The relative absence of areas where brain activation is stronger when decreasing negative affect vs. passively attending to negative information is striking. The most salient difference between the findings of our study and those represented in extant work is that, with a mean age of 63 years, our sample is significantly older. In the affective domain, older adults report less frequent and briefer episodes of negative affect (Carstensen et al., 2000), and they rate negative pictures as less arousing and exhibit less amygdala activation in response to them compared to younger adults (Mather et al., 2004). In addition, older more than younger and middle-aged adults endorse passive emotion-focused strategies for handling emotionally charged interpersonal problems (Blanchard-Fields et al., 1995).

Issues of cognitive function may play a role as well. Older individuals exhibit decrements in performance on tasks associated with cognitive control and dorsolateral PFC function, including poorer visual working memory performance, and decreased ability to decrease task-irrelevant information (Gazzaley et al., 2005), but not tasks involving emotion and social decision-making that are dependent on VMPFC function (MacPherson et al., 2002). Older adults also exhibit poorer visual working memory performance, and decreased ability to decrease task-irrelevant information (Gazzaley et al., 2005).
As a whole, these findings suggest that age-related cognitive impairment and/or changes in affective processing may explain the reduced involvement of dorsal and lateral regions of PFC during our emotion regulation task. Our subjects’ intact performance on a brief cognitive screen and the fact that they exhibited robust pupil and both dorsal and lateral brain responses in the increase condition makes a cognitive impairment explanation unlikely. Age-related changes in affective processing remain a distinct possibility, however. Aging may be associated with a more efficient, less effortful ability to decrease negative affect, either because reducing negative affect is a relatively automatic process, or because older adults are less intensely aroused by negative stimuli in the first place. This would make it unnecessary to engage dorsal and lateral regions of PFC in the service of cognitive control, which would result in few differences in PFC involvement in active attenuation compared to passive experience of negative affect. Independent of brain activation, tacit support for less cognitive control when decreasing compared to either attending to or increasing responses to the negative stimuli is found in the pupil diameter data. Although reducing negative affect exhibited evidence of sustained processing, the average peak pupil diameters for decreasing and attending were indistinguishable, suggesting no difference in allocation of cognitive resources.

With age comes changes in brain structure, including atrophy (Coffey et al., 1992). The pattern of findings reported herein, including the absence of decrease main effects, and the patterns of correlations between VMPFC and the amygdala may be the result of
such atrophy in this older sample. Although we demonstrate that the VMPFC-amygdala association is not accounted for by baseline signal estimates, it is important to note that baseline signal serves only as a rough proxy for volume. Brain atrophy may only manifest in changes in task-related signal increases and not in baseline signal. Formal volumetric assessments are warranted in future studies comparing older and younger samples.

In addition to the aged nature of our sample, there are methodological differences that may in part account for the reduced incidence of dorsal and lateral PFC clusters when reducing negative affect in this study. For one, our analysis of regulation main effects on brain responses was very tightly controlled. At the single-subject level, we explicitly evaluated the regulation response independent of the initial reaction to the pictures. Thus, our estimates of regulation-related signal change represent unique variance after controlling for signal change representing the initial response to the pictures. Second, at the group level, we conducted voxelwise ANOVAs which simultaneously partitioned the variance associated with each condition (e.g., “decrease”), controlling for variance in the other two conditions (e.g., “attend”, “increase”). These two strategies provide a more stringent criterion relative to studies that contrast only two conditions at a time. This is evident in the emotion regulation study that most closely parallels the procedures reported herein (Ochsner et al., 2004). These authors report that in a more stringent analysis to identify regions specifically involved in increasing compared to decreasing negative affect (controlling for unregulated responses), the only frontal
regions that emerged were two clusters in the superior frontal gyrus and one in the medial frontal gyrus (BA10), two regions that show the analogous effect, i.e., increase > both attend & decrease, in the present manuscript. This is a substantially smaller subset than those reported for the increase > look comparison (Ochsner et al., 2004). Importantly, two of the three clusters emerging from this more restricted test are small enough to be of questionable reliability, a problem common in earlier fMRI work on instructed emotion regulation (cf., Ochsner et al., 2002, 2004; Phan et al., 2005). Using a Monte Carlo simulation for a whole brain analysis that is limited to gray matter only with moderate smoothness (FWHM = 6mm) and a voxelwise threshold of $p = 0.001$, the minimum cluster size needed to reject the null hypothesis at a corrected $p < 0.05$ is approximately 300 mm$^3$. At this threshold, many of the effects that were reported in prior published work would fail to reach significance. It is therefore possible that some of the previous findings are spurious, which may partially explain the failure to replicate those effects here.

In addition to analytic differences, prior work has limited recruitment to female subjects only whereas we report on both males and females. Men and women differ with respect to the types of stimuli that elicit negative emotional responses, and in the intensity with which those responses are manifest (Bradley et al., 2001). We do not have sufficient power to determine whether sex interacts with regulation condition to predict brain or pupil diameter, but presumably this is serving as another source of variability, perhaps making it more difficult for us to reveal main
effects. Moreover, in prior work, the regulation instruction often is provided prior to the onset of the picture stimulus, which means that the type of regulation being studied may be fundamentally different than the type we are studying. Indeed, Gross (1998) has distinguished between antecedent- and response-focused emotion regulation, indicating that differences between them in physiology may reflect a difference in effortful processing.

Recent work by Ochsner et al. (2004) suggests that the nature of the strategies subjects select to effect increases and decreases in negative affect will influence the brain regions that are involved in regulating emotion. In the current report, subjects were explicitly asked to use one of two cognitive reappraisal strategies to increase their negative affect and, similarly, one of two strategies to decrease their negative affect. Regardless of which direction affect was shifted (i.e., more versus less negative), subjects were instructed to manipulate either the level of self-involvement or the negativity of the outcome. Thus, while we explicitly asked participants to use one of two strategies, we provided latitude to draw on the strategy that best fit a given picture and regulation condition, which more accurately reflects the flexibility we experience when regulating emotion outside the confines of the laboratory. This flexibility, however, comes with a cost since the selection of strategy may interact with regulation condition (i.e., subjects may have manipulated the negativity of outcomes in the increase condition but decreased self-involvement in the decrease condition) and also with age. This variability in the use of regulatory strategies, particularly when decreasing negative affect, thus may
have contributed to the relative absence of decrease main effects in dorsolateral and dorsomedial regions of PFC. By the same token, this variability may also have provided a lens through which to view the mediating role of VMPFC in the inverse association between BA 10 and the amygdala. Whereas during the training experience, we verified that subjects were using the strategies as described, we did not interview them regarding the strategies they used during the scan nor did we collect on-line subjective ratings of affect. Assessing strategies used remains a question for future research.

Finally, evidence supports the existence of hemispheric asymmetries related to emotion processing, particularly in frontal cortex (see Davidson, 2004 for a review). Although asymmetry during emotion regulation was not the focus of the current investigation, the concentration in this report on the left rather than right amygdala deserves mention. As reported earlier, an inverse association between the amygdala and VMPFC was evident with the left but not the right amygdala. For three reasons, however, we conclude that our data do not suggest strong asymmetric effects in the amygdala. For one, hemisphere did not interact with regulation condition when predicting amygdala responses. Second, if we lower the statistical threshold, we observe inverse associations between right amygdala and regions of VMPFC that are similar to those observed between left amygdala and VMPFC. Finally, although smaller in magnitude, the correlations reported between left amygdala and other variables (e.g., frontal regions, cortisol) for the decrease – attend contrast are echoed when instead examining right amygdala. Existing data (e.g., Phelps et al., 2001) suggest that left
rather than right amygdala may be involved when the representation of the negative stimulus depends on elaboration and interpretation by the participants, processes likely represented during deliberate regulation of responses to negative picture stimuli. This may explain why left rather than right amygdala is slightly more prominent in our correlation/regression analyses (but see Baas et al., 2004 for a meta-analysis in which higher incidence of left than right amygdala response in studies of emotion is not explained by elaborate processing, nor by stimulus type, task instructions, or differential habituation rates).

Reference List


