parameters: TR (repetition time) = 2000 ms, TE (echo time) = 30 ms, flip angle = 60°, FOV = 24 cm, matrix = 64 × 64, single shot, in-plane resolution = 3.75 × 3.75 mm, and slice thickness = 5 mm. The spiral-in/out sequence was shown to be effective in recovering BOLD signal in frontal regions important to this study (Preston et al., 2004). A T1-weighted spin echo anatomical scan was acquired in the same plane as the functional slices prior to acquisition of functional scans (TR = 500 ms, TE = 14 ms, in-plane resolution = 0.9375 mm, and slice thickness = 5 mm).

fMRI data preprocessing

Analysis of functional neuroimages (AFNI; Cox, 1996) was used for preprocessing and statistical analysis of these data. During preprocessing, every brain volume of each participant's functional run was quantitatively and visually examined to identify artifacts due to either subject head movement or to MR scanning system properties (e.g., spikes in the magnetic field or thermal noise). To correct for head movement, each functional time series was aligned to a base image approximately in the middle of the first 2-min film clip using a 3-dimensional, iterated, least squares, co-registration algorithm provide in the AFNI library (3dvolreg). Fourier interpolation was used to realign images to the base image. The motion correction procedure shifted images around three rotational axes (pitch, yaw, and roll) and in three directions (x: left to right, y: anterior to posterior, and z: superior to inferior). Estimates of these six motion correction parameters provide indirect measures of the extent of head motion at each time point. Individual brain volumes with greater than ±1.5 mm motion correction in x, y, or z directions were eliminated from further analyses. This resulted in the elimination of 13 brain volumes for one participant and 3 brain volumes for a second participant. Because there was no evidence of stimulus-correlated motion effects between film type and motion correction in x, y, or z directions, all functional runs were included in subsequent statistical analyses. All functional runs were subjected to an outlier detection and interpolation algorithm (program 3dDespike) to modify potentially spurious time points within each voxel's MR signal time series.

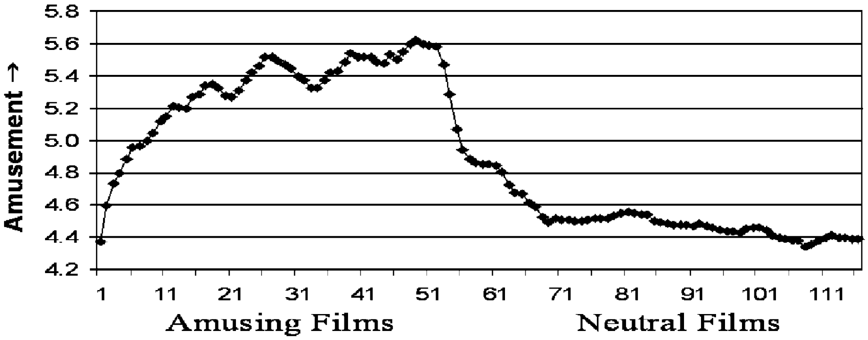
fMRI statistical analysis

Two different analysis approaches were used to analyze BOLD responses to sad and amusing films. First, block contrast analyses of sad vs. neutral and amusing vs. neutral film clips were conducted. In this analysis, separate sets of two neutral film clips matched on duration and number of actors in the two amusing and two sad film clips, respectively, were used as a comparison baseline. The block contrast analysis examines the differential BOLD signal between two distinct conditions (e.g., BOLD signal during sad and neutral film clips). Second, we conducted subject-specific regression analyses to assess the linear association of continuous emotion ratings and BOLD signal. This subject-specific regression analysis uses moment-to-moment changes in self-reported ongoing emotional experience as a regressor of BOLD responses during a single condition, namely, sad or amusing films only. The emotion rating regressor is a continuous self-report on a continuous scale of emotion intensity. These ratings were reduced into 2 s bins (to match the duration of a BOLD signal time point, namely, one brain volume collected every 2 s). The resultant subject-specific emotion rating regressor was convolved with a gamma variate model (Cohen, 1997) of the hemodynamic response function to account for delay to peak BOLD responses. Using a linear regression model, we specifically focused on detection of BOLD signal that varied linearly with changes in emotion ratings. Previous studies have indicated that the transfer function between stimulus input and BOLD response may not be linear (Cohen, 1997) and that the shape and magnitude of the fMRI BOLD response may not reflect a simple linear relationship to the underlying neural activity or to behavior (Boynton et al., 1996). However, we decided to test the simple linear relationship of emotion intensity and BOLD signal because of prior findings demonstrating that subject-specific reports of emotional intensity predicted brain responses linearly, for example, in amygdala and nucleus accumbens (Phan et al., 2004a,b).

For each approach, we employed (a) whole-brain analyses and (b) search region of interest analyses for three subcortical small volume-corrected a priori anatomical ROIs. Direct whole-brain contrasts of amusing vs. sad films were not conducted because such analyses invariably confound individual differences in neural and psychological responses to positive and negative emotion films and do not visualize regions of significant BOLD response that were equally activated by both types of emotion-generative films. Using neutral films as a baseline in the block contrasts provides a more consistent basis for making interpretations of the differential BOLD response for each type of emotion film.

To conduct statistical analyses on the functional BOLD signal, we used 3dDeconvolve to implement linear regression models to fit stimulus reference vectors to the MR time series at each voxel for each participant. Second-level one-sample *t* tests were conducted according to a random-effects analysis in order to enhance the generalizability of the results. For the block contrast analysis, stimulus reference vectors were coded 1 and −1 to compare BOLD response for two amuse vs. two matched neutral clips and for two sad vs. two matched neutral films clips. In the subject-specific regression analysis, continuous emotion ratings served as regressors of BOLD signal during amusing and sad films, separately. Individual subject statistical maps were then spatially smoothed using a Gaussian kernel of FWHM = 3.75 mm^3, resampled into 3.75 mm^3 isotropic voxels (which only entailed resampling of the slice thickness dimension from 5 mm to 3.75 mm, thereby not introducing to the in-plane dimensions error

A. Average emotion ratings for two amusing and two neutral film clips



B. Average emotion ratings for two sad and two neutral film clips

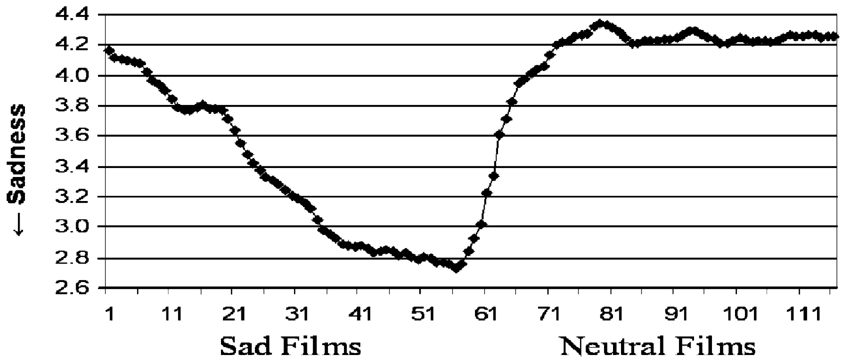


Fig. 2. Average emotion intensity ratings for 13 female participants in 2-s bins. (A) Increasing values represent increasing amusement ratings. (B) Decreasing values represent increasing sadness ratings.

related to the resampling interpolation algorithm), and spatially normalized into Talairach and Tournoux atlas coordinate space. One-sample t tests were conducted for both the block contrast and subject-specific regression analyses.

To correct quantitatively for the multiple comparisons inherent in the statistical analysis of tens of thousands of brain voxels, AlphaSim, a Monte Carlo simulation bootstrapping program in the AFNI software library, was employed to identify a joint voxel-wise threshold and minimum cluster volume threshold combination to set a cluster-wise P value of less than 0.05 corrected for multiple comparisons (Forman et al., 1995). Based on experimenter-selected parameters, including 10,000 sampling iterations, a voxel-wise threshold of $P < 0.005$, and an isotropic spatial smoothing Gaussian kernel of full-width half-maximum (FWHM) = 3.75 mm^3, the AlphaSim program determined that a minimum cluster volume threshold of 263 mm^3 (5 voxels × 3.75 mm^3) was required to protect against the probability of false positives (i.e., type I error) at a cluster-wise level of $P < 0.02$ in the whole brain analyses. To prevent false-negative results in whole brain analyses for smaller subcortical brain search regions of interest, namely, amygdala, thalamus, and caudate, the joint voxel and cluster threshold approach described above was also applied to a priori Talairach-defined bilateral anatomical masks for each of these three brain structures.

Significant BOLD responses are reported in the tables by location of the voxel with the highest signal magnitude in Talairach coordinates, Brodmann areas, and neuroanatomical labels for regions included in each cluster. To provide a standardized dependent variable interpretable across studies, BOLD responses are reported in Z values for the group t test results. Identification of neuroanatomical structures associated with areas of significant functional BOLD signal was determined using Talairach and Tournoux atlas (1988), Talairach Daemon (Lancaster et al., 2000), and Atlas of the Human Brain (Mai et al., 1997).

Results

Initial state measures

On state measures collected immediately before entering the MR scanner, participants reported minimal sadness (mean = 1.0, SD = 1.3, range: 0 (none) to 4 (moderate)) and moderate happiness (mean = 3.2, SD = 2.0, range: 0 (none) to 6 (a lot)).

Continuous emotion ratings

Continuous self-reported retrospective sadness and amusement intensity ratings collected with the rating dial in the MR scanner during the second film viewing demonstrated that participants experienced the target sad and amusing emotion states during initial film viewing. Emotion ratings were measured on a continuous scale (1 = extremely sad, 4 = neutral, 7 = extremely amusing), collected at 40 Hz, and reduced to 2 s bins, the time required to obtain a single brain volume during MR scanning (time to repetition = 2 s). This resulted in approximately sixty 2 s observations of emotion ratings for each 2 min film clip.

A repeated-measures MANOVA was used to examine differences on variables related to amusing and sad films. The emotion intensity ratings demonstrated that the amusing film clips (Bill Cosby and Robin Williams) were perceived as significantly more amusing than neutral film clips ($\text{mean}_{\text{Amusing}} = 5.58 \pm 0.47$ vs. $\text{mean}_{\text{Neutral}} = 4.27 \pm 0.36$; $F(1,12) = 58.3$, $P < 0.001$, $\text{eta}^2 = 0.83$; Cohen, 1988) and the sad film clips (Stepmom and The Champ) were perceived as significantly more sad than neutral film clips ($\text{mean}_{\text{Sad}} = 3.31 \pm 0.38$ vs. $\text{mean}_{\text{Neutral}} = 4.27 \pm 0.36$; $F(1,12) = 49.0$, $P < 0.001$, $\text{eta}^2 = 0.80$). The percent change in emotion intensity ratings from the neutral films was not significantly different for amusing films (mean = 32.5% ± 18.8) and for sad films (mean = 21.6% ± 10.3) and yielded a small effect size ($\text{eta}^2 = 0.20$). Fig. 2 shows the average emotion ratings across all 13 participants for the two amusing and two neutral, and two sad and two neutral film clips. Average emotion ratings for the neutral films did not vary significantly and demonstrated a narrow range of variance.

A greater number of discrete peaks in the continuous emotion intensity ratings was observed for amusing (1.77 ± 0.93) compared to sad films (1.27 ± 0.56), ($F(1,12) = 8.67$, $P < 0.05$, $\text{eta}^2 = 0.42$), and a faster rise time to first peak in emotion ratings for amusing (30.0 ± 13.5 s) compared to sad films (48.5 ± 14.0 s), ($F(1, 12) = 12.80$, $P < 0.005$, $\text{eta}^2 = 0.52$), but there was no reliable difference in recovery from last peak in emotion ratings to baseline (mean emotion rating of the first neutral film that preceded all emotion film clips) between amusing (97.2 ± 40.7 s) and sad films (106.4 ± 38.1 s).

Table 1
Block contrast analysis of sad > neutral films

Brain regions	BA	Volume (mm^3)	$x\ y\ z$[a]	Maximum Z score
Frontal lobes				
Medial PFC	9	844	0 56 23	5.33
Dorsomedial PFC	6	316	0 8 64	3.72
R IFG	47	580	41 23 −7	4.51
L IFG	45, 47	264	−49 26 1	4.11
Temporal lobes				
R MTG/STG	21	422	45 −7 −11	4.41
R STG	22	369	53 −37 8	3.88
R posterior STG	21	316	64 −49 4	5.04
L STG	22	1213	−45 −11 −4	5.13
Posterior insula	13			
Parietal lobes				
Medial precuneus	31	316	−7 −64 27	4.62
Occipital lobes				
Medial lingual gyrus	18	844	−4 −75 4	4.21
L lingual gyrus	18	316	−11 −67 −3	3.87
L lingual gyrus	19	264	−15 −56 −6	4.12
Subcortical				
R amygdala		369	15 −4 −11	6.00
L amygdala		369	−16 −6 −11	3.96
L posterior thalamus		844	−4 −26 12	4.24
L anterior thalamus		422	−4 −7 8	4.29
Culmen, Declive		580	−7 −60 −7	4.35

Note. $Z \geq 2.811$, t value threshold ≥ 3.424, voxel $P < 0.005$, cluster $P < 0.02$, minimum cluster volume threshold $\geq$ 263 mm^3 (5 voxels × 3.75 mm^3), connectivity radius = 3.75 (face-to-face), spatial smoothing Gaussian kernel FWHM = 3.75 mm^3.

BA = Brodmann area, IFG = inferior frontal gyrus, L = left, MTG = middle temporal gyrus, PFC = prefrontal cortex, R = right, S = superior, STG = superior temporal gyrus.

[a] Talairach and Tournoux coordinates of maximum BOLD signal intensity voxel.

State amusement and sadness measured just before entering the MR scanner were not significantly associated with emotion ratings during amusing, sad, or neutral films, indicating that film-induced changes in emotion experience were independent of baseline state emotion.

Block contrast analyses

The sad vs. neutral films block contrast resulted in significantly enhanced BOLD responses, as shown in Table 1 and Fig. 3A, in medial (BA 9) and dorsomedial (BA 8) prefrontal cortex, bilateral inferior frontal gyrus (BA 45, 47), left posterior insula (BA 13), right and left posterior superior temporal gyri (BA 21, 22), right middle temporal gyrus (BA 21), medial precuneus (BA 31), left lingual gyrus (BA 18,19), cerebellum, thalamus, and bilateral amygdala.

The amusing vs. neutral films block contrast resulted in significantly greater BOLD responses, as shown in Table 2 and Fig. 4A, in dorsomedial PFC (BA 6, 8), right posterior superior temporal gyrus (BA 22), right putamen, and left globus pallidus.

Table 2
Block contrast analysis of amuse > neutral films

Brain regions	BA	Volume (mm^3)	x y z[a]	Maximum Z score
Frontal lobes				
Dorsomedial PFC	8	263	−4 34 49	4.13
Dorsomedial PFC	6	263	−7 15 57	3.58
Temporal lobes				
R posterior STG	22	738	60 −41 16	3.92
R posterior STG	22	263	64 −37 16	3.75
Subcortical				
R putamen		316	34 −19 −7	4.08
L globus pallidus		263	−15 −7 4	4.56

Note. $Z \geq 2.811$, t value threshold ≥ 3.424, voxel $P < 0.005$, cluster $P < 0.02$, minimum cluster volume threshold ≥ 263 mm^3 (5 voxels × 3.75 mm^3), connectivity radius = 3.75 (face-to-face), spatial smoothing Gaussian kernel FWHM = 3.75 mm^3.

BA = Brodmann area, L = left, PFC = prefrontal cortex, R = right, STG = superior temporal gyrus.

[a] Talairach and Tournoux coordinates of maximum BOLD signal intensity voxel.

Subject-specific regression analysis

For sad films, the regression analysis using sadness intensity ratings resulted in significant activations, as shown in Table 3 and Fig. 3B, in the frontal lobes, including medial PFC (BA 9, 10) and right inferior frontal gyrus (BA 45), in the temporal lobes, including left posterior middle (BA 39) and right posterior superior (BA 22) temporal gyri, in a medial posterior region covering both

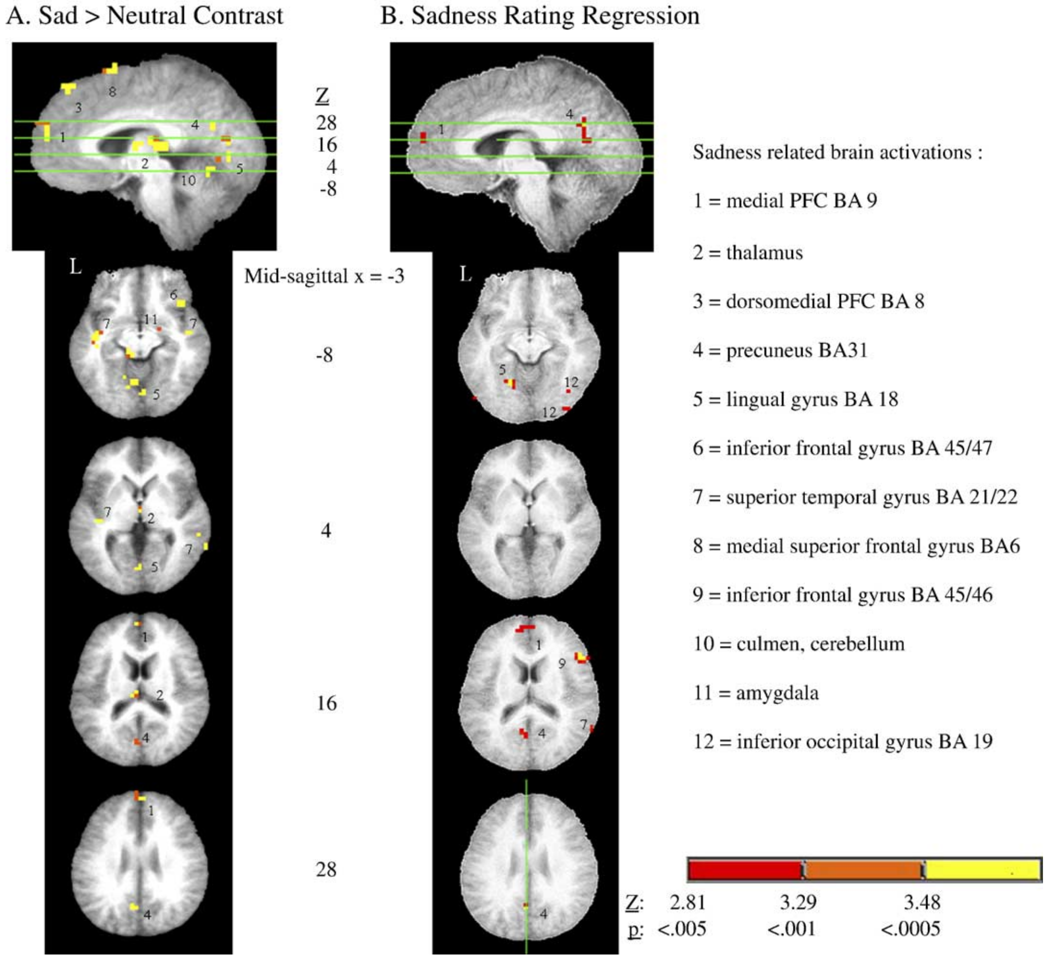


Fig. 3. BOLD responses for (A) the Sad > neutral block contrast and (B) the subject-specific regression analysis using sadness ratings.

posterior cingulate and precuneus (BA 31), in several ventral occipital areas, including right fusiform (BA 18), inferior (BA 19), and middle (BA 18) occipital gyri, left lingual gyrus (BA 19), and subcortically in left amygdala and thalamus.

For amusing films, as shown in Table 4 and Fig. 4B, the regression analysis using amusement intensity ratings resulted in significant activations in the frontal lobes, including medial (BA 9), dorsomedial (BA 6, 8), and bilateral inferior (BA 44), and left dorsolateral (BA 9) frontal areas as well as left posterior cingulate (BA 31). In the temporal lobes, activations were observed in left and right middle temporal gyri (BA 21, 37, 39) and right superior temporal gyrus (BA 22). Subcortical activations included right hippocampus, left thalamus, and right caudate.

Comparison of block contrast and subject-specific regression analyses

We examined the overlapping and distinct brain activations found by the block contrast and the subject-specific regression analyses for each type of emotion films. For sad films, similar regions of BOLD response that resulted from both data analytic methods included the medial PFC, right IFG, right posterior STG, medial precuneus, left lingual gyrus, left amygdala, and thalamus. The sad vs. neutral films block contrast resulted in distinct activations in dorsomedial PFC, left IFG, left STG, medial lingual gyrus, right amygdala, and the cerebellum (not found with the subject-specific regression analysis). The subject-specific regression analysis found distinct activations in left posterior MTG, right fusiform gyrus, right inferior, and middle occipital gyrus (not found by the block contrast analysis).

For amusing films, similar BOLD responses that resulted from both data analytic approaches included two distinct areas in the dorsomedial PFC. The amusing vs. neutral films block contrast resulted in distinct brain activations in right posterior superior temporal gyrus, right putamen, and left globus pallidus. The subject-specific regression analysis detected distinct activations in medial, inferior, and dorsolateral PFC regions, posterior cingulate, middle and superior temporal gyri as well as subcortical hippocampus, thalamus, and caudate.

Discussion

Affective neuroscience aims to elucidate the neural bases of emotional responding. One significant challenge, however, has

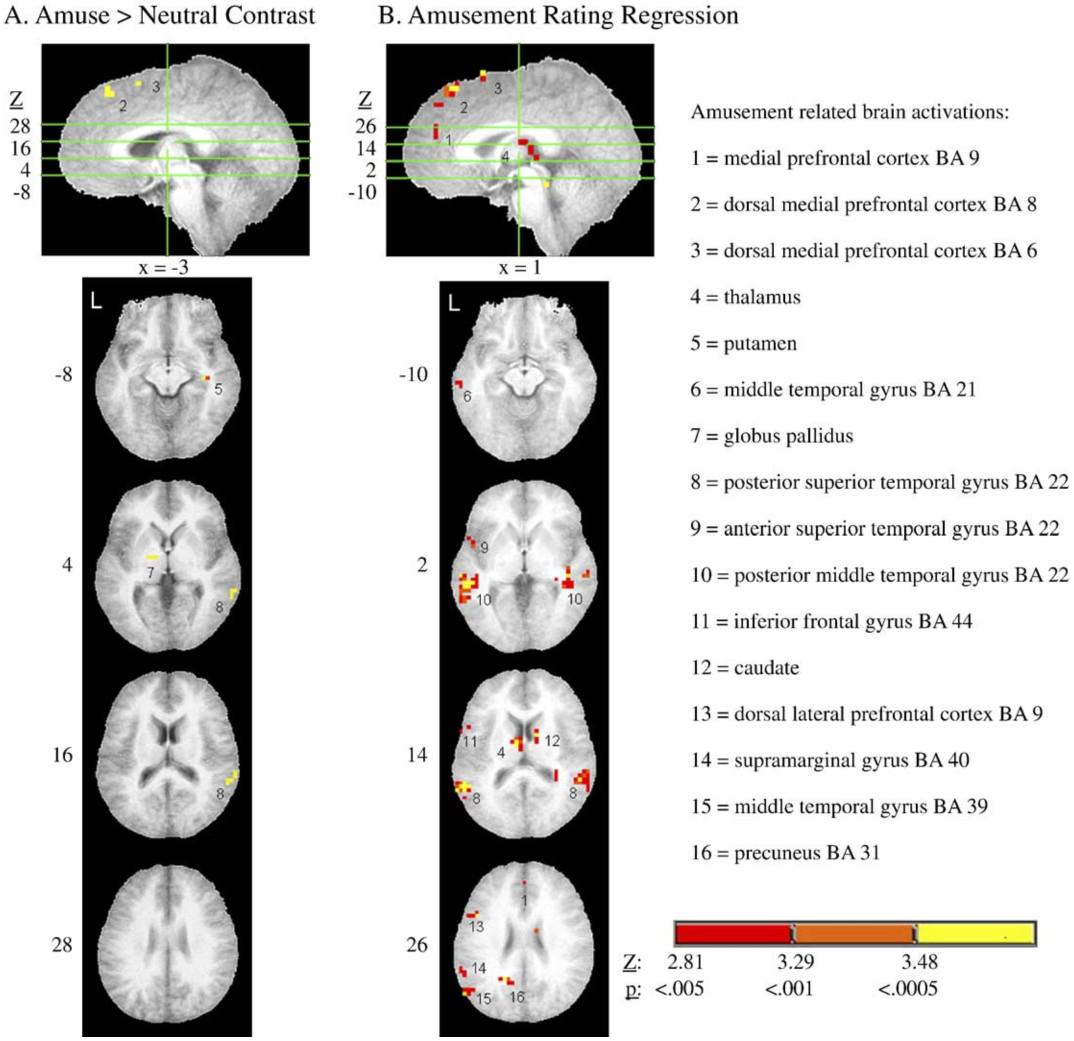


Fig. 4. BOLD responses for (A) the Amuse > neutral block contrast and (B) subject-specific regression using amusement ratings.

Table 3
Subject-specific regression analysis using sadness rating

Brain regions	BA	Volume (mm^3)	*x y z*[a]	Maximum *Z* score
Frontal lobes				
Medial PFC	9, 10	475	−7 53 19	3.17
R IFG	45	580	53 23 16	3.90
Temporal lobes				
L posterior MTG	39	264	−56 −67 12	2.99
R posterior STG	22	369	60 −52 16	3.20
R posterior STG	22	264	56 −45 19	3.25
Parietal lobes				
Medial precuneus/ Posterior cingulate	31	686	−4 −60 27	3.50
Occipital lobes				
R fusiform gyrus/Inferior occipital gyrus	19, 18	793	26 −82 −11	3.44
L lingual gyrus/ Parahippocampal gyrus	19	738	−19 −56 −7	3.73
R inferior occipital gyrus	19	369	41 −79 −14	3.44
R inferior occipital gyrus	19	369	38 −67 −3	3.25
R middle occipital gyrus	18	264	49 −79 −3	3.27
Subcortical				
L amygdala[b]		211	−22 −7 −10	3.42
L thalamus[b]		158	−4 −8 8	3.03

Note. $Z \geq 2.811$, t value threshold ≥ 3.424, voxel $P < 0.005$, cluster $P < 0.02$, minimum cluster volume threshold ≥ 263 mm^3 (5 voxels × 3.75 mm^3), connectivity radius = 3.75 (face-to-face), spatial smoothing Gaussian kernel FWHM = 3.75 mm^3.

BA = Brodmann area, IFG = inferior frontal gyrus, L = left, MTG = middle temporal gyrus, PFC = prefrontal cortex, R = right, STG = superior temporal gyrus.

[a] Talairach and Tournoux coordinates of maximum BOLD signal intensity voxel.

[b] Search volume of interest corrected cluster $P < 0.05$.

been to create experimental conditions that adequately capture the dynamic unfolding of emotion responses and that make sufficient allowance for the dramatic individual differences that are evident in emotional experience. In this study, we used dynamic emotion-generative film stimuli and a subject-specific sampling method for obtaining continuous emotion intensity ratings within the MR scanner. Our goals in this study were (1) to compare differences in detection of BOLD responses between conventional analyses using block contrasts and subject-specific regression analyses using dynamic emotion ratings, and (2) to identify neural bases of amusement and sadness experience.

Block contrast vs. subject-specific regression approaches

One crucial finding was the observation of a relationship between the data analytic approach used to examine emotion-related neural response and the specific emotion experience (i.e., amusement or sadness) induced by emotion-generative film stimuli. Specifically, for sad films, both the block contrast and subject-specific regression using emotion ratings analyses resulted in above-threshold BOLD responses, with the block contrast analysis resulting in greater signal magnitude and number of activation clusters. However, for amusing films, while both analytic approaches yielded significant BOLD responses, subject-specific regression resulted in a greater number and larger spatial extent of BOLD responses than did the block contrast approach.

One explanation for this pattern of results arises from the differential sensitivity of block contrast vs. subject-specific emotion ratings to model time-varying fluctuations in ongoing emotion experience induced by the film clips. As evidenced by the significantly greater number of discrete peaks in emotion intensity ratings and the faster rise to first peak during amusing compared to sad films, amusement and sadness experiences in this study were associated with markedly different temporal profiles as they evolved over time. The humorous jokes delivered in the amusing comedic routines are characterized as punctate events that may induce acute shifts in ongoing amusement experience. Thus, the subject-specific amusement rating may be more closely coupled, than the static block contrast model, to the experience of amusement and its neural substrates as they oscillate over time in response to the amusing film clips.

Sadness, on the other hand, appears to have a much slower and smoother temporal evolution as it gradually rises to peak intensity in response to sad films, at least as induced by these films. The relative advantage shown by the sad vs. neutral film block contrasts compared to subject-specific sadness ratings suggests that sadness experience and its concomitant neural

Table 4
Subject-specific regression analysis using amusement rating

Brain regions	BA	Volume (mm^3)	*x y z*[a]	Maximum *Z* score
Frontal lobes				
L IFG	44	1529	−56 8 8	3.90
L DLPFC/IFG	9	316	−45 11 27	3.68
Dorsomedial PFC/SFG	6	316	−7 15 57	3.45
Dorsomedial PFC/SFG	8	1213	0 34 53	4.13
Dorsomedial PFC/SFG	6	475	0 11 64	3.49
Medial PFC	9	264	4 45 23	3.34
R IFG	44	686	49 11 8	3.54
L posterior cingulate	31	580	−19 −52 27	3.68
Temporal lobes				
L posterior MTG	39	10,389	−56 −67 27	4.32
L MTG	21	316	−56 −7 −3	3.46
R posterior MTG	37	264	49 −52 4	3.15
R STG	22	264	56 −26 1	3.47
Subcortical				
R hippocampus		4482	30 −30 −3	4.22
L anterior thalamus		949	−7 −4 16	3.84
L posterior thalamus		422	−4 −26 8	3.27
R caudate body		791	4 0 19	3.76

Note. $Z \geq 2.811$, t value threshold ≥ 3.424, voxel $P < 0.005$, cluster $P < 0.02$, minimum cluster volume threshold ≥ 263 mm^3 (5 voxels × 3.75 mm^3), connectivity radius = 3.75 (face-to-face), spatial smoothing Gaussian kernel FWHM = 3.75 mm^3.

BA = Brodmann area, DLPFC = dorsolateral prefrontal cortex, IFG = inferior frontal gyrus, L = left, MTG = middle temporal gyrus, PFC = prefrontal cortex, R = right, SFG = superior frontal gyrus, STG = superior temporal gyrus.

[a] Talairach and Tournoux coordinates of maximum BOLD signal intensity voxel.

activation are characterized by a more steady-state, non-fluctuating profile that can be approximated by a box-car regressor as used in block contrasts.

The differential sensitivity of block contrast and time varying subject-specific regression approaches for detecting amusement and sadness-related BOLD signal may have important implications in interpreting the results of studies that focus on emotions that are characterized by markedly different patterns of temporal unfolding. Negative results in previous studies may be due to a mismatch between the phenomenon being examined and the data analytic models we use to infer underlying neural activations in neuroimaging studies. Thus, greater consideration of the temporal characteristics of different types of emotions and of individual differences in subject-specific emotion responses as they evolve over time is warranted both in the design and analysis of emotion-generative experiments.

The neural bases of amusement and sadness: common and distinct activations

The subject-specific regression analyses using amusement or sadness ratings resulted in similar areas of activation during amusing or sad films in medial PFC, right inferior frontal gyrus, posterior cingulate gyrus, and bilateral posterior middle temporal gyrus. The anterior medial PFC has been implicated in self-referential processing (e.g., Kelley et al., 2002; Macrae et al., 2004), emotional awareness (Lane et al., 1998), self-focused attention to emotion (Drevets and Raichle, 1998; Lane et al., 1997b), emotional self-regulation (Davidson, 2000), emotion decision making (Damasio, 1996), and in executive top-down cognitive regulation of emotion related limbic and paralimbic brain regions (Ochsner et al., 2002). The medial PFC has been characterized as a general processor of emotion and according to a meta-analytic review is one of the most frequently observed areas of activation across all types of emotion stimuli (Phan et al., 2002). Activation of medial PFC has been observed in young girls (BA 10; Levesque et al., 2003) and adult females (BA 10; Eugene et al., 2003) during viewing of sad films and in professional actors during self-induced sad state (Pelletier et al., 2003). The right inferior frontal gyrus (BA 44, 45) has been implicated in the assessment of facial emotion (Nakamura et al., 1999). Areas in bilateral posterior portions of middle temporal gyri have been associated with speech comprehension (Crinion et al., 2003; Specht and Reul, 2003) and face perception (e.g., Bartels and Zeki, 2004). The posterior cingulate or retrosplenial gyrus (BA 31) is often found in response to affective visual tasks (Maddock, 1999) and subserves visual attention to emotion stimuli. This specific set of brain regions was identified by subject-specific emotion ratings, suggesting that the time courses of neural response covaried with conscious subjective experience and self-report.

Additional brain regions detected in the sad vs. neutral films block contrast that were also found during amusing films included dorsomedial PFC and anterior and posterior regions of thalamus. The dorsomedial PFC may be part of a medial PFC network that exerts top-down modulation of more ventral PFC and subcortical brain regions (Ochsner et al., 2002). Thalamic activation has been associated with memory, executive functioning and attention (Van der Werf et al., 2003), emotion film- and recall-generated emotion (Reiman, 1997), and with happy and sad films (Lane et al., 1997a,b,c).

Neural activations that differentiated amusement and sadness experience were also found in this study. Amusing films uniquely produced subcortical activation in the right caudate, right putamen, left globus pallidus, and right hippocampus. The caudate has been found in positive emotion states (Lane et al., 1997b), romantic love (Bartels and Zeki, 2000), and in a meta-analytic review of 55 PET and fMRI emotion studies, the basal ganglia was observed in nearly 70% of happiness induction studies (Phan et al., 2002). The hippocampus activation may be associated with memory processes of retrieval of associations cued by components of the amusing film clips.

Sad films distinctly activated portions of the visual object processing pathways in the ventral occipito-temporal (inferior and middle occipital gyri, fusiform gyrus, lingual gyrus, posterior middle and superior temporal gyri) as well as the dorsal amygdala (bilaterally in the block contrast and only left in the subject-specific regression analysis). A recent PET study of film-induced emotions found bilateral amygdala activation during sad (and during amusing) films (Aalto et al., 2002). The amygdala has been implicated in vigilance to and detection of salience (Davis and Whalen, 2001), dispositional affective style (Davidson and Irwin, 1999), and amygdala activity has been associated with increasing intensity of sad facial expression (Blair et al., 1999). Left amygdala has also been noted during appraisal of negative emotion (Ochsner et al., 2002). A recent meta-analysis of left vs. right amygdala failed to find systematic hemisphere-specific functions, but noted that left amygdala activation is more commonly found (Baas et al., 2004).

Limitations and future directions

There were several limitations of the present study. We only used two exemplars of sad and amusing films. A greater number and wider variety of both sad and amusing film clips as well as the inclusion of female comedians among the amusing film stimuli would enhance the generalizability of the results of this study. Closer matching of visual properties in the emotion and non-emotion film clips, including luminance, color, number of scene shifts, may remove potential confounds not controlled in this study. Also, because we assumed a linear relationship between emotion ratings and BOLD responses and did not test for more complex relationships, we may not have detected other types of associations between emotion ratings and BOLD responses.

Future studies might benefit from several considerations. Because individual differences among participants might influence the temporal unfolding of the components that constitute an emotional response, the inclusion of state and trait personality, mood, and emotion measures would facilitate a more detailed understanding of the complex relationship of affective dispositions, emotion appraisal, and emotion regulation propensities. Inclusion of both male and female participants would support an examination of the impact of gender on the temporal profile of emotional responding. The addition of other measures that index other channels of emotion responses such as simultaneous EEG, pupilometry, facial EMG, and video recording of face expressions would enrich the analysis of ongoing dynamic emotion experience. Comparison of film viewing only vs. film viewing plus online emotion ratings (see Hutcherson et al., in press) would facilitate an understanding of the effect of simultaneous emotion rating on neural responses underlying emotion experience.

References

Aalto, S., Naatanen, P., Wallius, E., Metsahonkala, L., Stenman, H., Niemi, P.M., Karlsson, H., 2002. Neuroanatomical substrata of amusement and sadness: a PET activation study using film stimuli. NeuroReport 13, 67–73.

Baas, D., Aleman, A., Kahn, R.S., 2004. Lateralization of amygdala activation: a systematic review of functional neuroimaging studies. Brain Res., Brain Res. Rev. 45, 96–103.

Barrett, L.F., 2004. Feelings or words? Understanding the content in self-report ratings of experienced emotion. J. Pers. Soc. Psychol. 87, 266–281.

Bartels, A., Zeki, S., 2000. The neural basis of romantic love. NeuroReport 11, 3829–3834.

Bartels, A., Zeki, S., 2004. Functional brain mapping during free viewing of natural scenes. Hum. Brain Mapp. 21, 75–85.

Blair, R.J., Morris, J.S., Frith, C.D., Perrett, D.I., Dolan, R.J., 1999. Dissociable neural responses to facial expressions of sadness and anger. Brain 122, 883–893.

Boynton, G.M., Engel, S.A., Glover, G.H., Heeger, D.J., 1996. Linear systems analysis of functional magnetic resonance imaging in human V1. J. Neurosci. 16, 4207–4221.

Cohen, J., 1988. Statistical Power Analysis for the Behavioral Sciences, 2nd ed. Erlbaum, New Jersey.

Cohen, M.S., 1997. Parametric analysis of fMRI data using linear systems methods. NeuroImage 6, 93–103.

Cox, R.W., 1996. Software for analysis and visualization of functional magnetic neuroimages. Comput. Biomed. Res. 29, 162–173.

Craske, M.G., Tsao, J.C.I., 1999. Self-monitoring with panic and anxiety disorders. Psychol. Assess. 11, 466–479.

Crinion, J.T., Lambon-Ralph, M.A., Warburton, E.A., Howard, D., Wise, R.J., 2003. Temporal lobe regions engaged during normal speech comprehension. Brain 126, 1193–1201.

Damasio, A.R., 1996. The somatic marker hypothesis and the possible functions of the prefrontal cortex. Philos. Trans. R. Soc. London, Behav. Biol. Sci. 351, 1413–1420.

Davidson, R.J., 2000. Affective style, psychopathology, and resilience: brain mechanisms and plasticity. Am. Psychol. 55, 1196–1214.

Davidson, R.J., 2002. Anxiety and affective style: role of prefrontal cortex and amygdala. Biol. Psychiatry 5, 68–80.

Davidson, R.J., 2003. Darwin and the neural bases of emotion and affective style. Ann. N. Y. Acad. Sci. 1000, 316–336.

Davidson, R.J., Irwin, W., 1999. The functional neuroanatomy of emotion and affective style. Trends Cogn. Sci. 3, 1–21.

Davis, M., Whalen, P.J., 2001. The amygdala: vigilance and emotion. Mol. Psychiatry 6, 13–34.

Drevets, W.C., Raichle, M.E., 1998. Reciprocal suppression of regional cerebral blood flow during emotional versus higher cognitive processes: implications for interaction between emotion and cognition. Cogn. Emot. 12, 353–385.

Elfenbein, H.A., Mandal, M.K., Ambady, N., Harizuka, S., Kumar, S., 2002. Cross-cultural patterns in emotion recognition: highlighting design and analytical techniques. Emotion 2, 75–84.

Eugene, F., Levesque, J., Mensour, B., Leroux, J.M., Beaudoin, G., Bourgouin, P., Beauregard, M., 2003. The impact of individual differences on the neural circuitry underlying sadness. NeuroImage 19, 354–364.

Forman, S.D., Cohen, J.D., Fitzgerald, M., Eddy, W.F., Mintun, M.A., Noll, D.C., 1995. Improved assessment of significant activation in functional magnetic resonance imaging (fMRI): use of a cluster-size threshold. Magn. Reson. Med. 33, 636–647.

Glover, G.H., Lai, T.F., 2001. Spiral-in/out BOLD fmri for increased SNR and reduced susceptibility artifacts. Magn. Reson. Med. 46, 515–522.

Gross, J.J., 2001. Emotion regulation in adulthood: timing is everything. Curr. Dir. Psychol. Sci. 10, 214–219.

Gross, J.J., Levenson, R.W., 1995. Emotion elicitation using films. Cogn. Emot. 9, 87–108.

Hagemann, D., Naumann, E., Maier, S., Becker, G., Lürken, A., Bartussek, D., 1999. The assessment of affective reactivity using films: validity, reliability and sex differences. Pers. Individ. Differ. 26, 627–639.

Hutcherson, C.A., Goldin, P.R., Ochsner, K.N., Gabrieli, J.D., Feldman Barrett, L., Gross, J.J., in press. Attention and emotion: does rating emotion alter neural responses to amusing and sad films? NeuroImage.

Kelley, W.M., Macrae, C.N., Wyland, C.L., Caglar, S., Inati, S., Heatherton, T.F., 2002. Finding the self? An event-related fMRI study. J. Cogn. Neurosci. 14, 785–794.

Kring, A.M., Gordon, A.H., 1998. Sex differences in emotion: expression, experience, and physiology. J. Pers. Soc. Psychol. 74, 686–703.

Lancaster, J.L., Woldorff, M.G., Parsons, L.M., Liotti, M., Freitas, C.S., Rainey, L.H., Kochunov, P.V., Nickerson, D., Mikiten, S.A., Fox, P.T., 2000. Automated Talairach atlas for functional brain mapping. Hum. Brain Mapp. 10, 120–131.

Lane, R.D., Reiman, E.M., Ahern, G.L., Schwartz, G.E., Davidson, R.J., 1997a. Neuroanatomical correlates of happiness, sadness, and disgust. Am. J. Psychiatry 154, 926–933.

Lane, R.D., Reiman, E.M., Bradley, M.M., Lang, P.J., Ahern, G.L., Davidson, R.J., et al., 1997b. Neuroanatomical correlates of pleasant and unpleasant emotion. Neuropsychologia 35, 1437–1444.

Lane, R.D., Fink, G.R., Chau, P.M., Dolan, R.J., 1997c. Neural activation during selective attention to subjective emotional responses. NeuroReport 8, 3969–3972.

Lane, R.D., Reiman, E.M., Axelrod, B., Yun, L.S., Holmes, A., Schwartz, G.E., 1998. Neural correlates of levels of emotional awareness. Evidence of an interaction between emotion and attention in the anterior cingulate cortex. J. Cogn. Neurosci. 10, 525–535.

Larsen, J.T., Norris, C.J., Cacioppo, J.T., 2003. Effects of positive and negative affect on electromyographic activity over zygomaticus major and corrugator supercilii. Psychophysiology 40, 776–785.

LeDoux, J.E., 2000. Emotion circuits in the brain. Annu. Rev. Neurosci. 23, 155–184.

Levenson, R.W., 1994. Human emotions: a functional view. In: Ekman, P., Davidson, R.J. (Eds.), The Nature of Emotion: Fundamental Questions. Oxford University Press, New York, pp. 123–126.

Levenson, R.W., Gottman, J.M., 1985. Physiological and affective predictors of change in relationship satisfaction. J. Pers. Soc. Psychol. 49, 85–94.

Levesque, J., Joanette, Y., Mensour, B., Beaudoin, G., Leroux, J.M., Bourgouin, P., Beauregard, M., 2003. Neural correlates of sad feelings in healthy girls. Neuroscience 121, 545–551.

Macrae, C.N., Moran, J.M., Heatherton, T.F., Banfield, J.F., Kelley, W.M., 2004. Medial prefrontal activity predicts memory for self. Cereb. Cortex 14, 647–654.

Maddock, R.J., 1999. The retrosplenial cortex and emotion: new insights from functional neuroimaging of the human brain. Trends Neurosci. 22, 310–316.

Mai, J.K., Assheuer, J., Paxinos, G., 1997. Atlas of the Human Brain. Academic Press, San Diego, CA.

Mauss, I.B., Levenson, R.W., Wilhelm, F.W., McCarter, L., Gross, J.J., in press. The tie that binds? Coherence among emotion experience, behavior, and physiology.

Nakamura, K., Kwashima, R., Ito, K., Sugiura, M., Kato, T., Nakamura, A., Hatano, K., Nagumo, S., Kutoba, K., Fukuda, H., Kojima, S., 1999. Activation of the right inferior frontal cortex during assessment of facial emotion. J. Neurophysiol. 82, 1610–1614.

Ochsner, K.N., Bunge, S.A., Gross, J.J., Gabrieli, J.D., 2002. Rethinking feelings: an FMRI study of the cognitive regulation of emotion. J. Cogn. Neurosci. 14, 1215–1229.

Pelletier, M., Bouthillier, A., Levesque, J., Carrier, S., Breault, C., Paquette, V., Mensour, B., Leroux, J.M., Beaudoin, G., Bourgouin, P., Beauregard, M., 2003. Separate neural circuits for primary emotions? Brain activity during self-induced sadness and happiness in professional actors. NeuroReport 14, 1111–1116.

Phan, K.L., Wager, T., Taylor, S.F., Liberzon, I., 2002. Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. NeuroImage 16, 331–348.

Phan, K.L., Taylor, S.F., Welsh, R.C., Decker, L.R., Noll, D.C., Nichols, T.E., Britton, J.C., Liberzon, I., 2003. Activation of the medial prefrontal cortex and extended amygdala by individual ratings of emotional arousal: a fMRI study. Biol. Psychiatry 53, 211–215.

Phan, K.L., Taylor, S.F., Welsh, R.C., Ho, S.H., Britton, J.C., Liberzon, I., 2004a. Neural correlates of individual ratings of emotional salience: a trial-related fMRI study. NeuroImage 21, 768–780.

Phan, K.L., Wager, T.D., Taylor, S.F., Liberzon, I., 2004b. Functional neuroimaging studies of human emotions. CNS Spectrosc. 9, 258–266.

Preston, A.R., Thomason, M.E., Ochsner, K.N., Cooper, J.C., Glover, G.H., 2004. Comparison of spiral-in/out and spiral-out BOLD fMRI at 1.5 T and 3 T. NeuroImage 21, 291–301.

Reiman, E.M., 1997. The application of positron emission tomography to the study of normal and pathologic emotions. J. Clin. Psychiatry 58, 4–12.

Scherer, K.R., 2000. Psychological models of emotion. In: Borod, J.C. (Ed.), The Neuropsychology of Emotion. Oxford University Press, New York, pp. 137–162.

Specht, K., Reul, J., 2003. Functional segregation of the temporal lobes into highly differentiated subsystems for auditory perception: an auditory rapid event-related fMRI-task. NeuroImage 20, 1944–1954.

Talairach, J., Tournoux, P., 1988. Co-Planar Stereotaxic Atlas of the Human Brain. Thieme Medical, New York.

Taylor, S.F., Phan, K.L., Decker, L.R., Liberzon, I., 2003. Subjective rating of emotionally salient stimuli modulates neural activity. NeuroImage 18, 650–659.

Van der Werf, Y.D., Scheltens, P., Lindeboom, J., Witter, M.P., Uylings, H.B., Jolles, J., 2003. Deficits of memory, executive functioning and attention following infarction in the thalamus; a study of 22 cases with localised lesions. Neuropsychologia 41, 1330–1344.

Wager, T.D., Phan, K.L., Liberzon, I., Taylor, S.F., 2003. Valence, gender, and lateralization of functional brain anatomy in emotion: a meta-analysis of findings from neuroimaging. NeuroImage 19, 513–531.