Supplementary Material

Neural Activation During Reappraisal

Frontal Effects. We expected to replicate prior work in older adults by demonstrating that, relative to a maintain control condition, medial PFC regions including dorsal cingulate would be more active when increasing and decreasing negative emotion. As predicted, groupwise analyses revealed frontal clusters in bilateral dorsal medial frontal gyrus (MFG; BA 6; cluster #9 in Supplementary Table 1, includes portions of supplementary motor area), bilateral dorsal cingulate cortex (cluster #4), right middle and inferior frontal gyrus (cluster #8), and in bilateral subgenual anterior cingulate cortex (sACC; BA 25; cluster #5). Supplementary Figure 1 depicts these regions overlaid on an average high resolution anatomical scan. Increasing and decreasing negative emotion resulted in higher signal change than maintaining negative emotion in the medial frontal gyrus, dorsal cingulate gyrus, and subgenual PFC.

Published reports describing the neural circuits involved in voluntary emotion regulation have consistently implicated a number of different regions of prefrontal cortex (PFC) including lateral ventral, ventromedial, dorsomedial, and dorsolateral regions (Banks et al., 2007; Beauregard et al., 2001; Bechara, 2004; Eippert et al., 2007; Goldin et al., 2008; Harenski & Hamann, 2006; Johnstone et al., 2007; Kalisch et al., 2006; Kim & Hamann, 2007; Levesque et al., 2003; Ochsner et al., 2002; Ochsner et al., 2004; Ohira et al., 2006; Phan et al., 2005; Urry et al., 2006; van Reekum et al., 2007; Wager et al., 2008). In the current study, almost all frontal effects were exhibited in midline structures, including the sACC, dorsal cingulate gyrus, and left dMFG in the vicinity of the supplementary motor area. An exception would be the middle and inferior frontal effect, in which we observed signal deactivation that was greatest in the increase condition. Thus, we did not observe effects in which increasing and decreasing produced greater
activation than maintaining in lateral prefrontal cortex across the entire sample, effects one would expect given the cognitive demands of the task. We have previously conjectured that perhaps the age of the sample played a role in the absence of lateral PFC effects (see Supplemental Material for Urry et al., 2006 for a discussion of this issue), an argument that is applicable to this study too. Age comparisons will be an important next step, particularly since recent work indicates that there are age differences in emotion regulation ability (Phillips et al., 2008).

In addition to the possible contribution of aging, there are other factors governing the primarily medial effects we see in this study. One may be the use of a more active control condition in the present study, in which participants were instructed to maintain their emotional response. Previous studies used more passive control conditions involving simply attending to or viewing the pictures. The process of maintaining an emotional response likely draws on some of the same cognitive control operations as increasing and decreasing, thus a subtraction between conditions would eliminate areas implicated in those processes. This and other possible factors (e.g., second exposure to the unpleasant pictures, number of active reappraisal goals, number of trials and participants, timing with which reappraisal instructions are delivered, and significance and voxel contiguity thresholds) should be systematically addressed in future studies.

Amygdala Regions of Interest. Left and right amygdala regions-of-interest (ROIs) were defined using the Talairach Daemon (Lancaster et al., 2000) packaged with AFNI as reported previously (Urry et al., 2006; van Reekum et al., 2007) and submitted for analyses in SPSS. A multivariate GLM testing the within-subjects effects of reappraisal goal (increase, maintain, decrease) and hemisphere (left, right) on amygdalar response revealed a significant main effect of reappraisal goal, $F(2,24) = 3.84, p = .035, \eta^2_p = .24$. Supplementary Figure 2a depicts the
uncorrected $F$ values in six coronal slices all of which traverse the Talairach atlas-defined amygdala ROIs. Mean AUC when increasing negative emotion, $M = 2.76$, $SE = .69$, was higher than when both maintaining, $M = 1.08$, $SE = .46$, $p = .030$, and decreasing, $M = 1.31$, $SE = .78$, $p = .039$. There was no difference in amygdala activation between maintaining and decreasing, $p = .798$. Supplementary Figure 2c presents the peristimulus plots of the hemodynamic response functions (HRF) in the right and left amygdalae when increasing, maintaining, and decreasing negative emotion. Although the pattern of means suggested a hemispheric difference in the effect of regulation condition on the amygdala (see Supplementary Figure 2b), particularly for the decrease condition, the reappraisal goal X hemisphere interaction was not significant, $F(2,24) = 2.03$, $p = .154$, $\eta^2_p = .14$. There was no main effect of hemisphere, $F < 1$.

Thus, replicating our own work (Johnstone et al., 2007; Urry et al., 2006) and that of others too, at least conceptually (Eippert et al., 2007; Ochsner et al., 2004), we found that mean signal in both the left and right amygdala was higher when using reappraisal to increase compared to maintain negative emotional responses to the pictures. In our case, the difference between increasing and maintaining was observed when calculating mean signal across the entire volume of the amygdala in each hemisphere. Using this mean ROI approach across all participants, we did not observe amygdala signal to be significantly lower when decreasing negative emotion.

Several studies have reported signal decreases in the amygdala when decreasing negative emotion (Eippert et al., 2007; Goldin et al., 2008; Ochsner et al., 2002; Ochsner et al., 2004; Ohira et al.; 2006; Phan et al., 2005), and in each case they did so using a voxelwise approach with small volume correction rather than mean ROI approach. Other studies have failed to reveal lower amygdala activation when decreasing. For example, using the mean ROI approach, we
observed less activation when decreasing compared to attending to negative images with a different older sample (men and women ages 61-65 years; van Reekum et al., 2007), but amygdala signal when decreasing compared to attending to negative images was not reliably different in two of our previous studies, one a study of healthy older people (men and women ages 62-64 years; Urry et al., 2006) and the other a study of healthy compared to clinically depressed men and women ranging in age from 19 to 60 years (Johnstone et al., 2007). Using a voxelwise approach with small volume correction, Kim and Hamann (2007) similarly did not observe a significant difference between watching and decreasing responses to negative pictures in a small sample of women ranging in age from 18 to 29 years, nor did Kalisch et al. (2005) for reappraisal of threat of pain using detachment in a sample of 16 men and women ages 20 to 34 years. The effect of reappraisal on the amygdala may depend on methodological variation across studies and/or individual differences. With respect to individual differences, we have shown, for example, that people showing a greater decrease in amygdala activation when decreasing negative emotion exhibit a steeper pattern of decline in diurnal cortisol secretion and greater activation of ventromedial prefrontal cortex (Urry et al., 2006), and larger pupil diameters (Johnstone et al., 2007; Urry et al., 2006).

Subjective Ratings of Difficulty, Effort, and Success

At the end of each of the three emotion regulation scan runs, participants rated their current sleepiness on a 4-point scale (1 = “not at all sleepy”, 2 = “somewhat sleepy”, 3 = “moderately sleepy”, and 4 = “very sleepy”) in response to the cue “How sleepy are you right now?” (data not reported). They also rated three additional condition-specific questions regarding task difficulty (e.g., “How difficult was it to MAINTAIN the intensity of your responses?”), how hard they tried (“How much did you try to MAINTAIN the intensity of your
responses?”), and how successful they were (“How successful were you at MAINTAINING the intensity of your responses?”). These questions were asked about each of the three reappraisal goals, and were rated on a 4-point scale (1 = “not at all”, 2 = “somewhat”, 3 = “moderately”, and 4 = “very”). The data were averaged across scan runs and submitted to multivariate GLMs and pairwise comparisons to interpret significant main effects.

All three conditions were rated as being similarly difficult, $F(2,22) = .63, p = .541, \eta^2_p = .05$, increase $M = 2.17, SD = 0.61$, maintain $M = 2.21, SD = 0.68$, decrease $M = 2.33, SD = 0.77$. Participants reported trying harder when decreasing, $M = 3.52, SD = 0.58$, than both maintaining, $M = 3.40, SD = 0.68$, $p = .031$, and increasing, $M = 3.33, SD = 0.76$, $p = .010$, $F(2,22) = 4.00, p = .033, \eta^2_p = .27$. Ratings of effort when maintaining and increasing were not significantly different, $p = .250$. Participants felt less successful when increasing, $M = 2.59, SD = 0.64$, compared to maintaining, $M = 2.75, SD = 0.71$, $p = .034$. Participants reported equal success when decreasing, $M = 2.64, SD = 0.63$, compared to maintaining, $p = .215$, and when increasing compared to decreasing, $p = .568$, $F(2,22) = 2.66, p = .092, \eta^2_p = .20$.

Given our interest in cognitive effort in this report, we calculated linear and quadratic contrasts of ratings of effort and conducted regression analyses predicting quadratic activation in the three medial frontal regions of interest in the main text. None of these analyses revealed significant associations. The ratings of effort were provided on a 4-point scale thus a restricted range that may have hampered our ability to demonstrate significant associations. Moreover, these ratings were collected retrospectively at the end of each scan run, which may also help explain the lack of correspondence with medial frontal activation. It is also possible that perceptions of effort simply are not generated by these medial frontal regions.

_Gaze Behavior_
We recorded gaze behavior using eye tracking to determine to what extent our reappraisal findings might depend on attentional deployment (van Reekum et al., 2007), an alternative emotion regulatory strategy (Gross & Thompson, 2007). Gaze behavior was acquired with the same system described for pupil diameter. Point of gaze was calibrated by asking participants to foveate nine circles at known coordinates distributed across the goggle display. Fixations were identified when the point of gaze remained with an area spanning 20 pixels in diameter for a minimum of 50 ms throughout the 8-second period of interest.

Two trained assistants independently drew rectangular and elliptical areas of interest (AOIs) on each of the pictures using iView Analysis software (v. 1.09.29, SensoMotoric Instruments), as described in van Reekum et al. (2007). In brief, AOIs were drawn around the object(s) that decisively imbued the pictures with affective meaning. Gaze duration was then calculated as the sum of fixations falling within these AOIs divided by whole-picture gaze duration, i.e., the amount of time participants spent fixating anywhere on the display. This was calculated separately for the first (“early”) and second (“late”) halves of the 8-second reappraisal period. The final variable of interest was calculated by subtracting gaze duration during the 4-second period preceding delivery of the regulation instruction from gaze duration during the early and late halves of the reappraisal period. A multivariate GLM assessed the effect of reappraisal goal (increase, maintain, decrease) and time (early, late) on gaze duration. For analyses involving eye tracking variables, \( n = 21 \) (15 females) as a result of poor data quality for five male participants.

**Effects of Reappraisal on Gaze Behavior, an Index of Attentional Deployment.** A significant interaction between reappraisal goal (increase, maintain, decrease) and time (early, late) was observed for gaze duration, \( F(2,20) = 6.80, \ p = .006, \ \eta^2_p = .41 \). There were no
differences as a function of reappraisal goal during the early period. During the late period, however, decreasing negative emotion, $M = -.07$, $SE = .03$, was associated with the biggest decline in gaze duration followed by maintaining, $M = -.04$, $SE = .02$, and then increasing, $M = -.01$, $SE = .02$. The difference between decreasing and increasing was statistically significant, $p = .033$. Looking at the interaction by instead comparing early and late gaze duration within each reappraisal condition, we found that the decline in gaze duration between the early, $M = .00$, $SE = .02$, and late intervals was significant for decreasing, $p = .002$, but not for increasing, early $M = -.02$, $SE = .01$, or maintaining, early $M = -.01$, $SE = .01$, both $ps > .05$. These findings indicate that attentional deployment varied as a function of reappraisal goal.

**Does Attentional Deployment Account for Reappraisal-Related Change in Neural Activation?** We ran a series of multivariate repeated measures GLMs testing the main effect of reappraisal goal (increase, maintain, decrease) with gaze duration for each condition entered as a covariate. The dependent measure was mean BOLD signal estimates extracted from each of the nine regions listed in Supplementary Table 1. Importantly, in no case did the presence of the covariates eliminate the significant main effect of reappraisal goal or change the basic pattern of differences between conditions. Moreover, the between-subjects effects of the gaze duration covariates (and their interaction with reappraisal goal) generally failed to explain significant variance in neural activation in these regions. These findings suggest that, although attentional

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1 Negative values for object gaze duration indicate a decrease in time spent looking at the emotional areas of the pictures during reappraisal relative to the amount of time looking at the emotional areas prior to delivery of the reappraisal instruction.

2 Out of 30 between-subjects effects of gaze duration on neural activation, only 2 were significant. Specifically, gaze duration in the enhance condition explained significant variance in activation of the bilateral subgenual ACC (cluster #5 in Supplementary Table 1), and gaze duration in the maintain condition explained significant variance in activation of the right fusiform (cluster #2). In addition, gaze duration in the enhance condition interacted with reappraisal goal, and with reappraisal goal and hemisphere in explaining amygdala activation. Again, these few effects did not change the pattern of effects described for reappraisal goal.
deployment varied as a function of reappraisal goal, this variation did not account for reappraisal-related change in neural activation.

Note: Please refer to the References section of the main text for references cited in this Supplementary Material.
Supplementary Table 1: Descriptive labels and Talairach coordinates for clusters emerging from voxelwise ANOVA comparing reappraisal goals across the entire sample.

<table>
<thead>
<tr>
<th></th>
<th>Brain region (Brodmann Area)</th>
<th>cluster size (mm³)</th>
<th>x</th>
<th>y</th>
<th>z</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>B. brainstem (L. red nucleus, R. substantia nigra), R. parahippocampus, R. lingual gyrus, R. culmen</td>
<td>3584</td>
<td>5</td>
<td>-37</td>
<td>-4</td>
</tr>
<tr>
<td>4</td>
<td>B. dorsal cingulate gyrus</td>
<td>2384</td>
<td>5</td>
<td>-1</td>
<td>48</td>
</tr>
<tr>
<td>5</td>
<td>B. subgenual ACC (BA 25)</td>
<td>1880</td>
<td>-3</td>
<td>13</td>
<td>-18</td>
</tr>
<tr>
<td>9</td>
<td>L. dorsal medial frontal gyrus (BA 6)*</td>
<td>792</td>
<td>-1</td>
<td>-7</td>
<td>56</td>
</tr>
</tbody>
</table>

* increase, decrease > maintain*

| 1 | L. fusiform, lingual gyrus, culmen                                                               | 13272              | -7  | -55 | 0   |
| 2 | R. fusiform, declive, culmen                                                                     | 6680               | 23  | -53 | -6  |
| 6 | L. precentral gyrus                                                                              | 1672               | -43 | -5  | 40  |
| 7 | R. lingual gyrus**                                                                               | 1120               | 11  | -75 | 2   |

* increase > maintain, decrease*

| 8 | R. middle and inferior frontal gyrus                                                             | 1104               | 39  | 35  | -2  |

*Notes. Clusters are numbered according to size from biggest to smallest. n = 26. L = left; R = right; B = bilateral; ACC = anterior cingulate cortex; BA = Brodmann Area.

* p = .08 for Decrease > Maintain in this cluster.

** p = .08 for Maintain > Decrease in this cluster.
Supplementary Figure Captions

Supplementary Figure 1. Here we present a visual depiction of the results of the voxelwise repeated measures ANOVAs comparing increasing, maintaining, and decreasing responses to negative pictures. Clusters are overlaid on the average high resolution, Talairach-transformed T1 image computed across all 26 participants, shown in radiological convention (R = L). The colors within each cluster represent uncorrected F values for the test of the regulation main effect, with yellow values indicating the voxels with the strongest effects, thresholded at $p < .01$. The numbers next to each cluster refer to the # recorded in the first column of Supplementary Table 1.

Supplementary Figure 2. Here we depict the results of the GLM analysis comparing increasing, maintaining, and decreasing responses to negative pictures within the Talairach-defined amygdala ROI. This ROI is shown in six coronal slices. The sagittal slice to the left shows the anterior-posterior location of each of those six coronal slices. The colors within the ROI represent F values for the test of the regulation main effect, thresholded at $p < .05$ with yellow values indicating the voxels with the strongest effects. The amygdala ROI is overlaid on the average high resolution, Talairach-transformed T1 image computed across all 26 participants, shown in radiological convention (R = L). Crosshairs are centered on Talairach coordinates $x = 23$, $y = -5$, and $z = -12$. Panel b shows the mean AUC signal estimates for the left and right amygdala. Panel c depicts the peristimulus time course of emotion regulation in the left and right amygdala separately. Increasing responses to negative pictures is represented by the green lines, maintaining by the yellow lines, and decreasing by the red lines. The shaded area represents the time points that were summed to produce the mean AUC signal estimates that are depicted in panel c.
a.

| z = -12 |
|---|---|
| x = 23 |

b.

- **AUC**
  - **left**
  - **right**

- **F value**
  - 5.82

```
AUC
2.5
2.0
1.5
1.0
0.5
0.0
```

```
left
right
```

decrease maintain increase

c. **left amygdala**

```
% signal change
2  4  6  8  10  12  14  16  18  20
```

time (s)

decrease maintain increase

right amygdala

```
% signal change
2  4  6  8  10  12  14  16  18  20
```

time (s)

decrease maintain increase