Remembering the good times: neural correlates of affect regulation

Rebecca E. Cooney[a], Jutta Joormann[b], Lauren Y. Atlas[a], Fanny Eugène[a] and Ian H. Gotlib[a]

[a]Department of Psychology, Stanford University, Stanford, California, USA and [b]Department of Psychology, University of Miami, Coral Gables, Florida, USA

Correspondence to Rebecca E. Cooney, Department of Psychology, Building 420, Jordan Hall, Stanford University, Stanford, CA 94305, USA
Tel: + 1 415 285 3502; fax: + 1 650 725 5699; e-mail: rcooney@psych.stanford.edu

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The ability to regulate one's mood state effectively is critical to emotional and physical health. Recent investigations have sought to delineate the neural mechanisms by which individuals regulate mood states and emotions, positing a critical role of a dorsal system that includes the dorsolateral prefrontal cortex and anterior cingulate. This study extended these efforts by examining the neural correlates of retrieving positive autobiographical memories while experiencing a negative mood state in a sample of healthy female adults. We demonstrated that mood-incongruent recall is associated with activation in ventrolateral and ventromedial prefrontal cortices (including orbitofrontal cortex and subgenual cingulate). These findings suggest that mood-incongruent recall differs from other affect regulation strategies by influencing mood through a ventral regulatory network. *NeuroReport* 18:1771–1774

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Introduction

A growing literature attests to the importance of successful emotion regulation for physical and mental health [1]; we know little, however, about the mechanisms that underlie recovery from negative mood states and emotions. Although investigators have identified strategies that people commonly use to regulate negative emotions and are examining how and why these strategies work [2], few researchers have assessed patterns of brain activation related to the process of recovery from negative affect.

Scientists examining the neural correlates of sad mood have found activations in the medial prefrontal cortex and temporal lobes, and in the subgenual anterior cingulate cortex (Brodmann Area 25), which has been postulated to play a critical role in the experience and modulation of sad mood [3]. The few studies that have examined the regulation of negative affect have focused on the neural correlates of reappraisal [4] and suppression [5,6]. In general, these studies have implicated a top-down modulation of ventral and limbic structures by dorsal brain regions, such as the dorsolateral prefrontal cortex, in the successful regulation of affect [7]. In addition, investigators have found ventromedial and ventrolateral areas, including the orbitofrontal cortex (BA 11), subgenual anterior cingulate cortex (BA 25, 32), and BA 10, to be associated with the generation and regulation of emotion [8]. Consequently, researchers have suggested that different emotion regulatory strategies recruit different brain regions [7].

Investigators have found that people recall mood-incongruent memories when they are experiencing a negative mood [9], and that recalling positive memories reduces negative affect [2,10]; the mechanisms underlying the mood-enhancing quality of this strategy, however, are not known. This study was designed to examine the neural correlates of both the induction of a sad mood state and the recall of positive autobiographical memories while experiencing sad mood. As mood-incongruent recall is not a direct attempt to change the negative mood state, we expected less involvement of dorsal brain regions in the use of this strategy. Instead, we hypothesized that recalling positive autobiographical memories while experiencing negative mood generates mood-incongruent thoughts and, therefore, a novel and more positive mood state. On the basis of results of studies of neural aspects of autobiographical memory (e.g. [11]), we expected mood-incongruent autobiographical recall to recruit more ventral structures, including the ventromedial prefrontal cortex, specifically in the orbitofrontal cortex and in the rostral and subgenual anterior cingulate cortex.

Method

Participants

Fourteen female participants were recruited from the community through an electronic message board. Only women were recruited because of sex differences in neural activation during the experience of sadness [12] and during retrieval of autobiographical memories [13]. Participants were between the ages of 18 and 60 years (mean age=33.5, SD=12.34), were fluent in English, had completed at least some college, and had no head trauma or brain injury.

Procedure

Mood-repair task

A 1-min baseline scan was conducted while participants focused on a fixation cross. Participants then saw a screen with a text prompt that remained on for 1 min asking them

to recall a happy, positive memory from their high school years (positive recall 1; PR1). They then viewed a sad film clip of a young girl dying of cancer (4 min). Before watching the clip, participants were instructed via audiotaped instructions to get into the feeling of the movie as intensely as possible and to imagine how they would feel if they were in this situation. After they watched the film clip, they heard audiotaped instructions asking them to focus on their feelings (2 min). Participants then saw a screen with a text prompt for 1 min asking them to elaborate their sad mood by 'really getting into the feeling' generated by the sad film clip (mood elaboration, ME). They then received a text prompt to recall a second positive memory for 1 min (positive recall 2; PR2). During each 1-min scan with a text prompt (PR1, ME, and PR2), the prompt remained on the screen. Participants rated their mood on a 4-point visual analog scale (1=very sad–4=very happy) before and after each scan. Four scans were collected: baseline, PR1, ME, and PR2. Participants then described the memories they had recalled in the scanner.

Functional MRI data acquisition and analysis

Scans were conducted on a 1.5T GE Signa scanner (GE, General Electric, General Electric, Fairfield, Connecticut, USA). Functional images were acquired using a T2* in-/out-spiral pulse sequence (TE=40 ms, flip=90) [14] consisting of 24 4-mm interleaved slices acquired axially (in-plane resolution 3.75×3.75 mm, no gap) at a temporal resolution of 2 s (2.00 TR). High-resolution structural scans were collected using a T1-weighted spoiled grass (TR=100 ms; TE=7 ms, flip=90) sequence.

All preprocessing and analyses were performed with Analysis of Functional Neuro Images (AFNI) [15]. Voxel time series data were concatenated, slice time corrected, and corrected for motion, excluding participants who moved more than 1.5 mm. Data were spatially smoothed with a 4 mm Gaussian smoothing kernel, and high-pass filtered. Before analysis, functional images were coregistered to anatomical images.

The preprocessed time series data for each participant were analyzed with multiple regression. Four contrast vectors were created: ME vs. baseline, PR1 vs. baseline, PR1 vs. PR2, and PR2 vs. baseline. Models included regressors for each contrast vector and included terms for residual motion and trend regressors. Resulting individual participant *t*-statistic maps were transformed into *z*-scores and warped into Talaraich space. We computed a group map thresholded at $P=0.0001$ with a spatial extent of greater than 8 contiguous voxels.

Results

Mood ratings

Participants' transcribed memories were rated by two independent raters on a 10-point scale with respect to how happy the recalled event would be for an average person. The interrater agreement was $r=0.68$ for the first memory and $r=0.71$ for the second memory. The two memories recalled by the participants did not differ in their average happiness ratings [$M=7.00$, SD=1.08; $M=6.60$, SD=0.69, $t(11) < 1$]. Mood ratings were obtained from participants in the scanner at baseline, after PR1, after ME, and after PR2. A one-way repeated-measures analysis of variance yielded a significant main effect for time, $F(3,39)=43.33$, $P<0.01$. Follow-up paired *t*-tests indicate that participants' mood ratings increased from baseline to recalling the first positive autobiographical memory, $t(13)=2.48$, $P<0.05$, decreased after the negative ME, $t(13)=7.77$, $P<0.01$, and increased again after recalling the second positive autobiographical memory, $t(13)=8.04$, $P<0.01$, indicating that the sad mood induction was successful and that recalling positive memories improved participants' mood state.

Functional MRI contrasts

Sad mood elaboration

To identify brain regions involved in the generation and elaboration of the sad mood induced by the film clip, we contrasted the ME scan with the baseline scan (Fig. 1). Table 1 (a) shows extensive activations in both anteromedial and lateral sections of orbitofrontal cortex, extending bilaterally through the inferior frontal gyrus (BA 47) and orbitofrontal cortex (BA 11) into the putamen and nucleus accumbens. Activations were also found in right posterior parahippocampal gyrus and superior temporal gyrus (BA 22).

Mood regulation

We examined two contrasts designed to assess the neural substrates associated with the use of mood-incongruent autobiographical recall to regulate a sad mood. The first contrast (PR2 vs. baseline) was designed to yield activations associated with recall of positive autobiographical memories following a sad mood induction. This contrast (Table 1 (b); Fig. 2A) yielded activations in the left superior frontal gyrus (BA 10), left middle frontal gyrus (BA 10), and orbitofrontal cortex (BA 11). Although encouraging, this contrast cannot differentiate activation associated generally with the recall of positive memories from activation specific to mood-incongruent autobiographical recall. Thus, the second contrast (PR2 vs. PR1) was designed to yield neural activations unique to the recall of 'mood-incongruent' positive autobiographical memory (i.e. structures that are differentially active during recall of a positive autobiographical memory while in a sad mood). Activations during this contrast are listed in Table 1 (c) and depicted in Fig. 2B, with loci in the ventromedial prefrontal cortex that included bilateral and contiguous activation extending from a region of posterior

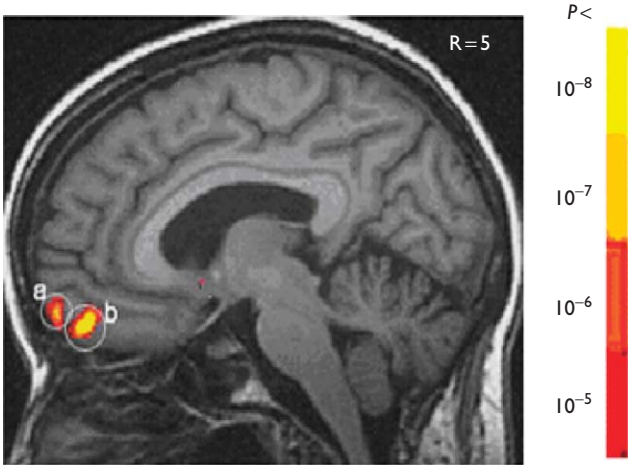

Fig. 1 Mood elaboration. Mood elaboration vs. baseline. Activations in (a) right medial frontal gyrus/BA10 (5,60, −14; $Z=4.86$) and (b) right orbital gyrus/BA11 (6,52, −19; $Z=6.85$).

Table 1 Areas of increased activation in response to contrasts of interest

Region/BA	Vox.	*x*	*y*	*z*	Max *Z*
(a) Mood elaboration (mood elaboration > baseline)					
L. putamen	65	−19	11	−7	6.08
R. superior temporal gyrus (22)	44	53	11	−3	5.64
R. orbitofrontal cortex (11)	26	30	38	−14	5.69
R. medial prefrontal cortex/ orbitofrontal cortex (10/11)	22	8	53	−18	6.85
R. parahippocampus	20	23	−11	−18	6.21
L. inferior frontal gyrus (47)	14	−49	26	−3	5.49
(b) Mood incongruent recall (positive recall 2 > baseline)					
L. superior frontal gyrus (10)	18	−19	71	−7	5.29
L. medial frontal gyrus (10)	11	−41	49	−7	5.20
L. orbitofrontal cortex (11)	9	−15	30	−14	5.03
(c) Mood regulation (positive recall 2 > positive recall 1)					
L. subgenual cingulated cortex (25)	38	−8	15	−18	6.12
R. subgenual cingulated cortex (25)	25	8	15	−18	5.15
L. fusiform gyrus (20/36)	17	−38	−34	−14	5.93
R. fusiform gyrus (20)	15	45	−30	−14	5.60
L. inferior frontal gyrus (47)	11	−41	26	−11	5.71
R. orbitofrontal cortex (11)	9	26	34	−14	5.63
L. anterior cingulated cortex (32)	9	−8	34	−11	4.42

Activations reported (extent > 8), P=0.0001, uncorrected.
BA, Brodmann's area; L, left; R, right; Vox., number of activated voxels within a cluster. Coordinates in Talaraich and Tournoux space. Max *Z* indicates *z*-score at the peak activation of each loci.

orbitofrontal cortex to subgenual anterior cingulate (BAs 25, 32), activation along the fusiform gyrus extending posterior from BA 20 and BA 36, and anterior prefrontal cortical activation in left inferior frontal gyrus (BA 47).

Discussion

This study investigated neural aspects of the instantiation of sad mood and of the use of mood-incongruent autobiographical memory to regulate that mood. Consistent with results of behavioral studies [2,10], viewing a sad film clip and being instructed to elaborate the resultant sad mood significantly worsened participants' mood state; subsequently recalling a positive autobiographical memory significantly improved the sad mood. We also found that the induction and elaboration of a sad mood state were associated with increased neural responding in the orbitofrontal cortex, a region that has been found to be active during the experience of sadness in studies using a range of experimental paradigms, such as viewing sad films without elaboration instructions [16] and guided imagery/visualization [17]. In addition to orbitofrontal cortex, we found the experience of a sad mood state to be associated with increased activation in ventral striatal areas, replicating previous work [18].

The primary goal of this study, however, was to extend this research by assessing the neural correlates of mood-incongruent autobiographical recall in the service of recovery from a sad mood state. We hypothesized that, in contrast to previously studied strategies such as reappraisal or suppression, the regulation strategy of mood-incongruent autobiographical recall would be associated with activations in more ventral regions of the emotion processing circuit of the brain, specifically in the ventromedial prefrontal cortex. In the first contrast (PR2 vs. baseline), we found activation in the orbitofrontal cortex, and also in ventrolateral prefrontal cortex (including BA 10 and BA 47); we did not find increased activation in dorsolateral prefrontal cortex.

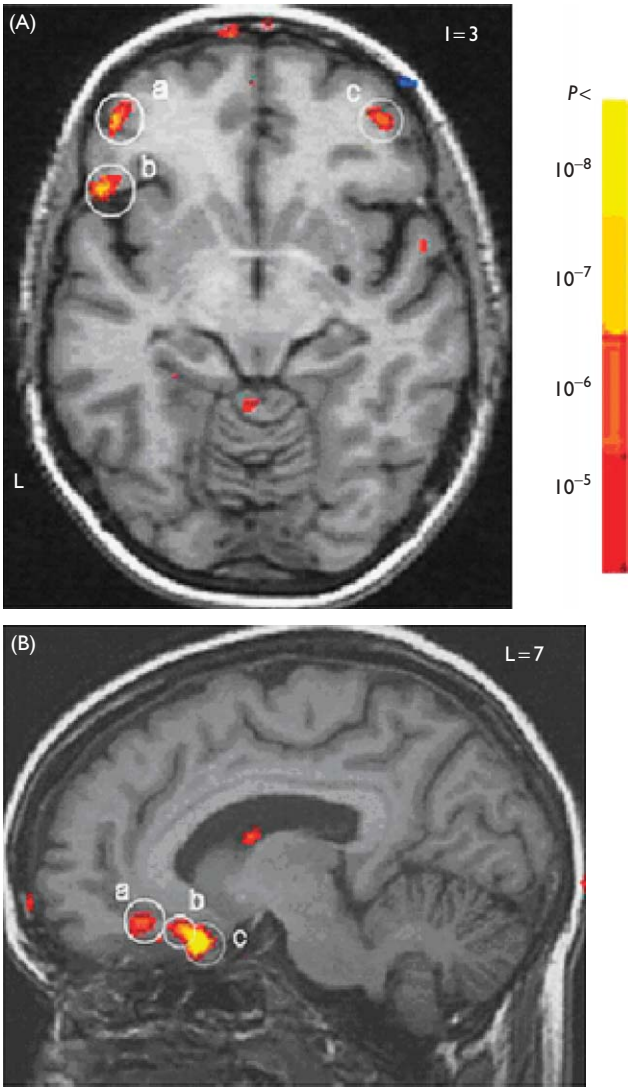

Fig. 2 Mood regulation. (A) Positive recall two vs. baseline. VLPFC activations centered at (a) left middle frontal gyrus/BA11 (−45, 42, −3; Z=5.03); (b) left inferior frontal gyrus/ BA47 (−50, 20, −1; Z=5.46); and (c) right middle frontal gyrus/BA11 (42, 42, −1; Z=5.22). (B) Positive recall 2 vs. positive recall 1. Activations centered at (a) left anterior cingulate/ BA32 (−7,34,−10; Z=4.42); (b) left subgenual cingulate cortex/BA25 (−7, 20, −13; Z=5.33), and (c) left subgenual cingulate cortex/BA25 (−7, 14, −18; Z=6.12).

Although earlier studies have focused primarily on the role of dorsal regions in regulating more ventral, emotion generating, brain areas, it is important to note that the ventral regions of prefrontal cortex have been implicated in studies assessing the utilization of affect regulation strategies [4,6].

The second contrast (PR2 vs. PR1) was designed to distinguish neural activations during mood-incongruent positive autobiographical recall from activations during recall of a positive autobiographical memory before a sad mood induction. In this analysis we found increased activation in orbitofrontal cortex and in two regions of the anterior cingulate cortex, BA 32 and BA 25, implicating the ventromedial prefrontal cortex in an emotion regulatory capacity. Interestingly, we found orbitofrontal cortex activation during both the experience of sad mood and the retrieval of positive memory. Orbitofrontal cortex activation

has been found not only to be associated with the experience of sadness, but further, to be recruited during both sad and happy emotional and autobiographical memory retrieval processes [11]. Moreover, studies explicitly examining emotional processing have found increased activation in this region in the suppression or reappraisal of negative affect [4–6]. It is important to note that the orbitofrontal cortex is highly interconnected with other regions that are involved in the processing of emotion, including the anterior cingulate cortex and both lateral and medial prefrontal cortex [19]. Indeed, it is possible that the flexible recruitment of the orbitofrontal cortex in the service of experiencing and regulating both negative and positive mood states is critical to healthy emotional functioning.

These results also suggest an important role of the ventromedial prefrontal cortex, and specifically of the subgenual cingulate, in regulating negative affect through mood-incongruent autobiographical recall. The ventromedial prefrontal cortex has been conceptualized as a seat of neural integration of cognitive and affective processes [20]. Investigators have found activation in the subgenual cingulate and adjacent structures during the experience of sadness in both healthy individuals and people diagnosed with major depression [3,21]. Interestingly, other studies of healthy participants have reported activation in the subgenual cingulate and associated areas during induced happiness [22,23]. Taken together, these findings suggest that the subgenual cingulate is important in regulating negative affect through the processing of mood-enhancing information.

Overall, our results indicate that regulating negative affect through mood-incongruent autobiographical recall recruits ventral brain regions, in particular orbitofrontal cortex and ventromedial prefrontal cortex, but not more dorsal areas, such as dorsolateral prefrontal cortex. The results suggest that whereas affect regulation through reappraisal and suppression is effortful and is associated with top-down regulation of ventral systems through dorsal brain regions like dorsolateral prefrontal cortex and dorsal anterior cingulate, regulation through mood-incongruent autobiographical recall is associated with more bottom-up activation of ventral brain regions like subgenual anterior cingulate cortex and orbitofrontal cortex. These results reinforce the position that affect can be regulated in different ways and, further, indicate that these various strategies are associated with distinct patterns of neural activation.

Conclusion

Successful affect regulation is critical to maintaining physical and mental health. The present results indicate that recalling positive autobiographical memories following induced sad mood recruits ventral brain regions, such as the subgenual anterior cingulate cortex and orbitofrontal cortex. This design can now be used to assess affect regulation in individuals with psychopathology and to interrogate disruptions in the network of structures that underlie emotion regulation.

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