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NeuroImage 23 (2004) 483 – 499

For better or for worse: neural systems supporting the cognitive down- and up-regulation of negative emotion

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Received 11 September 2003; revised 11 June 2004; accepted 22 June 2004

Functional neuroimaging studies examining the neural bases of the cognitive control of emotion have found increased prefrontal and decreased amygdala activation for the reduction or down-regulation of negative emotion. It is unknown, however, (1) whether the same neural systems underlie the enhancement or up-regulation of emotion, and (2) whether altering the nature of the regulatory strategy alters the neural systems mediating the regulation. To address these questions using functional magnetic resonance imaging (fMRI), participants up- and down-regulated negative emotion either by focusing internally on the self-relevance of aversive scenes or by focusing externally on alternative meanings for pictured actions and their situational contexts. Results indicated (1a) that both up- and down-regulating negative emotion recruited prefrontal and anterior cingulate regions implicated in cognitive control, (1b) that amygdala activation was modulated up or down in accord with the regulatory goal, and (1c) that up-regulation uniquely recruited regions of left rostromedial PFC implicated in the retrieval of emotion knowledge, whereas down-regulation uniquely recruited regions of right lateral and orbital PFC implicated in behavioral inhibition. Results also indicated that (2) self-focused regulation recruited medial prefrontal regions implicated in internally focused processing, whereas situation-focused regulation recruited lateral prefrontal regions implicated in externally focused processing. These data suggest that both common and distinct neural systems support various forms of reappraisal and that which particular prefrontal systems modulate the amygdala in different ways depends on the regulatory goal and strategy employed.

Keywords: Emotion; Neural system; Up- and down-regulation

Introduction

To cope with trying times, individuals employ a wide variety of emotion-regulatory strategies (Gross, 1998; Ochsner and Gross, 2004). One common strategy alters the trajectory of an unfolding emotional response by mentally transforming, or reappraising, the meaning of the emotion-eliciting situation. In comparison to other regulatory strategies, such as suppressing emotion expressive behavior, reappraisal appears to provide one of the most flexible and effective means of diminishing the negative impact of an aversive event (Gross, 2002; Gross and Levenson, 1993; Richards and Gross, 2000). Reappraisal is used not just to mentally better our bad situations, however. It also is used to mentally make bad situations worse. In some cases, cognitively up-regulating negative emotion may be desirable, as when athletes cultivate aggression before a big game. In others it may be understandable, as when we imagine the worst while passing a traffic accident. And in still others it may be maladaptive, as our worry mushrooms into anxiety and depression (Nolen-Hoeksema, 2000; Segerstrom et al., 2000). Whether used to make ourselves feel better or worse, reappraisal plays an important regulatory role in maintaining our mental and physical well-being (Davidson et al., 2000; Gross, 1998). Despite growing recognition of reappraisal's importance, however, little is known about the underlying psychological and neural mechanisms.

A model of the brain organization of emotional reappraisal (Ochsner et al., 2002) was proposed by analogy to well-studied forms of cognitive control such as working memory and response selection (D'Esposito et al., 2000; Miller and Cohen, 2001). On this view, the emotion-modulatory effects of reappraisal stem from interactions between cognitive control processes implemented in prefrontal and cingulate regions and emotional appraisal processes implemented in multiple emotion-related structures, including the amygdala (Ochsner and Gross, 2004; Ochsner et al., 2002). This model's predictions are consistent with the handful of neuroimaging studies that have investigated the neural correlates of reappraisal. Three studies have examined the down-regulation of either aversive affect (Ochsner et al., 2002), sadness (Levesque et al., 2003), or sexual arousal (Beauregard et al., 2001), and all found

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doi:10.1016/j.neuroimage.2004.06.030

reappraisal-related prefrontal activations in combination with modulations of regions associated with different types of emotion processing, including the amygdala. A fourth study found that reappraisal could maintain amygdala activation to aversive photos after they disappeared (Schaefer et al., 2002) but did not report maintenance-related prefrontal activations. To date, no studies have examined the use of reappraisal to up-regulate emotion, and it is therefore not known whether up-regulation involves neural systems similar to those underlying the down-regulation of emotion.

Although all four of these studies found prefrontal and/or amygdala participation in reappraisal, the specific prefrontal and emotion-processing-related activations have varied across studies. Part of this variability may be attributable to the use of different reappraisal strategies by participants, both within and across studies. Some studies specifically instructed participants how to actively reinterpret the meaning of events depicted in stimuli (Ochsner et al., 2002), whereas others provided an instruction either to suppress emotion by becoming detached (Beauregard et al., 2001) or to maintain an emotion (Schaefer et al., 2002) without specifying exactly how participants were to do this. Different reappraisal strategies may recruit different cognitive control systems and thus be associated with different patterns of brain activation. As of yet, however, there has been no systematic attempt to test this possibility.

To clarify and extend our understanding of the neural bases of reappraisal, the present study used functional magnetic resonance imaging (1) to directly compare the effect of using reappraisal to down- and up-regulate negative emotion, and (2) to examine the effects of two different reappraisal strategies that were equally effective at achieving these regulatory goals.

On the cognitive control side of reappraisal, there is reason to believe that the up- and down-regulation of emotion will depend upon similar prefrontal control systems because both involve generating an alternative interpretation for the meaning of an event, and prior work suggests that these processes depend upon prefrontal cortex (Ochsner and Gross, 2004; Ochsner et al., 2002). However, there also is reason to believe that the up- and down-regulation of emotion will depend upon distinct prefrontal control systems because the reinterpretations used to make oneself feel better or worse may differ in systematic ways. When generating a reappraisal that makes one feel worse, for example, one might retrieve emotion knowledge and emotion labels that can be used to describe an event in increasingly negative terms. Thus, one might add insult to the injury depicted in an image by describing it as horrific, terribly painful, and unlikely to heal. By contrast, the down-regulation of negative emotion is not likely to involve the retrieval of emotion knowledge per se, but rather may involve mediating interference between negative bottom-up appraisals of stimuli and neutralizing top–down reappraisals of them (Bechara et al., 2000; Ochsner and Gross, 2004; O'Doherty et al., 2003; Rolls, 2000). By directly contrasting activations related to increasing or decreasing negative emotion via cognitive reappraisal, the present study can help identify their common and distinct neural correlates.

On the emotional appraisal side of reappraisal, we hypothesized that cognitive control regions supporting reappraisal would modulate regions involved in appraising the affective qualities of stimuli and events. Consistent with this hypothesis, prior work has shown that using reappraisal to down-regulate negative emotion diminishes amygdala activity (Ochsner et al., 2002), which plays an important and pervasive role in encoding evocative, arousing, and especially aversive events (Anderson and Phelps, 2001; Anderson et al., 2003; Hamann et al., 2000; LeDoux, 2000; Morris et al., 1998; Whalen et al., 1998). The present study sought to extend prior findings by determining whether the up- and down-regulation of emotion elicited by aversive images involve differential modulation of the amygdala, with cognitive up-regulation associated with greater amygdala activation and cognitive down-regulation associated with lesser amygdala activation.

To systematically examine the effects of different types of cognitive reappraisal, we asked participants to reappraise aversive images using strategies that either focused on the self-relevance of an event or focused on situational aspects of the event. Whereas self-focused strategies alter the personal relevance of events, making one feel more or less connected to what is going on, situation-focused strategies reinterpret the nature of the events themselves, reevaluating others' actions, dispositions, and outcomes. The distinction between self- and situation-focused reappraisal strategies builds on psychological theories that demonstrate the special role for self-relevant information in memory, emotion, and motivation (Baumeister, 1998) and an emerging cognitive neuroscience literature that has identified distinct medial prefrontal systems important for self-referential processing (e.g., Gusnard et al., 2001; Kelley et al., 2002; Lane et al., 1997). Either type of strategy can be used to increase or decrease emotion, albeit by different means, and the present study sought to determine the neural correlates of self- and situation-focused types of cognitive reappraisal.

Methods

Participants

Twenty-four female participants (M age = 20.6 years) were recruited in compliance with the human subjects regulations of Stanford University and were paid US$60 for voluntary completion of this study. We used only one sex because several studies have suggested that there are sex differences in response to negative visual materials (e.g., Canli et al., 2002; Cahill et al., 2001), and we wanted to avoid this source of variability.

Behavioral paradigm

Participants were instructed to increase and decrease their negative emotions in response to aversive images using one of two strategies (see Fig. 1A). Participants assigned to the self-focus group were instructed to think about the personal relevance of each image as it appeared. When increasing negative affect, they were to increase their sense of subjective closeness to pictured events, imagining themselves or a loved one as the central figure in a photo, imagining themselves present as pictured actions unfolded, and in general heightening their sense of personal or subjective experience for the sights and sounds of the event they were viewing. When decreasing negative emotion, participants in the self-focus group were instructed to increase their sense of objective distance, viewing pictured events from a detached, third-person perspective. Thus, a participant viewing an image of a sick person in the hospital might increase her negative emotion by imagining that she could be that individual, or that she was present observing that individual and their agonized expression of pain as they lay in their hospital bed. To decrease negative emotion participants could

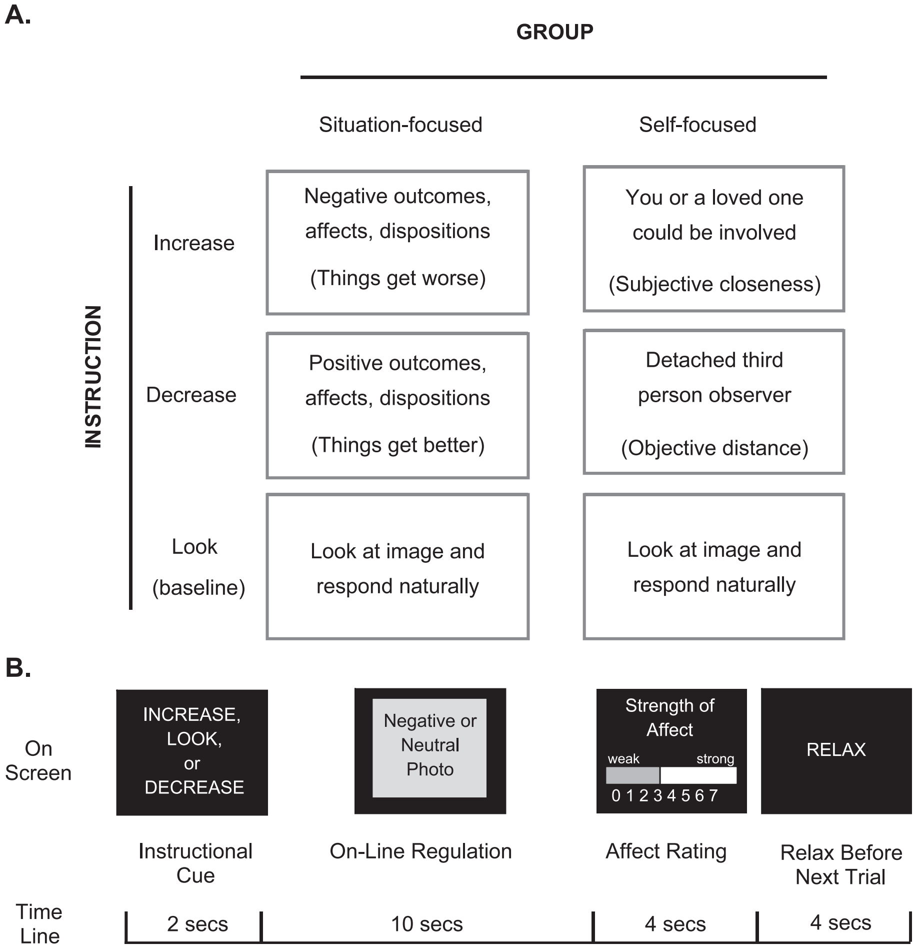

Fig. 1. (A) Schematic diagram showing the six different conditions in the present study defined by the crossing of two factors: type of instruction (to increase emotion, decrease emotion, or in a baseline condition, look at a stimulus and respond naturally) and strategy group (employing a reappraisal strategy that either focuses on reinterpreting aspects of a pictured situation or on reinterpreting the self-relevance of pictured events). (B) Timeline for events on each trial. An initial cue instructs participants to increase, decrease, or look, which is followed by a photo presentation period during which participants follow this instruction. Participants then provide a rating of their current negative affect and finally have a moment to relax before the onset of the next trial.

view the sick person from the detached, clinical perspective of one not personally connected in any way to the pictured individual and the context in which she is situated.

Participants assigned to the situation-focused group were instructed to reinterpret the emotions, actions, and outcomes of individuals as depicted in their situational context. To increase negative emotion using this strategy, it was emphasized that the participant should imagine events in the image getting worse. To decrease negative emotion, participants in the situation-focused group were asked to imagine pictured events getting better. Thus, in the case of the sick person pictured in the hospital, the situation-focused strategy might involve imagining that person is in great pain, has been suffering for quite a long time, and tragically is unlikely ever to recover. To decrease negative emotion, one could imagine that the sick individual is only tired, possessed of a strong constitution, and is likely to recover quickly.

Participants randomly assigned to each of the two instructional groups (12 self-focused and 12 situation-focused) were cued to increase or decrease their negative emotion on a series of 162 randomly intermixed trials. Twenty-seven images were shown for each of six types of trials defined by crossing three types of instruction (increase, decrease, or look) and two valences of stimuli (negative and neutral; Fig. 1A). Each image was shown only once for a given participant, and assignment of images to instruction types was counterbalanced across participants. On increase and decrease trials, participants reappraised images as described above. On look trials, participants were instructed simply to look at the image and let themselves respond naturally. This trial type served as a baseline for comparison with the increase and decrease reappraisal trials. Negative and neutral images were selected from the International Affective Picture System (Lang et al., 1993) and were balanced for valence and arousal across instruction types. Neutral images were included primarily to provide a buffer against habituation to negative images and are not a focus of the analyses presented here.

Each trial was composed of four events (Fig. 1B). First, a cue word (increase, decrease, or look) appeared centrally for 2 s. Second, an aversive or neutral image appeared centrally for 10 s. While the image remained on the screen, participants performed the evaluation operations specified by the prior instructional cue. Third, a rating scale appeared immediately after presentation of the photo. This scale allowed participants to rate the current strength of their negative affect after having looked, increased, or decreased their negative emotion and served as a behavioral index of the success of reappraisal. The scale consisted of a horizontal rectangular bar with anchors of 0 and 7 to indicate relative strength of negative affect. At the beginning of the 4-s rating period, the bar grew from left to right and participants pressed a key when the bar grew to a size that corresponded to the strength of their current negative feeling. This bar provided a continuous index of participants' subjective experience of negative emotion. Fourth, the word relax appeared for 4 s in the center of the screen in capital letters, indicating that participants should relax until the next trial began.

Pretraining and posttesting

Three to 5 days before scanning, participants completed a separate training session in the Psychology Department at Stanford University. During this session, participants received careful instruction and guidance in the performance of the reappraisal strategy they subsequently used in the scanning session. This training phase had two parts. In part one, participants read a brief description of the strategy they were to employ and then viewed a series of images for which they were asked to spontaneously generate appropriate reappraisals. The experimenter helped shape these reappraisals so that they fit the self- or situation-focused strategy the participant was instructed to use. Experimenters also instructed participants not to reappraise stimuli using other strategies not relevant to that participant's group assignment. In part two, the participant completed a block of 21 practice trials whose length was equivalent to one of the scans the participant would later complete in the scanner. At the end of this practice block, the experimenters debriefed participants to ensure that they were able to effectively reappraise and address any questions the participant might have. This training phase ensured that participants clearly understood the specific type of strategy they were to employ inside the scanner and could effectively implement that strategy to reappraise negative images. It was emphasized that participants should do their best to reappraise when asked to do so on any given trial and should accurately report the strength of their negative affect whether or not they felt reappraisal had been successful in changing the way they felt.

After completing the scanning session, participants completed a set of computer guided ratings in a separate room. Each image presented in the scanner was presented again, and participants were asked to rate how much effort they had exerted to perform the self- or situation-focused reappraisals. These ratings provide a measure of the extent to which participants were effortfully engaged in the task as requested.

MRI data acquisition

Twenty-five axial slices (4-mm-thick, 1-mm gap) were collected at 3T (GE Signa LX Horizon Echospeed scanner) with a T2*-sensitive gradient echo spiral-in or -out pulse sequence (30 ms TE, 2000 ms TR, two interleaves, 60° flip angle, 24-cm field of view, 64 × 64 data acquisition matrix). T2-weighted flow-compensated spin-echo scans were acquired for anatomical localization using the same slice prescription (2000 ms TR; 85 ms TE). The spiral in/out sequence has been found particularly valuable in reducing susceptibility dropout in frontal and medial temporal brain regions (Glover and Law, 2001; Preston et al., 2004). High order shimming was performed before functional scans using the scanner's software (developed in the Lucas Center for GE; Glover, 1999). Stimulus presentation and data acquisition were controlled using Psyscope software running on a Macintosh G3 computer. Responses were made with the index finger of the right hand using one button on a four button response box. An LCD projector displayed stimuli on a screen mounted on a custom head coil fitted with a bite-bar to limit head motion.

Data analysis

Functional images were slice time corrected and motion corrected using SPM99 (Wellcome Department of Cognitive Neurology). Anatomical images were coregistered to the mean functional image and normalized to a standard template brain; the functional images were then normalized using those parameters and interpolated to 2 × 2 × 2 mm voxels. Functional images were smoothed with a Gaussian filter (6 mm full width-half maximum). A high-pass filter with a cutoff period of 120 s was applied to remove drifts within sessions.

Fixed effects for each participant were modeled using a mixed design. The 2-s instruction period and 4-s rating period were modeled with a canonical hemodynamic response function at the onset of each period; the 10-s regulation period and 4-s relaxation period were modeled as a boxcar regressor convolved with the canonical hemodynamic response. A general linear model analysis was used in SPM99 to create contrast images for each participant summarizing differences between trial types. These images were used to create SPM{t} maps for the group. Statistical maps for group analyses were thresholded at $P < 0.001$ uncorrected for multiple comparisons. Maxima are reported in ICBM152 coordinates as in SPM99.

On the basis of prior results (e.g., Ochsner et al., 2002) and theoretical considerations (e.g., Ochsner and Gross, 2004), a small set of regions were hypothesized a priori to be involved in reappraisal. These regions included the amygdala and prefrontal regions thought to be involved in cognitively increasing or decreasing negative emotion. Amygdala voxels were identified using a small volume correction for a structurally defined a region of interest derived from amygdala coordinates specified in the Talairach atlas and transformed into ICBM space. Prefrontal voxels were identified from functionally defined regions of interest derived from specific contrasts of increase and decrease trials relative to the look baseline condition (described below). To specifically characterize activation in these ROIs, activation time courses were extracted from the peak voxel in each region. Peak voxel activations were selected rather then average cluster activations because prior research has shown peak voxel activity to be more strongly correlated with electrophysiological measures of activation (Arturs and Boniface, 2003).

Results

Prior to group analysis of behavioral or imaging data, outlier checks were performed to identify individuals showing affect ratings, or changes in affect when increasing or decreasing emotion, that were greater than 2.5 SD from the mean of the entire group. One participant in the situation-focused group was identified as an outlier and her data were removed from all subsequent analyses.

Behavioral results

Subjective reports of negative affect

An ANOVA on affect ratings for negative photos with strategy group as a between-subject factor and type of instruction as a within-subject factor revealed a significant main effect of type of instruction [$F(2,42) = 57.94$, $P < 0.0001$] and no other significant effects (Fig. 2A). Thus, reappraisal was successful both at increasing and decreasing negative emotion, and success of reappraisal did not vary as a function of strategy (F for the interaction <1.62, $P > 0.21$). Planned comparisons demonstrated that when increasing negative emotion, participants reported significantly greater negative affect [$M = 6.22$ $t(22) = 6.83$, $P < 0.0001$] than on look trials when they let themselves respond naturally ($M = 5.62$). When decreasing negative affect, participants reported significantly less negative affect [$M = 4.39$; $t(22) = 6.67$, $P < 0.0001$] than on baseline look trials. For comparison purposes, affect ratings for look trials with neutral photos also are shown in Fig. 2A. Affect reports for these trials

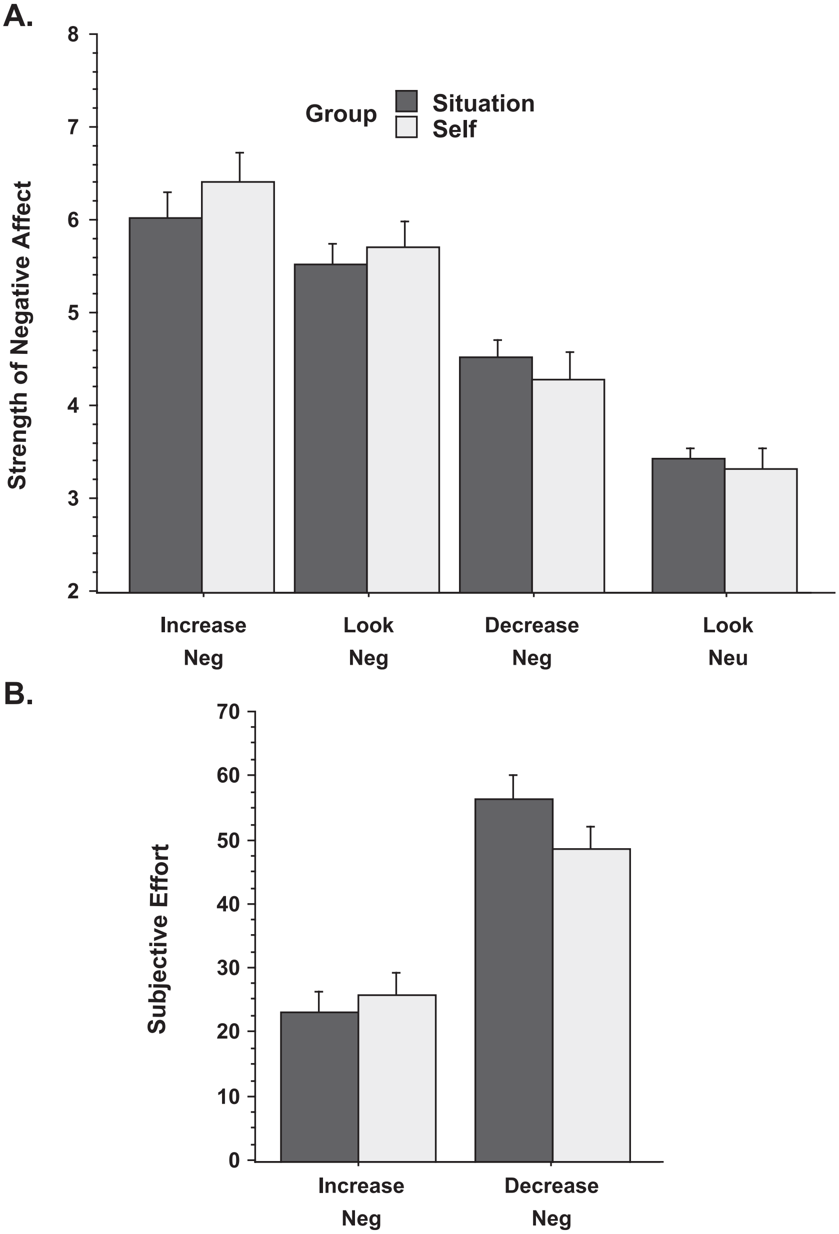

Fig. 2. (A) Self-reports of negative affect on increase, look, and decrease trials with negative photos, and for comparison, look trials with neutral photos. Overall, there were main effects of reappraisal instruction—participants successfully and significantly increased or decreased negative emotion relative to look baseline trials. Reappraisal strategy did not significantly interact with this pattern of findings. (B) Effort ratings on increase and decrease trials. Overall, decreasing was rated as more effortful, and reappraisal strategy did not significantly interact with this pattern of findings.

were significantly smaller than for any trial type using negative photos [*M* = 3.37, *t*(22) > 7.67, *P* < 0.0001, for all comparisons].

Postscan effort ratings

Effort ratings were placed on a 100-point scale where 100 = greatest and 1 = least effort. An ANOVA on postscan effort ratings with strategy group as a between-subject factor and type of instruction as a within-subject factor revealed a significant main effect of type of instruction [$F(2,42) = 28.12$, $P < 0.0001$] and no other significant effects (Fig. 2B). Planned comparisons indicated that participants exerted greater effort when decreasing (*M* =52.47) than when increasing [*M* = 24.64; *t*(22) = 6.70, *P* < 0.0001] negative affect.

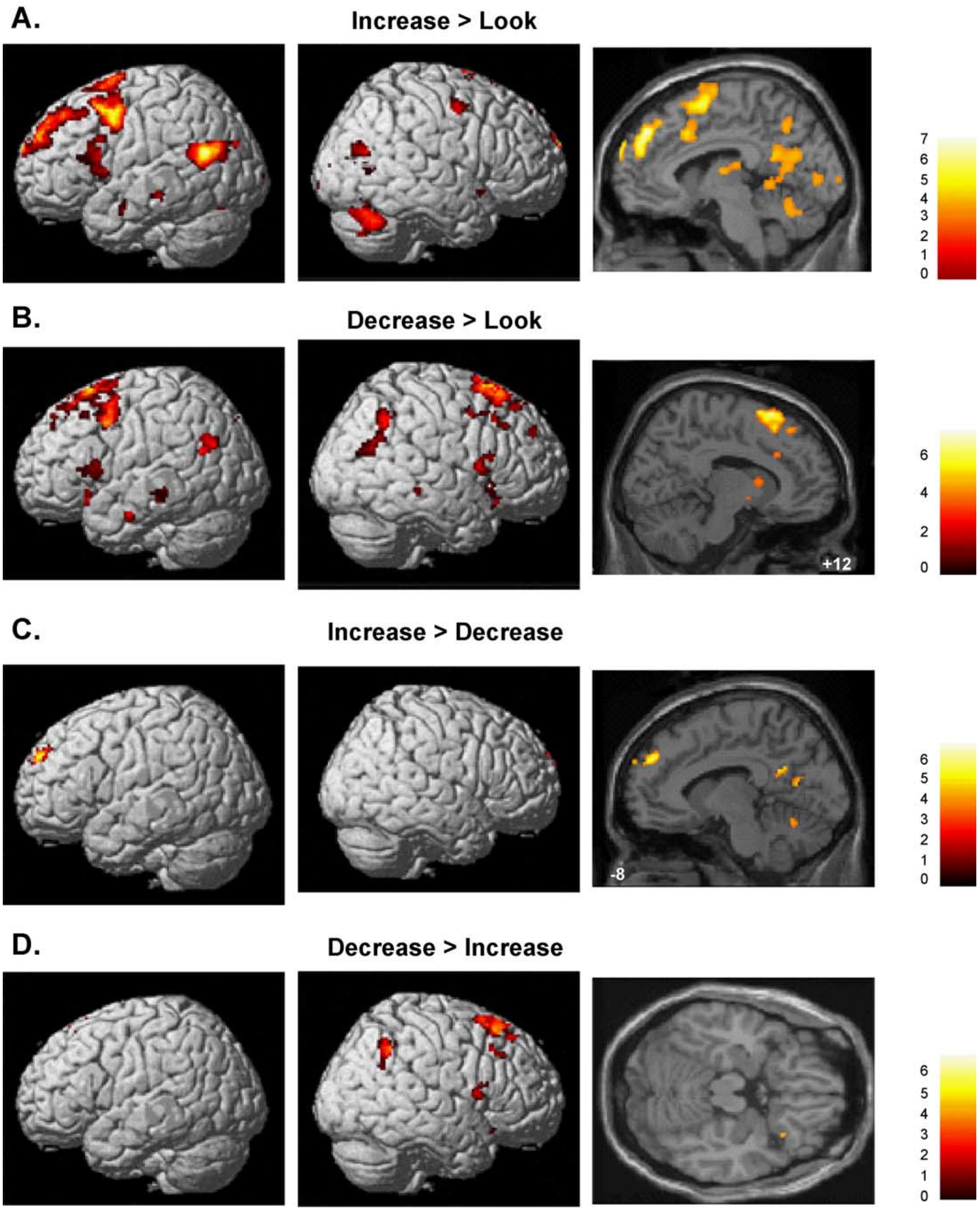

Fig. 3. Group contrasts showing activation when increasing or decreasing emotion. (A) Left two panels show left and right lateral views and rightmost panel shows left medial view of regions active in the increase–look contrast. Of note is the presence of left dorsal lateral and medial prefrontal as well as anterior cingulate cortical activation. (B) Left two panels show left and right lateral views and rightmost panel shows right medial view of regions active in the decrease–look contrast. Of note is bilateral activation of lateral and medial prefrontal cortex, including many left-sided regions similar to those used when increasing. (C) Regions uniquely activated when increasing as revealed by the increase–decrease contrast. Left rostral medial prefrontal cortex and posterior cingulate activation are most easily observed on the rightmost medial view of the left hemisphere. (D) Regions uniquely activated when decreasing as revealed by the decrease–increase contrast. Center panel shows right lateral prefrontal activation, and rightmost panel shows axial view of right lateral orbitofrontal activation.

Table 1
Group activations for increase > look contrast

Region of activation	Brodmann	Coordinates			Z score	Volume (mm^3)
		x	*y*	*z*		
Middle frontal gyrus	L6/9	-50	2	42	5.26	7344
Middle frontal gyrus	L6	-50	0	50	4.81	(L)
Middle frontal gyrus	L6	-36	12	52	4.33	(L)
Middle frontal gyrus	R6	60	-2	50	4.63	896
Middle frontal gyrus	R6	52	-6	58	3.43	(L)
Middle frontal gyrus	R6	56	6	54	3.40	(L)
Medial frontal gyrus	L6	-10	2	66	4.88	6968
Superior frontal gyrus	L6	-4	6	62	4.67	(L)
Cingulate gyrus	L32	-6	18	38	4.05	(L)
Medial frontal gyrus	L9	-6	48	40	5.34	9600
Superior frontal gyrus	L10	-4	66	26	4.72	(L)
Medial frontal gyrus	L9	-6	52	26	4.62	(L)
Medial frontal gyrus	R32	18	10	44	3.24	40
Inferior frontal gyrus	L44	-58	16	16	4.58	1728
Inferior frontal gyrus	L44	-58	12	6	4.24	(L)
Middle frontal gyrus	L9	-44	12	30	3.63	(L)
Postcentral gyrus	L3	-22	-30	54	3.23	40
Postcentral gyrus	R	24	-30	62	3.43	80
Superior temporal gyrus	L39	-50	-64	20	4.32	7136
Middle temporal gyrus	L39	-54	-72	22	3.98	(L)
Middle temporal gyrus	L39	-40	-72	22	3.72	(L)
Superior temporal gyrus	R38	48	14	-12	3.46	88
Middle temporal gyrus	L21	-66	-30	-10	3.61	264
Middle temporal gyrus	L21	-58	-4	-20	3.93	14
Middle temporal gyrus	R39	60	-72	20	4.54	1392
Middle temporal gyrus	R19	60	-78	10	3.70	(L)
Cuneus	L30	-24	-76	8	3.98	400
Precuneus	L7	-6	-62	46	3.52	408
Thalamus	L	-2	-16	12	3.60	944
Thalamus	L	-10	-8	-2	3.35	72
Thalamus	R	20	-14	10	3.17	48
Putamen	L	-22	6	0	3.93	1472
Putamen	L	-30	4	-6	3.15	(L)
Globus pallidus	R	14	-4	-2	4.54	840
Cerebellum	L	-10	-64	-24	3.87	6816
Posterior cingulate	L30/23	-6	-50	20	3.86	(L)
Precuneus	L31	-2	-68	22	3.74	(L)
Cerebellum	R	38	-62	-34	4.88	15136
Cerebellum	R	18	-72	-28	4.25	(L)
Cerebellum	R	32	-74	-28	4.00	(L)
Amygdala*	L	-18	-10	-14	2.52	128

Note. Clusters of five or more contiguous voxels whose global maxima meet a *t* threshold of 3.50, $P < 0.001$ uncorrected, are reported. Local maxima for these clusters are denoted with (L). Coordinates are in MNI space.

* Small volume corrected, two-tailed $P < 0.09$ corrected, $P < 0.006$ uncorrected.

Imaging results

Contrasts were performed to (1) identify regions involved in increasing or decreasing in emotion, regardless of strategy (i.e., regions associated with the main effects of increasing or decreasing), and (2) identify regions uniquely involved in self- or situation-focused reappraisal strategies (i.e., regions associated with the interaction of strategy and direction of reappraisal). For the first set of contrasts, we collapsed across strategy group and compared activations on increase, decrease, and look baseline trials for all 23 participants. For the second set of contrasts, we contrasted activations for each group to determine whether specific regions were more involved for self- or situation-focused reappraisal when increasing or decreasing emotion.

The effects of cognitively increasing and decreasing emotion

Recruited by reappraisal. Regions generally involved in increasing or decreasing emotion first were identified by greater activation in response to increase or decrease as compared to look trials (Figs. 3A and B and Tables 1 and 2). The overall results of each contrast showed many similarities, including significant activation of dorsal and ventral lateral prefrontal cortex, dorsal medial prefrontal cortex, anterior cingulate cortex, bilateral temporal–parietal junction, middle temporal gyrus, and subcortical regions including caudate, thalamus, and cerebellum. There were some notable dissimilarities as well: increase > look activations generally were left-lateralized and included specific activation of rostral medial and posterior cingulate cortex, whereas decrease > look activations generally were bilateral or right-lateralized and included specific activation of orbital frontal cortex.

These dissimilarities were confirmed by directly contrasting activations on increase and decrease trials (Figs. 3C and D; Table 4). To identify increase-related regions that were not recruited when decreasing, the increase–decrease contrast was masked by the increase–look contrast. This insured that only regions more active during increasing than during the baseline look condition could be identified as increase-specific by the increase–decrease contrast. The idea behind this masking procedure was first to identify a network of regions involved in increasing negative affect using the increase–look contrast, and second, given that such regions had been identified, to then determine which of those regions are additionally or selectively more active when increasing than when decreasing. In so doing, the masking procedure ensures that identified regions are functionally interpretable as increase-related by excluding from consideration any regions that were not more active when increasing negative emotion than when simply

Table 2
Group activations for decrease > look contrast

Region of activation	Brodmann	Coordinates			Z score	Volume (mm^3)
		x	y	z		
Superior frontal gyrus	L6	−10	18	62	5.14	17768
Superior frontal gyrus	L6	−2	16	62	5.11	(L)
Superior frontal gyrus	R6	10	20	64	5.05	(L)
Superior frontal gyrus	L6	−34	12	56	3.32	80
Superior frontal gyrus	L8/9	−16	46	42	3.29	88
Superior frontal gyrus	L8	−8	46	48	3.64	120
Superior frontal gyrus	R10	22	46	30	3.54	256
Middle frontal gyrus	L6	−46	6	54	4.70	3184
Middle frontal gyrus	L8	−46	8	44	4.02	(L)
Middle frontal gyrus	L9	−56	8	40	3.87	(L)
Middle frontal gyrus	L8	−36	22	48	3.27	56
Middle frontal gyrus	L8	−24	24	46	3.30	88
Middle frontal gyrus	R8	52	16	48	3.66	328
Middle frontal gyrus	R6/8	50	6	46	3.61	(L)
Middle frontal gyrus	R9	42	30	38	3.50	368
Middle frontal gyrus	R8	36	22	44	3.50	(L)
Inferior frontal gyrus	L45	−54	20	8	3.97	656
Inferior frontal gyrus	L44	−58	14	14	3.73	(L)
Inferior frontal gyrus	L47	−44	22	−8	4.04	416
Inferior frontal gyrus	L47	−30	22	−16	3.58	(L)
Inferior frontal gyrus	R44	58	10	12	4.13	792
Inferior frontal gyrus	R45	60	18	18	3.34	(L)
Inferior frontal gyrus	R47	50	18	−6	3.92	392
Inferior frontal gyrus	R47	34	24	−16	3.53	(L)
Cingulate gyrus	R32	12	24	30	3.48	216
Inferior parietal lobule	R40	60	−56	42	4.28	3000
Superior temporal gyrus	R39	62	−68	24	4.04	(L)
Superior temporal gyrus	R39	64	−62	30	3.59	(L)
Middle temporal gyrus	L39	−60	−72	28	3.75	1496
Angular gyrus	L39	−54	−64	32	3.66	(L)
Middle temporal gyrus	L39	−48	−60	22	3.53	(L)
Middle temporal gyrus	L21	−66	−32	−14	3.42	264
Middle temporal gyrus	L21	−68	−34	−6	3.25	(L)
Middle temporal gyrus	L21	−66	−26	−8	3.14	(L)
Middle temporal gyrus	R21	52	−32	−8	3.44	160
Inferior temporal gyrus	L20	−54	−8	−26	4.00	312
Caudate	L	−16	8	14	3.90	1496
Lateral globus pallidus	L	−20	−2	0	3.29	(L)
Caudate	L	−16	0	16	3.24	(L)
Caudate	R	18	10	12	4.86	2192
Lateral globus pallidus	R	16	2	−6	3.80	(L)

Note. Clusters of five or more contiguous voxels whose global maxima meet a t threshold of 3.50, $P < 0.001$ uncorrected, are reported. Local maxima for these clusters are denoted with (L). Coordinates are in MNI space.

looking at an image. Similarly, decrease-related regions were identified by masking the decrease–increase contrast with the decrease–look contrast. This ensured that only regions more active during decreasing than during the baseline look condition could be identified as decrease-specific by the decrease–increase contrast.

Increase-specific regions were primarily left-lateralized and included left rostral medial prefrontal cortex (BA 9/10) and the posterior cingulate cortex, whereas decrease-specific regions work exclusively right lateralized and included dorsolateral and lateral orbital prefrontal cortex. It should be noted that because of the masking procedure used to construct these contrasts, differential activation of the amygdala in the increase as compared to decrease conditions cannot be revealed. The reason for this is that voxel clusters modulated by up- or down-regulation of emotion do not overlap. Thus, for example, amygdala regions showing diminished activation when down-regulating (as identified in the decrease–look contrast) will not show up in the increase–decrease contrast because those down-regulated voxels are not also up-regulated in the increase–look contrast, which was used as a mask for that increase–decrease comparison.

Modulation by reappraisal. Small-volume corrected analyses were used to test the hypothesis that amygdala activation should be up-regulated (increase > look) when increasing negative emotion and down-regulated (look > decrease) when decreasing negative emotion (Fig. 4; Tables 1 and 3). For the increase > look contrast, significantly activated voxels were identified in the left amygdala at a slightly liberalized two-tailed threshold ($P < 0.09$ corrected, $P < 0.006$ uncorrected), which may be justified given a priori interest in the amygdala's role in reappraisal and our

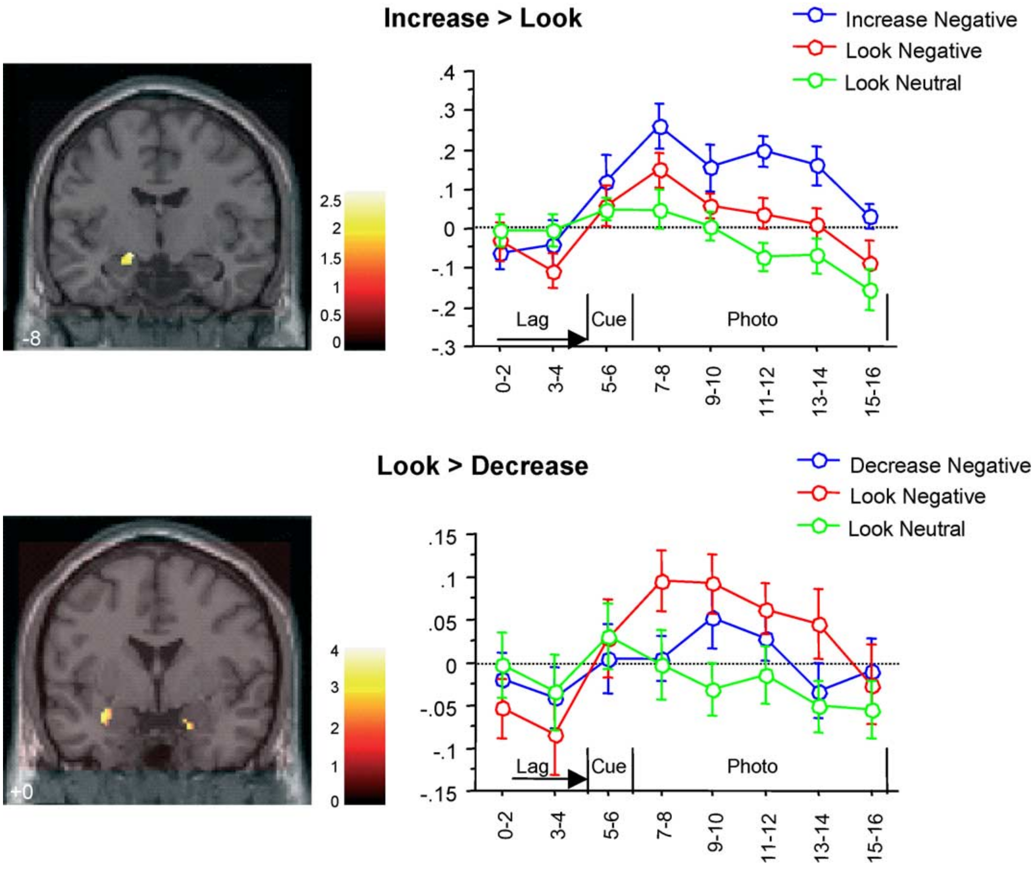

Fig. 4. Left panels show amygdala activation from group contrasts, whereas right panels show percent signal change activation time courses for the left amygdala peak voxel from each contrast. Time courses begin at the onset of a trial. With a 4- to 6-s hemodynamic response lag, and an initial 2- s instruction cue, modulation due to reappraisal may first be observed 6–8 s after trial onset, as shown in the portion of the time course corresponding to the photo presentation period, as indicated in the figure. Top panel shows left amygdala voxels active in the increase > look contrast, and bottom panel shows left and right amygdala voxels active in the look > decrease contrast, which respectively reflect up- and down-regulation of amygdala activity due to reappraisal. Time courses for peak voxels show significant modulation when increasing or decreasing negative emotion 6–8 s after trial onset, which may reflect up- or down-regulation of amygdala activity within the first 2 s that participants attempted to reappraise a photo. Activation time course for look trials with neutral photos is shown for comparison.

specific one-tailed prediction that amygdala activation should be greater on increase trials ($P < 0.09$ for a two-tailed comparison corresponds to $P < 0.045$ for a one-tailed comparison). Significant modulation of the right amygdala was not observed when increasing (P corrected < 0.18, $P < 0.01$ uncorrected). For the look > decrease contrast, downward modulation was significant for the left ($P < 0.007$ corrected, $P < 0.001$ uncorrected) and marginally significant for the right (two-tailed: $P < 0.087$ corrected, $P < 0.006$ uncorrected) amygdala. An additional emotion-processing region, bilateral insular cortex, was modulated when decreasing (Table 3).

To further characterize reappraisal-related amygdala modulations, activation time courses for the left amygdala peak activated voxels were extracted for each contrast. As shown in Fig. 4, up- or down-modulation of the amygdala began at the onset of the photo presentation period, and that increased or decreased amygdala activation was maintained while participants actively reappraised their emotion until the photo disappeared. T tests contrasting levels of percent signal change were used to confirm that reappraisal significantly up- or down-regulated amygdala activation. Activation was greater on increase as compared to look trials with negative stimuli for each 2-s TR during the photo presentation period when participants actively reappraised their emotional response [from 7–8 to 15–16 s, all one-tailed $t(22) > 2.00$, $P < 0.05$]. Activation was most significantly diminished on decrease as compared to look trials with negative stimuli at the beginning and at the end of the photo presentation period [for 7–8 and 13–14 s TRs, one-tailed $t(22) > 2.4$, $P < 0.05$; for 9–10 and 11–12 s TRs, $t(22) > 1.60$, $P < 0.12$; for 15–16 s TR, $t(22) < 1$].

Affect-activation relations. To determine whether and how activation in reappraisal-related regions predicted reappraisal-related affect change, correlational analyses were conducted that related self-reported increases (increase–look affect difference) or decreases (look–decrease affect difference) to a measure of activation (Beta values obtained from the SPM model fit for the photo presentation period on each trial type for each region of interest) in either the activated amygdala clusters listed in Tables 2 and 3 or in the increase- and decrease-specific prefrontal regions listed in Table 4. Increases in negative affect when up-regulating emotion did not significantly correlate with activation in the amygdala or in increase-specific prefrontal or cingulate regions. By contrast, decreases in negative affect when down-regulating emotion significantly correlated with decreases in both left

Table 3
Group activations for look > decrease contrast

Region of activation	Brodmann	Coordinates			Z score	Volume (mm^3)
		x	*y*	*z*		
Insula	L6/13/44	−48	−4	10	4.58	624
Insula	L13	−38	−26	18	3.78	528
Insula	L13	−40	−16	14	3.49	(L)
Insula	R13	44	−14	20	4.06	456
Insula	R13	40	0	16	3.45	64
Inferior parietal lobule	L40	−58	−24	22	3.34	88
Inferior parietal lobule	R40	50	−30	30	3.53	248
Inferior parietal lobule	R40	38	−58	44	3.44	144
Precuneus	R	24	−60	30	3.49	112
Amygdala*	L	−30	−2	−20	3.50	592
Amygdala*	L	−28	−4	−14	2.98	(L)
Amygdala**	R	20	0	−24	2.50	64

Note. Clusters of five or more contiguous voxels whose global maxima meet a *t* threshold of 3.50, $P < 0.001$ uncorrected, are reported. Local maxima for these clusters are denoted with (L). Coordinates are in MNI space.

* Small volume corrected, two-tailed $P < 0.007$ corrected, $P < 0.001$ uncorrected.

** Small volume corrected, two-tailed $P < 0.087$ corrected, $P < 0.006$ uncorrected.

amygdala ($r = 0.505$, $P < 0.01$) and right amygdala ($r = 0.504$, $P < 0.01$) activation, as well as increased activation in right orbitofrontal cortex ($r = -0.560$, $P < 0.005$). The reason for a failure to observe affect-activation correlations when increasing negative emotion may be related to an upper bound (or ceiling effect) on the amount that participants could increase their negative emotion above and beyond that already experienced during the look baseline condition. Because of a reduced range over which increases in negative affect could be observed, it may have been more difficult to observe correlations between restricted-range affect change scores and measures of change in brain activation. This hypothesis is supported by greater mean affect change and greater variability when decreasing ($M = 1.22$, SD = 0.88) as compared to increasing emotion [$M = 0.61$; SD = 0.43; $t(22) = 3.22$, $P < 0.01$].

The effects of specific types of cognitive emotion regulation strategies

To identify regions more activated when employing either a self- or situation-focused reappraisal strategy to increase or decrease emotion, two sample *t* tests compared activations between groups for all of the contrasts described above (Tables 5 and 6). These contrasts test for the interaction of strategy and type of reappraisal. For the increase > look contrast that identified regions involved in increasing emotion, no regions were more activated for the self-focused group; regions of temporal and parietal cortex were more activated for the situation-focused group (Table 5). For the decrease > look contrast that identified regions involved in decreasing emotion, the self-focused group showed more activation in right medial PFC, whereas the situation-focused group showed greater activation in both left and right lateral PFC (Table 6). Activation time courses for the peak voxel of representative medial and lateral right PFC regions are shown for the decrease–look contrast in Fig. 5. *T* tests contrasting percent signal change indicated (1) that only for the situation-focused group was left lateral frontal signal on decrease trials significantly greater than on

Table 4
Group activations for increase > decrease and decrease > increase contrasts

Region of activation	Brodmann	Coordinates			Z score	Volume (mm^3)
		x	*y*	*z*		
Increase > decrease						
Superior frontal gyrus	L9	−10	50	34	4.91	968
Superior frontal gyrus	L10	−4	64	32	3.75	136
Medial frontal gyrus	L10	−4	68	24	3.34	40
Posterior cingulate	L30	−8	−64	14	3.67	248
Posterior cingulate	L23	−6	−52	24	4.00	648
Posterior cingulate	L31	0	−62	24	3.47	(L)
Thalamus	L	−6	−12	10	3.26	88
Globus pallidus	R	18	−8	−2	3.41	56
Cerebellum	L	−18	−46	−16	3.83	672
Cerebellum	L	−14	−54	−18	3.76	(L)
Cerebellum	L	−8	−62	−18	3.50	(L)
Cerebellum	L	−4	−44	2	3.66	96
Decrease > increase						
Superior frontal gyrus	R8	16	26	56	4.86	3608
Superior frontal gyrus	R6	14	20	64	4.65	(L)
Superior frontal gyrus	R8	14	36	50	3.97	(L)
Middle frontal gyrus	R9	42	22	42	4.24	312
Inferior frontal gyrus	R44	56	12	16	4.27	384
Inferior frontal gyrus	R47	34	22	−18	3.23	40
Inferior parietal lobule	R40	64	−56	44	4.29	1592

Note. Clusters of five or more contiguous voxels whose global maxima meet a *t* threshold of 3.50, $P < 0.001$ uncorrected, are reported. Local maxima for these clusters are denoted with (L). Coordinates are in MNI space.

Table 5
Regions showing greater activation for the situation strategy group when increasing emotion

Region of activation	Brodmann	Coordinates			Z score	Volume (mm^3)
		x	*y*	*z*		
$\textit{Situation}_{(\textit{increase–look})} > \textit{self}_{(\textit{increase–look})}$						
Precentral gyrus	R3/4	14	−38	72	4.01	64
Middle temporal gyrus	L21	−64	−62	2	3.98	64
Middle temporal gyrus	R19	48	−86	16	3.58	416
Middle temporal gyrus	R19	54	−76	16	3.35	(L)
Superior occipital gyrus	R19	40	−86	22	3.13	(L)

Note. Clusters of five or more contiguous voxels whose global maxima meet a *t* threshold of 3.50, $P < 0.001$ uncorrected, are reported. Local maxima for these clusters are denoted with (L). Coordinates are in MNI space.

look trials during the photo presentation period in which participants down-regulated negative emotion [for 9–10 and 11–12 s TRs, one-tailed $t(22) > 2.60$, $P < 0.05$], and (2) that only for the self-focused group was right medial frontal signal significantly greater on decrease than on look trials [for 9–10, 11–12, and 13–14 s TRs, one-tailed $t(22) > 2.15$, $P < 0.05$; 15–16 s TR $t(22) = 1.93$, $P < 0.06$]. For the direct contrasts between increase and decrease trials that identified regions selectively involved in each type of reappraisal, neither group showed significantly greater activation relative to the other.

Discussion

Cognitive reappraisal was effective during the picture viewing paradigm such that participants significantly decreased negative

Table 6
Regions showing greater activation for the situation or self-strategy group when decreasing emotion

Region of activation	Brodmann	Coordinates			Z score	Volume (mm^3)
		x	*y*	*z*		
$\textit{Situation}_{(\textit{decrease–look})} > \textit{self}_{(\textit{decrease–look})}$						
Middle frontal gyrus	L10	−36	38	16	3.32	216
Inferior frontal gyrus	L45	−48	36	10	3.31	(L)
Middle frontal gyrus	R6	42	0	48	3.48	128
Middle frontal gyrus	R6	38	−8	62	3.46	80
Middle frontal gyrus	R46	56	30	30	3.75	168
Inferior frontal gyrus	L46	−50	30	18	3.90	360
Inferior frontal gyrus	L44	−52	6	22	3.47	168
Inferior frontal gyrus	R45	52	36	6	3.69	328
Precentral gyrus	L4	−28	−26	56	3.54	264
Precentral gyrus	L6	−38	−4	46	3.33	200
Superior temporal gyrus	L22	−60	−34	6	3.76	344
Superior temporal gyrus	L21/22	−66	−12	0	3.36	80
Inferior temporal gyrus	L37	−46	−64	−6	4.37	424
Inferior temporal gyrus	L19/37	−42	−74	−2	3.57	136
Supramarginal gyrus	L40	−58	−50	28	3.97	120
Cuneus	L	−24	−76	28	4.02	472
Middle occipital	L19	−26	−80	18	3.42	(L)
Cerebellum	L	−14	−70	−40	3.83	208
Cerebellum		0	−70	−26	3.78	864
Cerebellum	L	−10	−66	−26	3.40	(L)
Cerebellum	L	−30	−64	−40	3.55	88
Cerebellum	L	−22	−54	−36	3.45	112
Cerebellum	L	−16	−52	−28	3.44	296
Cerebellum	L	−12	−40	−26	3.26	(L)
Cerebellum	R	18	−44	−30	3.36	128
Cerebellum	R	10	−60	−28	3.32	128
$\textit{Self}_{(\textit{decrease–look})} > \textit{situation}_{(\textit{decrease–look})}$						
Cingulate gyrus	R32	6	30	−12	3.62	80
Inferior parietal gyrus	L40	−48	−66	50	3.34	64

Note. Clusters of five or more contiguous voxels whose global maxima meet a *t* threshold of 3.50, $P < 0.001$ uncorrected, are reported. Local maxima for these clusters are denoted with (L). Coordinates are in MNI space.

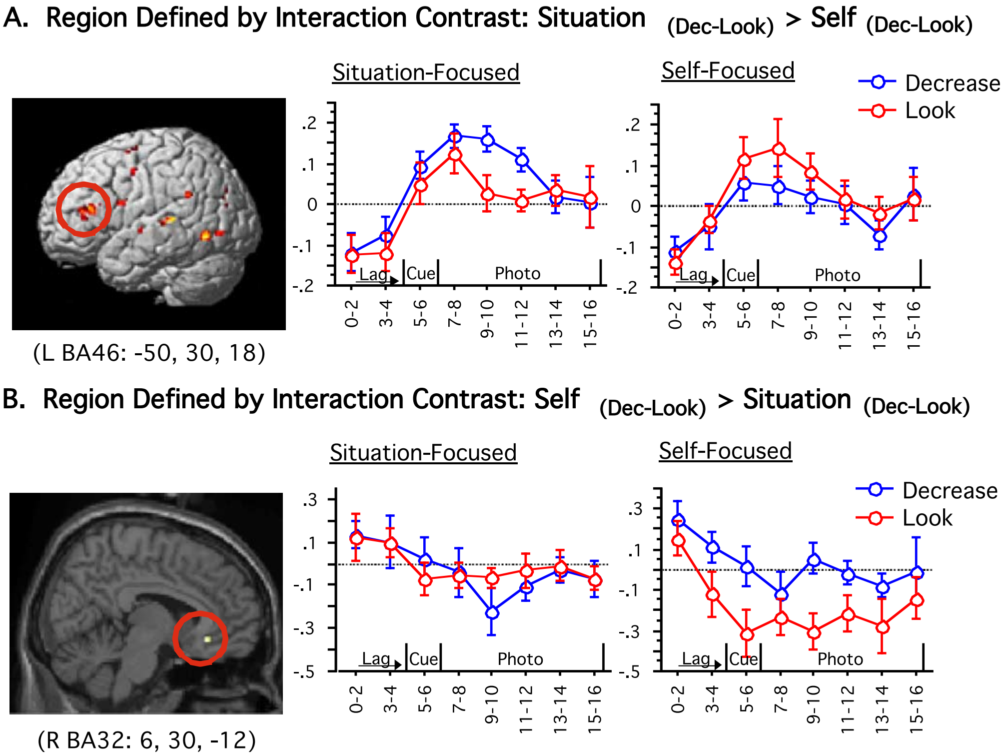

Fig. 5. Regions more active when using either a situation- or self-focused strategy to decrease emotion. Left panels show regions more engaged for the situation or self group when decreasing emotion. Center and right panels show percent signal change activation time courses for representative peak voxels from regions highlighted by the red circle in left panels. (A) Regions more active for the interaction contrast $\text{situation}_{(\text{decrease–look})} - \text{self}_{(\text{decrease–look})}$. Time courses show greater recruitment of this left lateral prefrontal region when decreasing negative emotion, but only for participants in the situation-focused group. (B) Regions more active for the interaction contrast $\text{self}_{(\text{decrease–look})} - \text{situation}_{(\text{decrease–look})}$. Time courses show greater recruitment of this right medial prefrontal region when decreasing negative emotion, but only for participants in the self-focused group. Inverted time courses for this medial prefrontal region are commonly observed (Gusnard and Raichle, 2001). Relative recruitment of lateral as compared to medial prefrontal regions by the situation- and self-focused reappraisal strategies suggests that these two strategies differ in their reliance on externally as compared to internally focused processes.

emotion when intentionally down-regulating emotional responses and significantly increased negative emotion when intentionally up-regulating emotional responses. Down-regulation was felt to be more difficult, which probably reflects the greater challenge in reversing, rather than enhancing, the initial emotional response to an aversive scene. Self- and situation-focused reappraisal strategies were equally effective. This is the first imaging study to examine both the cognitive and up- and down-regulation of emotion, which allows for consideration of the common and distinct neural systems involved in each kind of emotion regulation. This is also the first imaging study to systematically vary reappraisal strategy, which allowed for analysis of the neural systems involved specifically in self- versus situation-focused reappraisal.

Up- versus down-regulation of emotion

Up- and down-regulation of negative emotion involved both neural systems that were similarly activated and other systems that were selectively activated for one or the other kind of regulation. Both up- and down-regulating emotion (1) activated regions of left lateral prefrontal cortex implicated in working memory and cognitive control (Knight et al., 1999; Miller and Cohen, 2001; Smith and Jonides, 1999) that may support the generation and maintenance of reappraisal strategies, (2) activated regions of the dorsal anterior cingulate implicated in the on-line monitoring of performance (Botvinick et al., 2001; Ochsner and Feldmann Barrett, 2002), (3) activated regions of dorsal medial prefrontal cortex implicated in self-monitoring and self-evaluation of emotion (Gusnard et al., 2001; Lane et al., 1997; Ochsner and Gross, 2004; Simpson et al., 2001), and (4) modulated activation of the left amygdala, selectively decreasing or increasing its activation, respectively.

Although amygdala activation was modulated for both up- and down-regulation, the lateralization of these activations differed in the two conditions: whereas up-regulation increased activation in the left amygdala, down-regulation decreased activation bilaterally, albeit more significantly of the left side. Although the precise functional significance of lateralized amygdala activations (in general) is not clear, there are indications that the left amygdala may be associated with processing of and memory for affectively charged verbal stimuli (Buchanan et al., 2001; Hamann and Mao, 2002; Strange et al., 2000), the mental representation of an event that is eliciting fear (Phelps et al., 2001), and the induction of sad moods through verbal scripts (Schneider et al., 1997). Taken together, these data suggest that common modulation of the left amygdala by the up- and down-regulation of emotion may reflect the use of verbal strategies that can influence affective encoding in the amygdala. By contrast, modulation of the right amygdala during down-regulation may reflect the modulation of processes related to encoding the affective or arousing properties of nonverbal stimuli, as evidenced by right amygdala activation to film clips (Beauregard et al., 2001), the acquisition of classically conditioned responses (Furmark et al., 1997), and presentation of emotional facial expressions (Anderson et al., 2003).

The limited temporal resolution of fMRI also prevents a precise evaluation of the temporal dynamics of amygdala modulation. This study revealed amygdala modulations starting as early as the first 2-s epoch of reappraisal, but it is possible that faster-acting (and perhaps automatic) amygdala processes not detectable with this study's 2-s temporal resolution remained unaffected by the reappraisal process. Future studies employing a shorter TR and/or combined electrophysiological recording may serve to address this issue.

Up- and down-regulation also selectively recruited distinct regions of left rostral medial prefrontal and posterior cingulate cortex and right lateral or orbital prefrontal cortex, respectively. The reliance of up-regulation on left rostral medial and posterior cingulate cortices could reflect the role of these regions in generating words that describe emotional events (Crosson et al., 1999), which participants did when thinking about aversive scenes as even more affecting, horrific, sad, or shocking. In this way, emotion knowledge may be retrieved to add cognitive insult to the physical injuries depicted in photos.

The reliance of down-regulation on right lateral PFC could reflect the broad role of this region in behavioral inhibition and interference resolution (Bunge et al., 2001; Jonides et al., 1998), both of which are required when attempting to supplant negative stimulus appraisals with neutralizing top–down reappraisals. The reliance of down-regulation on right orbitofrontal cortex could reflect the role of this region in altering and updating the context-sensitive motivational relevance of stimuli (Bechara et al., 2000; Ochsner et al., 2001; Rolls, 2000). Reversal of stimulus-reward mappings activates lateral orbitofrontal cortex (O'Doherty et al., 2003) and is impaired by lateral OFC lesions (Dias et al., 1997; Rolls, 2000), which is consistent with the idea that reappraisal can cognitively reverse the aversive connotations of a stimulus. Altering the affective value of a stimulus may depend critically upon representation of an event in orbitofrontal cortex and amygdala (Rolls, 2000), as suggested by significant correlations between increased activation of right orbitofrontal cortex, decreased bilateral amygdala activation, and decreases in negative affect when down-regulating emotion.

The fact that prefrontal activation reflecting overlap of processes related to up- and down-regulation was proportionally greater than that uniquely associated with each type of regulatory goal may reflect the degree of overlap in underlying processes—that is, regardless of the reappraisal goal, cognitively reframing an affective event may draw most heavily upon strategic verbal and visuospatial processes used to construct reappraisal narratives. To the extent that up- and down-regulation recruit processes specifically associated with elaborating the affective properties of the stimulus as compared to mediating interference between competing appraisals and reappraisals, additional prefrontal control systems are recruited.

These findings replicate and extend our initial findings concerning the use of reappraisal to down-regulate negative emotion (Ochsner et al., 2002). In that study, we observed only left PFC involvement and no lateral orbitofrontal activation when decreasing negative emotion and modulating amygdala activation. The present study may have had substantially greater power to detect reappraisal-related activations and hence may have detected bilateral and orbital PFC involvement in the cognitive down-regulation of emotion. Sources of greater power may include (1) the use of 23 as compared to 15 participants, (2) the use of a spiral in–out as compared to spiral out pulse sequence that is more sensitive to detecting activation in prefrontal cortex and other regions (Glover and Law, 2001; Preston et al., 2004), and (3) more rigorous and extensive prescan training in reappraisal. Consistent with this argument, when the height threshold for the decrease–attend contrast from our prior study was lowered to 0.05, a bilateral pattern of activation is observed that very closely resembles the pattern observed in the present decrease–look contrast at a 0.001 threshold. One other difference between the results of the two studies may have been attributable to a change in instructions in the baseline condition. In the initial study but not in the present one, we observed modulation of medial orbitofrontal cortex by reappraisal, as revealed by greater activation in an attend baseline condition than in a reappraisal condition in which participants decreased negative emotion. This difference may be due to the fact that in the present study, we asked participants to look at images and respond naturally; whereas in the initial study, we specifically instructed participants to attend to their feelings. Selective attention can enhance processing (Culham and Kanwisher, 2001), which may have led to greater medial orbital frontal activation relative to the present study.

Taken together, past and present findings are consistent with the hypothesis that reappraisal involves interactions between prefrontal systems that implement cognitive control processes and systems that appraise the affective properties of stimuli, such as the amygdala.

Self- versus situation-focused reappraisal

Self-focused reappraisals, which modified the personal relevance for a given image, and situation-focused reappraisal, which reinterpreted the actions and outcomes for a given image, had two notable similarities: similar success in modulating emotion, and common activation of many of the prefrontal and amygdala systems described above.

These two strategies did differ in their relative reliance on medial as compared to lateral prefrontal cortex, however, but only when down-regulating emotion. Self-focused reappraisal differentially recruited medial PFC when decreasing emotion. This medial PFC region, corresponding to BA 32, has been associated with self-referential judgments (e.g., Kelley et al., 2002), and more generally with processes thought to reflect a default self-monitoring state of brain activation (Gusnard et al., 2001). When adopting a detached and distanced perspective, participants may have continuously monitored the self-relevance of aversive scenes to ensure that they were remaining distant from them. On the other hand, situation-focused reappraisal differentially recruited regions of lateral PFC generally implicated in the maintenance and manipulation of information about stimuli in the external world (D'Esposito et al., 2000). A similar pattern of differential medial versus lateral prefrontal recruitment has been observed when participants either judged the valence of their own emotional response to a photo or judged the valence of the emotion expressed by the central figure depicted in those photos (Ochsner et al., 2004). Taken together, these findings support the hypothesis that beyond their common reliance on a core network of reappraisal-related systems, self- and situation-focused reappraisal strategies depend upon neural systems generally involved in internally focused as compared to externally focused processing, respectively (Christoff et al., in press).

The absence of differential medial or lateral PFC activation during up-regulation may be the result of task instructions, which unexpectedly may have diminished differences between the self- and situation-focused strategies. Participants in the self-focused reappraisal group were informed that they could increase emotion by imagining either themselves or a loved one involved taking part in, or associated with, pictured events. This may have diminished reliance on self-reflective processing, as suggested by prior studies showing medial PFC activation only for self, but not close-other, related judgments (Wyland et al., 2003). Furthermore, it is possible that imagining increased self-involvement with complex events recruits lateral prefrontal systems mediating attention to, and elaboration of, aspects of those events (as when imagining what it would be like to be a sick person lying in a hospital bed, for example) very much like the processes recruited by situation-focused reappraisal.

Nature of reappraisal-related dynamics

Although the present study provides some initial answers to questions concerning the nature of neural mechanisms underlying the up- and down-regulation of emotion, it raises a number of questions as well.

One question is why down-regulation recruited both left and right PFC, whereas up-regulation recruited primarily left-lateralized systems. One possibility is that this difference is due to down-regulation being more effortful and therefore recruiting bilateral as compared to unilateral prefrontal regions. This explanation is unlikely, however, because multiple regions were more active when increasing than when decreasing, which should not have been observed if effort alone was driving observed prefrontal activations A second possibility is that the observed findings reflect differences in the amount of negative affect experienced when increasing as compared to decreasing emotion. This explanation also appears unlikely, however, because greater left PFC activation was observed as negative emotion increases, and greater right PFC activation was observed when emotion decreases, which is exactly the opposite of what would be expected based on prior work associating positive emotion with left, and negative emotion with right, PFC (e.g., Canli et al., 1998; Davidson, 2000). A third possibility, and one that we advanced above, is that differential PFC activation when up- and down-regulating emotions reflect the recruitment of cognitive processes specifically related to each regulatory goal: Up-regulating negative emotion may recruit left PFC systems used to self-generate affective descriptors that intensify emotion, whereas down-regulating negative emotion may recruit right PFC systems used to mediate interference between competing prepotent affective responses and cognitively controlled reappraisals.

A second question concerns the active role that prefrontal control processes play in modulating amygdala activation. Various researchers have proposed a reciprocal relationship between cognitive and emotional processes. Some have suggested that deactivation of emotion systems is an indirect byproduct of most any type of cognitive processing (Drevets and Raichle, 1998; Mayberg et al., 1999), whereas others suggest that the relationship is more specific, occurring only when linguistic processes are used to label affective stimuli (Lieberman, 2003). A similar view is that reappraisal is simply a form of distraction and disrupts emotion processing in much the same way that any secondary task disrupts a primary task (McRae et al., 2002). On these views, the down-regulation of emotion via reappraisal occurs not because one has actively transformed the meaning of a stimulus, but simply because one has engaged in effortful cognitive processing that either draws resources away from, or is wired up to disrupt (Lieberman, 2003), emotion processing. The present results challenge these views, however, because none can account for the fact that the effortful cognitive processing engaged when one is attempting to up-regulate negative emotion not only makes one feel worse, but also increases amygdala activity. This finding should not have been observed if emotion processing is inhibited simply by engaging in any type of cognitive processing or is disrupted only when labeling emotional states and stimuli, which our participants did when up-regulating emotion.

In our view, the most likely explanation for the present results is that the active mental transformation of the meaning of an event is responsible for up- or down-regulating amygdala activity, a conclusion that is supported by the finding of prefrontal–amygdala interactions underlying other recent studies examining reappraisal (Beauregard et al., 2001; Levesque et al., 2003) or the use of cognitive control to maintain, if not necessarily transform, an emotional response (Schaefer et al., 2002). This is not to say that various types and applications of attention, cognitive load, or evaluative judgments might not modulate emotion processing (cf. Schaefer et al., 2003). Indeed, in the long term, it will be important to relate the mechanisms underlying reappraisal to the mechanisms underlying other ways in which cognition can regulate emotion.

Unfortunately, however, clarifying these relationships currently is difficult because results have been mixed from studies examining modulation of amygdala activation to fearful or threatening faces or images under conditions of full as compared to divided attention, or when directly as compared to indirectly evaluating the affective properties of these stimuli. Some studies show amygdala modulation (Hariri et al., 2000; Liberzon et al., 2000; Pessoa et al., 2002; Phan et al., 2003) and others show the amygdala response is invariant with respect to these manipulations (Anderson et al., 2003; Critchley et al., 2000; Vuilleumier et al., 2001; Winston et al., 2002). Although the precise reasons for these discrepancies are not clear, one possibility is that instructions in some cases may induce participants to reappraise the meaning of stimuli.

A third question concerns the importance to reappraisal of other cortical, subcortical, and cerebellar regions activated when increasing or decreasing emotion. Modulation of inferior parietal, occipital, and temporal cortices may reflect attentional selection of cognitively reorganized perceptual inputs held in working memory during reappraisal (Cabeza and Nyberg, 2000; Culham and Kanwisher, 2001; Smith and Jonides, 1999). Modulation of thalamus and various portions of the basal ganglia may reflect the recruitment of cognitive control circuitry that links prefrontal regions to subcortical structures in functional loops (Alexander et al., 1986). Modulation of cerebellum may reflect recruitment of circuitry important for the accurate selection and timing of linguistic and cognitive operations supporting the narrative reframes used when reappraising (Fiez, 1996; Prabhakaran et al., 2000) and is consistent with numerous studies showing cerebellum activation during emotion (e.g., Lane et al., 1997; Paradiso et al., 1999; Reiman et al., 1997).

Implications and future directions

The present findings have important implications for the design of neuroimaging studies of emotion. Given that the specific prefrontal systems engaged by reappraisal, and the nature of amygdala modulations reappraisal causes, both may vary systematically as a function of goal and strategy, studies should systematically control the way in which stimuli are appraised and reappraised in order to draw inferences about the relationship of prefrontal and amygdala activation to emotion. For studies that allow participants to freely experience photos, films, or memories, there is no way to know whether prefrontal and amygdala activations vary because participants spontaneously appraised or reappraised stimuli in different ways (Ochsner and Feldmann Barrett, 2002).

The present findings also have implications for the study of interindividual variability in emotion and emotion regulatory capacity. Future studies may identify individual differences in the tendency to experience negative emotion, and the ability to control it, that systematically influence the specific reappraisal-related systems identified here. Development, aging, and the presence of depression and anxiety thus may influence the way in which emotion systems generate responses and the efficacy with which reappraisal systems modulate them (Davidson, 2000; Mather et al., 2004), leading either to deficits in the ability to make one's self feel better by down-regulating negative emotion or to improved ability to make one's self feel worse by up-regulating negative emotion (for a discussion, see Ochsner and Gross, 2004).

Acknowledgments

The authors thank Janet Eckart, Ambili Ramachandran, and Karen Milch for assistance with data collection and analysis, a NARSAD Young Investigator grant to the first author, National Science Foundation grant BCS-93679, and National Institute of Health grants MH58147 and MH066957 for support of this research.

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